Behind the Sweetness

The past, present, and future of artificial sugar sweeteners

Great topic. Reduce # of parentheses because it doesn't acknowledge the importance of what you're saying. They should be used sparingly. Very interesting topic and you made it engaging to read. Put references throughout text. A
The History

First discovered accidentally in 1879 by Constantine Fahlberg and Ira Remsen, artificial sugars have played an important yet controversial role in our society for several decades. The compound that was initially discovered through poorly applied laboratory safety (Apparently, the dinners of both men one night were exceptionally sweet, and the compound was traced back to the laboratory by tasting residues of chemicals on clothes and throughout the lab!) was saccharin, a compound that was found to have a potency of roughly three hundred times that of ordinary sucrose (table sugar), while leaving a strange aftertaste. Another discovered benefit of the product was that it was not readily metabolized within the body, and therefore did not contribute any caloric value to the body. The potential benefits of saccharin were immediately recognized by Fahlberg, who went on to patent and mass-produce saccharin without mention of Remsen ("Remsen merely grew irate"). By 1907, saccharin was already in use as a replacement for sugar in foods for diabetics. Use of saccharin became more widespread due to sugar rationing during WWI, and by the 1960's, saccharin was used on a large scale for diet soft drinks (many times, saccharin is combined with other artificial sugars in soft drinks in order to reduce the undesired aftertaste, many times with no avail). Saccharin is now most commonly found in the sweetener "Sweet’N Low," which is found in most restaurants, and several diet soft drinks are sweetened with saccharin, the most well known being Coca-Cola’s "Tab," introduced in 1963. Saccharin is stable when heated, is relatively inert in the human body, and can be stored for long periods of time.

figure 1: Sweet’N Low sweetener
The Science

A question that immediately arises when discussing artificial sweeteners is how it makes things extremely sweet while contributing no calories to the body. In order to understand this process better, it is necessary to examine exactly what calories are. A calorie is a measure of energy, more specifically a gram calorie is the energy needed to increase the temperature of one gram of water by 1 degree Celsius. Therefore, by definition, all substances have some amount of calories. The calories that contribute to the human body are actually "food calories," the energy that is contributed to the body through metabolism in order to carry out processes of the body. These calories can only be utilized through metabolic processes (see figure below) of the body, such as respiration.

figure 2: Metabolic pathways of the body
Compounds such as proteins, fats, and carbohydrates (sugar) can be readily broken down by the body and used to create energy (adenosine triphosphate – ATP) for the body’s various processes. If compounds are not in the exact form needed to produce this energy, the body may be able to break compounds down into the required form, or else the compounds are excreted from the body as waste. This happens to be the case for saccharin and most of the other various artificial sugar sweeteners. The artificial sugar sweeteners that are ingested cannot readily be broken down into components that can enter any metabolic cycles and be used as energy for the body, rendering them effectively useless to the body, which excretes the compounds as waste. This benefit of not having any caloric value to the body allows for the liberal use of the product by anyone, especially diabetics who must regulate glucose levels in the body (glucose is a common energy intermediate used in the body’s metabolic processes).

The explanation for the high potency of artificial sugars lies within the definition and mechanism of taste itself. Taste is one of the five primary senses and refers specifically to the ability to detect flavors. In order for humans to detect flavors, food normally contains certain compounds with specific chemical groups that can bind to receptor sites that send a sensory signal to the brain. Taste is a sensory function of the central nervous system, and the receptor cells for taste in humans are found on the surface of the tongue and back of the throat. These receptor sites function on a mechanism called “lock and key,” in which only specific chemical groups can bind with this receptor site, similarly to the way only certain keys can open certain locks. It has been found, though, that similar shaped functional groups may be able to bind to these sites as well, sometimes even stronger than the intended chemical group. This is the mechanism by which artificial sugar sweeteners produce their high potency sweetness.

Saccharin, for example, mimics the structure of sucrose and binds to its receptor site on the
tongue with a much stronger interaction, producing a potency of three hundred times that of sucrose (see figure below).

figure 3: Simple representative example of saccharin-receptor site interaction. This model may not be an exact representation.

