Safety assessment for sweeteners

The sixteenth century Swiss physician Paracelsus recognized that everything is toxic, depending on the dose. Selenium is a good example. It's a micronutrient (the human body contains 20 mg or less) that is needed for several enzymes involved in processing thyroid hormones. However, consumption of 1 mg or more per day can lead to a condition called selenosis, which can be fatal. We see the same thing with some sweeteners. For example, glycyrrhizin, the sweet substance in licorice, can have beneficial anti-inflammatory effects. Glycyrrhizin inhibits the body's ability to break down cortisol, so more cortisol accumulates, and cortisol does have anti-inflammatory effects. But too much cortisol can lead to serious consequences, and too much licorice can lead to too much cortisol.

With this in mind, the FDA and other regulatory agencies have established procedures to regulate what can be added to food, and how much can be added. In the United States, the 1958 Food, Drug & Cosmetic Act established rules for establishing the safety of "food additives" prior to their use in foods.

In order to obtain regulatory approval for a new food additive (including sweeteners), the manufacturer must carry out extensive safety testing. These studies must include short-term tests for genetic toxicity; metabolism and pharmacokinetic studies; short-term toxicity tests in rodents; 90 day toxicity tests in rodents and in non-rodents; reproduction studies in animals; one year toxicity in non-rodents; lifetime toxicity and carcinogenicity studies in rodents. These are followed by clinical studies in humans [1].

Safety testing must establish a level at which there is no observable adverse effect even with daily use; This level is called the "no observable adverse effect level (NOAEL). Regulatory agencies then set an Acceptable Daily Intake level (ADI) that is usually 1% of the NOAEL, to provide a 100-fold safety factor. The ADI is frequently expressed in terms of the number of milligrams per kilogram of body weight per day. To determine how many cans of diet soft drink you can consume per day, you need to know your weight (in kilograms), and the amount of sweetener used per can. For example, let's consider a 170 pound person (77 kilograms) drinking a diet cola with 180 milligrams of aspartame per can. The ADI for aspartame in the United States is 50 milligrams per kilogram per day, so our subject can consume 3,850 milligrams of aspartame per day (50 x 77). To get 3,850 milligrams of aspartame, this person would need to drink 21 cans of diet cola. And at that point, this person would have consumed one one-hundredth of the amount which might cause an adverse effect of any kind.

Following regulatory approval, The FDA often requires post-approval surveillance for new food additives. Aspartame, for example, underwent 8 years of post-approval surveillance following its approval in the early 1980s.

When the 1958 law was passed, it was obviously impractical to go back and test the safety of every existing food additive, and it would have been a waste of resources to do so for things that everyone already knows to be safe. Therefore, the law created the "GRAS exemption," where "GRAS" is an acronym for "generally recognized as safe." In order to qualify for GRAS status, there must be general consensus among qualified experts that a food additive is safe, based on widely available information. This usually includes published, peer-reviewed safety studies, or evidence that a substance has been consumed safely for hundreds or thousands of years. The GRAS process has been used, for example, in the case of rebaudioside and other stevia-based sweeteners. In order for a food additive to achieve GRAS status, someone (usually a manufacturer) must file a GRAS notification with the FDA. The FDA publishes all such notifications, and anyone interested may comment. After a period of time, the FDA may accept or reject the additive, or it may request further data. The Flavor and Extract Manufacturers Association (FEMA) is a U.S. trade group that has an expert panel which reviews some ingredients and periodically publishes a list of substances that it considers GRAS. These substances are assigned FEMA GRAS numbers. For example, neohesperidin dihydrochalcone is FEMA GRAS 3811.

Just because something is natural, that doesn't mean it is safe. Botulinum toxin is very natural, and very deadly. We see this in the case of licorice, which is natural and has been used for thousands of years--too much can cause serious health problems. We see it also in the case of methanol, a metabolic product of aspartame and many fruit juices.

The internet abounds with conspiracy theories about one sweetener or another gaining regulatory approval in nefarious ways. But the reality is that there are many regulatory agencies all over the world evaluating the safety data for each sweetener. These agencies are generally run by risk-averse bureaucrats and highly skilled scientists. The history books contain a number of sweeteners (dulcin and P-4000, to name two) that were found to be unsafe and were discarded. Those sweeteners that have achieved regulatory approval around the world are, with a high degree of certainty, safe.

References

[1] A.M. Rulis and J.A. Levitt, FDA's food ingredient approval process. Regul. Toxicol. Pharmacol. 53(1):20-31, 2009; http://www.caloriecontrol.org/pdf/Rulis_08.pdf