

Aspartame Information replies to the New York Times (distributed with The Daily Telegraph)

Melanie Warner's article "New Research, New Fears About a Sweetener's Risks?" which appears in the New York Times supplement circulated with the Daily Telegraph today, makes many misleading allegations about the safety of aspartame. This is not the first time that Ms Warner has chosen to attack the safety of low calorie sweeteners. On 15 May, 2005, the New York Times carried an article by Ms Warner that made allegations that Splenda was a possible carcinogen. The Aspartame Information Service has prepared the following point-by-point response to the allegations about aspartame as a service to readers of the New York Times. The original text of the article is shown in italics and the correct information appears below each quote.

When Dr. Morando Soffritti, a cancer researcher in Bologna, Italy, saw the results of his team's seven-year study on aspartame, he knew he was about to be injected into a bitter controversy over this sweetener, one of the most contentiously debated substances ever added to foods and beverages.

There is a high level of scientific consensus about the safety of aspartame. Aspartame is not only one of the most thoroughly tested ingredients in the food supply but has been approved for use by the Food and Drug Administration, by experts of the United Nations Food and Agriculture Organization and the World Health Organization, by the European Union and by regulatory agencies in more than one hundred countries. Furthermore, aspartame has been reviewed and found to be safe for the general population by the Council of Scientific Affairs of the American Medical Association. The Food and Drug Administration has affirmed the safety of aspartame no fewer than twenty six times over a period of more than a quarter of a century.

.Dr. Soffritti's study concluded that aspartame may cause the dreaded "c" word: cancer. The research found that the sweetener was associated with unusually high rates of lymphomas, leukemias and other cancers in rats that had been given doses of it starting at what would be equivalent to four to five 20-ounce bottles of diet soda a day for a 150 pound person.

Dr Soffritti's allegation that aspartame is linked to cancer is not supported by the data revealed in his paper. The claim that aspartame caused a higher level of tumors in female rats (but not male rats) is based solely on a comparison with the control group of female rats which had abnormally low levels of tumors. Furthermore, the alleged effect only appears in the female rats when the number of lymphomas and leukemia are combined. It is well known that these diseases have different causes. Combining these symptoms is like combining statistics on hay fever and the common cold and then asserting that they have the same cause.

At the same time, Dr. Soffritti's findings have energized a vociferous group of researchers, health advocates and others who say they are convinced that aspartame is a toxin associated with a variety of health troubles, including headaches, dizziness, blindness and seizures.

It is difficult to imagine how aspartame could be a toxin. Aspartame is a simple food ingredient which is made from two amino acids, the building blocks of protein that occur widely in the food we eat every day. They are found in eggs, meat, cheese, fish, cereals, fruit and mother's milk.

When we consume aspartame, it is broken down in the digestive system to very small quantities of common dietary components.

Dr Soffritti. says that since last July, he has been contacted by some of these critics, including a member of Parliament in Britain and a number of conspiracy theorists, some of whom say they have suffered from "aspartame poisoning" and filled Web pages with cloak-and-dagger speculation about why the FDA approved aspartame for sale a quarter-century ago.

The FDA's approval of aspartame for use in dry products in 1981 was followed by further approvals for various product categories in the 1980s and 1990s. In 1996, the FDA approved the use of aspartame as a general purpose sweetener for use in all foods and beverages.

No regulatory agency has yet acted on Dr. Soffritti's findings, although Roger Williams, a member of Parliament, called for a ban on aspartame in Britain last December.

The British parliamentary record shows that Roger Williams simply repeated a series of extreme and absurd allegations from the conspiracy theorists. Caroline Flint, the Parliamentary Under-Secretary of State for Health stated in her response "The current advice from the Food Standards Agency remains in place, namely that aspartame is safe for use in food."

Putting restrictions on aspartame would come at a significant cost.

This statement is true, but not in the way that Ms Warner intends. There is now a substantial body of scientific evidence which shows that aspartame helps people to control their weight. The public health costs of scaring people about a safe and wholesome food ingredient are indeed significant. Statistics from Europe show that overweight and obesity are associated with 70,000 new cancer cases every year.

Dr Soffritti. was concerned about the large numbers of people who use aspartame, particularly children and pregnant women. "If something is a carcinogen in animals," he said, "then it should not be added to food, especially if there are so many people that are going to be consuming it."