In figure 3, the representative receptor site contains a partial positive hydrogen (H+) that can hydrogen bond to the partial negative oxygen on the sulfur group of the saccharin molecule, as well as a partial negative oxygen which can bond to the partial positive hydrogen of the amine group on the saccharin molecule. In addition to these strong interactions, weaker van der Waals forces and like-like interactions of the non-polar region of the receptor site (site X in figure 3) can interact with the non-polar benzene ring of the saccharin molecule. These interactions all contribute to the very strong binding of saccharin and other various artificial sugar sweeteners, giving each compound a distinct potency based upon how well each compound can bind to the
receptor site. The potencies for various artificial sugar sweeteners as compared to sucrose are given below.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccharin</td>
<td>300 X</td>
</tr>
<tr>
<td>Cyclamate</td>
<td>30 X</td>
</tr>
<tr>
<td>Aspartame</td>
<td>180 X</td>
</tr>
<tr>
<td>Acesulfame</td>
<td>200 X</td>
</tr>
<tr>
<td>Sucralose</td>
<td>600 X</td>
</tr>
</tbody>
</table>

Figure 4: Potencies of various artificial sugar sweeteners

**The Players**

Since the discovery of saccharin, there have been several more discoveries of other artificial sweeteners, several in very much the same way as saccharin (poor laboratory practices). Currently, “Sweet’N Low,” “Equal,” and “Splenda” are the most commonly used artificial sugar sweeteners and can be found in most restaurants.

**Equal (NutraSweet):**

![Aspartame structure](image5.png)

![NutraSweet](image6.png)

figure 5: Aspartame structure  
figure 6: “NutraSweet” (Equal)
Aspartame (NutraSweet or Equal), probably the first or second most used artificial sugar to date, was discovered in 1965 by chemist Jim Schlatter who was doing research on gastric ulcer treatments. Similarly to the discovery of saccharin, Schlatter licked his finger before reaching for a piece of paper and discovered a sweet taste, which turned out to be Aspartame. Aspartame possesses a sweet taste with minimal bitterness, and the onset of sweetness is slightly slower than actual sucrose (sugar), but the sweetness may linger at times. Aspartame has a potency of 180 times that of sucrose, almost half of the potency of saccharin. Unlike saccharin, aspartame is not heat stable and does not have as long of a shelf life, making it undesirable for baking and storing. Unlike most artificial sweeteners, some aspartame can actually be readily metabolized in the body, resulting in a very small amount of calories. This is due to the fact that the primary component of aspartame, phenylalanine, is an essential amino acid and contains approximately 4 calories per gram. The actual amount of calories produced from this metabolism, though, is negligible, which is why “NutraSweet” is advertised as a 0 calorie sweetener.

**Splenda:**

![Sucralose Structure](image)

*figure 7: Sucralose Structure*

![Splenda](image)

*figure 8: “Splenda”*
Sucralose ("Splenda"), discovered in 1976, is a relatively new artificial sugar and is therefore not as common as saccharin or aspartame. It was not until 1998 that the FDA approved sucralose for commercial use, which is why "Splenda" is not as commonly found in some restaurants. Its discovery, another example of unsafe laboratory practices, involved a laboratory assistant mistaking the word "test" for the word "taste" when asked to "test the sample." Fortunately, the chemical turned out to be sucralose, a sucrose derivative. Sucralose is heat stable, can be stored for long periods of time without degrading, and has a potency of 600 times that of sucrose, making it one of the most potent artificial sugars. As advertised by the quote "made from sugar so it tastes like sugar," sucralose is the only artificial sugar that is derived from sucrose. As can be seen from the figure above, sucralose is just the sucrose structure with 3 chlorines substituted for hydroxyl groups, allowing it to bind effectively to the sweetness receptor site but preventing it from being readily metabolized.