As noted above, Dr Soffritti's data do not support his allegation that aspartame is a carcinogen. In the United Kingdom, the government's Department of Health Committee on Carcinogenicity reviewed the Soffritti paper and recorded the following conclusions in its minutes:

"Members considered that it was implausible that there should be only a small increase in tumor incidence over such a wide range of doses. They also commented that there may be a reasonable explanation for the differing historical control figures but that the low incidence in the female control group compared to all other groups cast doubt on the study. Members were critical of the study design in that rats were allowed to live until a natural death. It was noted that the statistical approach used, although survival-related, did not fully adjust for age-related effects."

The conclusions of the Committee on Carcinogenicity are available publicly and were supplied to Ms Warner.

Lyn Nabors, executive vice president of the Calorie Control Council, said Dr. Soffritti's study was not valid because the rats used in it had been allowed to live longer than the two-year standard established by the United States government's National Toxicology Program. "It's difficult to determine if the cancers you find are due to something else," Ms. Nabors said. "Just as in humans, the rat's body slows down later in life, and the aging process causes all kinds of things." But John R. Bucher, deputy director of environmental toxicology at the National Toxicology Program, the government's agency for research on toxic chemicals, called the design of the Ramazzini study "impressive" and "thorough," and said that he did not think the fact that rats were allowed to live until their natural deaths had skewed the results. Dr. Jose Russo, director of the breast cancer and environmental research center at the Fox Chase Cancer Center in Philadelphia, says that lifetime studies are "ideal" but that they are not done often, partly because they are more expensive than limited-time tests.

Dr Soffritti did not follow the internationally established protocol for animal carcinogenicity studies. A scientific consensus was established in the 1970s and was formalized in the publication in 1982 by the Food and Drug Administration in its "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food." This document includes "Guidelines for Oral Carcinogenicity Studies in Rodents" and specifically notes on page 57 that "Animals should be exposed to the test substance 7 days per week for at least 104 consecutive weeks" and that "Studies of greater than 130 weeks duration are not recommended." Rats, like people, develop a range of cancers in old age, and establishing cause and effect of tumors in rats which have died of old age is not possible. Dr Soffritti's experiment was conducted on rats that had died and therefore used an unreliable protocol which was abandoned by most researchers thirty or more years ago.

Dr. Russo, however, criticized the Ramazzini study for not allowing outside pathologists to analyze all of the tissue samples where cancerous tumors were found. "People need to see every tumor," he said. Dr. Bucher of the National Toxicology Program said pathologists at the program, with which Ramazzini collaborates, looked at 70 tumor slides. But with the study producing over 9,000 tumor-containing slides, James Swenberg, professor of environmental science at the University of North Carolina at Chapel Hill, says that this falls short of standard practice.

Previous findings by the Ramazzini researchers using a similar protocol to that employed in the aspartame experiment have been reviewed by the FDA's Cancer Assessment Committee, which noted that those reported data were "unreliable" due to a "lack of critical details . and . questionable histopathological conclusions. ."

While Dr. Soffritti's methods have drawn some criticism, the Ramazzini cancer lab, which is financed by private bank foundations, governments and 17,000 individual members, has earned considerable credibility since it was founded in 1971 for its pioneering research on chemicals.

Typically, an Italian not-for-profit organization is registered with an appropriate regional registrar where it has to deposit its statute and accounts. The Ramazzini Foundation does not appear to be registered with the relevant regional registrar. On the contrary, the Ramazzini Foundation is registered with the Bologna Chamber of Commerce as if it were a company. The Ramazzini group regularly receives funding from industry.

Dr. Soffritti said he was inspired to look at aspartame because of what he calls "inadequacies" in the cancer studies done by Searle in the 1970's. He said that those studies did not involve large-enough numbers of rats and did not allow them to live long enough to develop cancer. The Ramazzini study was conducted with 1,900 rats, as opposed to the 280 to 688 rodents used in Searle's studies, and the rats lived for up to three years instead of being sacrificed after two, which is the human equivalent of age 53. "Cancer is a disease of the third part of life," Dr. Soffritti said. "You have 75 percent of cancer diagnoses for people who are 55 years old or older. So if you truncate the experiments at 110 weeks and the rats are supposed to survive until 150 to 160 weeks, it means you avoid the development of cancer at the time when cancer would be starting to arise."

As noted above, rats, like people, develop cancers in old age. It is precisely because of this fact that it is very difficult to interpret the findings of life time rat studies. Four long-term carcinogenicity studies on aspartame conducted in accordance with international standards have found no relationship between aspartame and any form of cancer. In 2003, the U.S. National Toxicology Program (NTP) completed three carcinogenicity studies in which large amounts of aspartame were fed to groups of male and female transgenic mice (cancer models). These studies, sponsored by the U.S. government and conducted under accepted laboratory procedures, found no link between aspartame and cancer. Aspartame has been used by hundreds of millions of consumers around the world for over 20 years. With billions of man-years of safe use, there is no indication of an association between aspartame and cancer in humans.

Others have also challenged Searle's studies. Documents from the FDA and records from the Federal Register indicate that, in the years before the FDA approved aspartame, the agency had serious concerns about the accuracy and credibility of Searle's aspartame studies. A 1976 report from an FDA task force, for example, found that Searle's studies on aspartame and several of the company's pharmaceutical drugs were "poorly conceived, carelessly executed, or inaccurately analyzed or reported." It cited what it called a lack of training by the scientists analyzing tissue samples, a "substantial" loss of information because of tissue decomposition and inadequate monitoring of feeding doses.

Searle's studies were evaluated independently by the FDA, the Universities Associated for Research and Education in Pathology (UAREP) and by the Public Board of Inquiry convened in 1980. All three bodies concluded that aspartame was safe and not linked to cancer.

In response to the report, the FDA asked the Justice Department to open a grand jury investigation into whether two of Searle's aspartame studies had been falsified or were incomplete. In a 33-page letter in 1977, Richard A. Merrill, the FDA's chief counsel at the time, recommended to Samuel K. Skinner, then the United States attorney for the Northern District of Illinois, that a grand jury investigate the company, which was based in the Chicago suburb of Skokie, for "concealing material facts and making false statements in reports of animal studies conducted to establish the safety of the drug Aldactone and the food additive aspartame." A grand jury was never convened, however. Shortly after the letter was sent, Mr. Skinner left the Justice Department to join Sidley & Austin, a law firm that represented Searle. After 12 years at that firm, now Sidley, Austin, Brown & Wood, Mr. Skinner was appointed to be President George H. W. Bush's transportation secretary; later he became his chief of staff. In 1978, a year and half after Mr. Skinner left the United States attorney's office in Chicago, his deputy, William F. Conlon, also left to work at Sidley & Austin. Mr. Skinner, now a lawyer at Greenberg Traurig LLP, said that as soon as he began looking for a new job and interviewing with Sidley & Austin, he recused himself from the Searle investigation. Mr. Conlon, who is still at Sidley & Austin, did not return phone calls.

It is very difficult to take a political conspiracy theory seriously. The FDA has affirmed the safety of aspartame twenty six times, culminating in the agency's approval of aspartame as a general purpose sweetener in 1996.

Over the next few years, Searle's petition for aspartame approval led to much disagreement within the FDA. The commissioner at the time, Alexander M. Schmidt, convened a three-member public board of inquiry, which concluded that one of Searle's studies on rats showed an increase in brain tumors from aspartame. The board members - all of them scientists at universities - voted to withhold approval of aspartame until more studies were done.

A further long term study on aspartame was completed in 1980. In a letter to Commissioner Hayes regarding FDA approval of aspartame dated August 6, 1981, Dr. Nauta, Chairman of the Public Board of Inquiry stated: "We wish to express our endorsement of your final decision in this matter"

In any case, critics say that most of these studies were financed either directly or indirectly by manufacturers of aspartame, and that the results of aspartame studies tend to depend on who paid for them. In an analysis of 166 articles published in medical journals from 1980 to 1985, Dr. Ralph G. Walton, a professor of psychiatry at Northeastern Ohio Universities College of Medicine found that all 74 studies that were financed by the industry attested to sweetener's safety. Of the 92 independently funded articles, 84 identified adverse health effects. "Whenever you have studies that were not funded by the industry, some sort of problem is identified," said Dr. Walton, adding that he has not looked at studies performed since 1985. "It's far too much for it to be a coincidence."