**Safety First**

![Sweet’N Low warning label](image)

figure 9: "Sweet’N Low warning label
From its initial discovery, the potential benefits of saccharin were immediately recognized by the public who quickly adopted the new product with little knowledge of its potential hazards. Throughout the 1960’s, studies involving the use of saccharin suggested that it may be an animal carcinogen (cancer causing agent). The concern of saccharin’s potential hazards peaked in 1977 when a research study was published revealing a higher incidence of bladder cancer in rats after large doses of saccharin were ingested. The United States Food and Drug Administration proposed a ban on saccharin, which was met with huge opposition among the public, especially among diabetics. Even Theodore Roosevelt was a huge proponent of saccharin and has been quoted to have said, “Anyone who thinks saccharin is dangerous is an idiot.” The U.S. Congress eventually placed a moratorium on the ban and required that “Sweet’N Low” have the well known warning label on the packages indicating that saccharin may be a carcinogen. Since then, there have been extensive studies regarding the correlation between increased cancer and saccharin consumption, some showing a possible correlation and others showing no connection at all. The studies conducted in 1977 were highly criticized due to the fact that huge doses of saccharin, hundreds of times the normal daily usage of saccharin, were used in order to conduct the controversial experiments. In addition, the proposed biological mechanism believed to cause the cancer in rats is not compatible with the human anatomy due to differences in urine compositions between rats and humans. In 1991, these criticisms combined with fact that no experiment has shown a clear connection between saccharin and cancer finally resulted in the formal withdrawal of the 1977 proposal to ban the use of saccharin, and in 2000, Congress officially repealed the law requiring the infamous “Sweet’N Low” warning label.
Given the huge controversy with saccharin, all other artificial sugars have been well studied and tested in order to determine possible health hazards of its use. Aspartame has received huge public attention regarding its safety and the circumstances around its approval. There have been suggestions to continue further studies in the possible connection between aspartame and brain tumors, brain lesions, and lymphoma. It is already a known fact that people with phenylketonuria (PKU) lack the ability to degrade phenylalanine properly and that increased amounts of phenylalanine in the body (the main component of aspartame, see figure 5) can cause mental retardation. As to the possibility of adverse health effects to people without PKU, there is a continuing debate in the scientific and medical community as to whether any possible symptoms of brain tumors, lesions, and lymphoma are caused by long-term or short-term exposure to aspartame. Research as recent as February, 2006 has shown, after a seven year study, that aspartame is associated with unusually high rates of lymphomas, leukemia, and other cancers in rats after given doses equivalent to drinking four to five 20 ounce bottles of diet soda a day for a 150-pound person. The controversy and hazards regarding the use of aspartame are still inconclusive and will continue to be debated until further research has been conducted.
Of all of the artificial sweeteners, “Splenda” has the least amount of controversy associated with it. It has been studied for over 20 years and animal testing has shown that sucralose appears safe for anyone to use. A possible explanation for its lack of potential health hazards comes from the fact that sucralose is derived from sucrose, an ingredient people actually ingest. The chlorine substituted groups are the only difference between sucralose and sucrose, and given that humans naturally ingest small amounts of chlorine in water and other foods every day, it seems reasonable to assume that sucralose is a relatively safe product.

**Current Research and Beyond**

Currently, besides the research on the safety of the artificial sugars, research has been conducted on artificial sugars in order to find a possible way to make artificial sugars taste more like real sugar (sucrose). Due to artificial sugar’s high potency and therefore strong binding of the sweetness receptor site, there is usually a strong unpleasant aftertaste associated with its use. Research has shown that the artificial sugars may actually chemically inhibit the natural termination of the taste-receptor signal, resulting in the unpleasant aftertaste. A possible mechanism of this inhibition is the phosphorylation (addition of a phosphate group) of the taste sensors. Current research is going in to understanding this mechanism in depth and possibly coming up with a safe solution for preventing this phosphorylation of taste receptors. Ultimately, the final goal of the research is for artificial sugars to safely approach the taste of actual sucrose, a goal that may take several years of research to approach. If this goal is finally reached, the worldwide acceptance and applicability of artificial sugars will be realized for diabetes, obesity, or dieting in general.
References

1.) “Virtual Chembook”. Elmhurst College. Ophardt, Charles E.  

2.) “How can an artificial sweetener contain no calories”. Scientific American. A. Rivard 
   and Argyle, Minn.  
   <http://www.sciam.com/askexpert_question.cfm?articleID=0007F523-93FA-1CE2- 
   93F6809EC5880000>.

   <http://travel.nytimes.com/2006/02/12/business/yourmoney/12sweet.html?n=Top%2fNe 
   ws%2fScience%2fTopics%2fResearch>.


5.) “New research improves taste complexity for artificial sugars”. Decision News Media.  