Dr Walton's paper reveals that of the 92 pieces of "research," 85 (not 84) are said to identify an adverse reaction to aspartame. However, of the 85:

- Ten studies actually involve aspartate and not aspartame. Aspartate is the salt of aspartic acid. Aspartic acid is a very common component of food. These studies are therefore irrelevant to aspartame safety.
- 18 of the studies do not actually draw any negative conclusions about aspartame.
- Five are review articles, not peer-reviewed studies.
- Two are "brief reports" or "case reports", not peer-reviewed studies.
- Five are anecdotes, based on the writers' observations of patients.
- 11 are conference proceedings, which are not peer-reviewed studies.
- 19 are letters to various medical journals.
- Three are different reports of the same study.
- Two are exact duplicates of other documents appearing in the list.
- Three are different reports of the same allegations.

Dr. Walton, who, like some other psychiatrists, has studied aspartame from a neurological perspective, said he had also seen problems from the sweetener firsthand. At Safe Harbor Behavioral Health, a mental health facility in Erie, Pa., where he is clinical director, Dr. Walton said he had observed that for many people with mood disorders, such as depression or bipolar disorder, aspartame exacerbates the condition. "For people with panic disorders, for instance, we've seen that when we eliminate aspartame, it's much easier to control their illness," he said.

"The number of panic attacks goes down." Dr. Walton and others say that this is probably attributable to aspartame's phenylalanine component. (Aspartame is made up of two amino acids, phenylalanine and aspartic acid.) He said that an excess of phenylalanine could upset the body's balance of neurotransmitters, causing a range of neurological symptoms. Defenders of aspartame often point out that phenylalanine is naturally present in many protein-intensive foods. But Dr. William M. Pardridge, a professor of endocrinology at the David Geffen School of Medicine at the University of California, Los Angeles, says that when it comes from food, phenylalanine is absorbed into the brain more slowly. "If your blood phenylalanine level was increased five times, in my view there would be a safety concern," Dr. Pardridge said. "The question is whether aspartame use could ever increase levels that much, and the answer is yes. We've known that for 20 years."

The two amino acids in aspartame are in fact aspartic acid and phenylalanine (not phenylalanine). A serving of milk contains five times as much phenylalanine and eleven times as much aspartic acid as a soft drink sweetened with aspartame. People who frequently choose products with aspartame obtain over 98% of their phenylalanine and aspartic acid from other dietary sources. Aspartame is broken down by the digestive system to common dietary components and therefore brings nothing new to our diet. In order to reach a five-fold increase in blood phenylalanine levels, as suggested by William Pardridge, someone would have to drink forty cans of diet soft drink with one hour. That is, of course, impossible.

Dr. Soffritti said he had not studied the effects of phenylalanine. He theorized that the tumors in his study were related to the methanol, or wood alcohol, that is produced as the body metabolizes aspartame. When the body breaks down methanol, the result is formaldehyde, a known carcinogen. "I know that when I treat animals with methanol, you end up with lymphomas and leukemias," he said. But Dr. Kenneth E. McMartin, a methanol expert and professor of pharmacology, toxicology and neuroscience at the Louisiana State University Medical Center, said he believed that it was unlikely that someone could consume enough aspartame to let harmful levels of formaldehyde build up in the body.

The very small amount of methanol which is released when we eat or drink products with aspartame is not anything to be concerned about. Methanol occurs in fresh fruits and vegetables. There is as much methanol in a banana and more than twice as much in a serving of tomato juice as there is in a soft drink sweetened with aspartame. Traces of methanol also occur naturally in our blood, in our saliva, and on our breath. The amount of methanol released when we drink a soda sweetened with aspartame is about one twenty thousandth (1/20,000) of the volume of the drink. Methanol from aspartame cannot be detected in the blood of people who have consumed a single dose of aspartame equivalent to that in over 100 cans of soft drink.

Dr. Soffritti said he thought that more research and open debate were needed on whether aspartame was a carcinogen. "It is very important to have scientists who are independent and not funded by industry looking at this," he said. Michael F. Jacobson, executive director of the Center for Science in the Public Interest, a nutrition advocacy group, said he did not think that Dr. Soffritti's study could be considered definitive, but that it should prompt an "urgent re-examination. "For a chemical that is used by hundreds of millions of people around the world, it should be absolutely safe," Mr. Jacobson said. "There shouldn't be a cloud of doubt."

It is not surprising the Dr Soffritti or Michael Jacobson should urge a yet another re-evaluation of aspartame. It is because aspartame is such a popular ingredient that raising scare stories attracts media coverage, as this story in the New York Times demonstrates. Aspartame remains one of

the most thoroughly tested and scrutinized ingredients in our food supply. It also has an important role to play in helping people to avoid overweight and obesity, and their related diseases, including cancer.

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