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A review of potential carcinogenic effects of aspartame

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Abstract

Aspartame – a wildly popular, worldwide artificial sweetener that is 200 times sweeter than sugar without the associated calories or added sugar. It has caused a controversy of great importance due to certain findings connecting high aspartame intake with the appearance of malignant tumors. Relevant studies surfaced toward the start of the century classifying aspartame as a carcinogen, with a few additional prominent trials to support it in the last 20 years. These studies have been thoroughly debated by other strong control trials and reviews that poke many holes in defense of aspartame's safety. Due to the strength of their design and evidence, these papers are much more widely accepted, making the somewhat official stance of the scientific community that aspartame is not cancerous. There still leaves much room for additional exploration on proper daily limits of aspartame and other potentially dangerous effects besides associations with tumors.

Introduction

Aspartame (N-[L-α-Aspartyl]-L- phenylalanine, 1-methyl ester) is one of the most widely used artificial sweeteners in the world, making up approximately 62% of the total market for artificial sweetening [1]. In contrast to standard sugar, aspartame can sweeten products without adding additional kilocalories [1]. It is a lower-calorie option in comparison to standard food and beverage products sweetened with sugar. Since it is about 200 times sweeter than normal sugar, it can be used in small amounts while still having a strong sweetening effect, making it more effective for health and/or weight loss efforts [2].

The FDA approved aspartame for use in 1981 and it quickly rose in popularity, as now over 200 million people worldwide are regularly consuming aspartame in over 6,000 food, beverage, and hygiene products [1]. The most common products containing aspartame are soda, low-calorie beverages, cereal, gum, instant coffees, yogurt, and many medications [3]. While there are many other commonly used sweeteners such as sucralose (known as Splenda) or saccharin (known as Sweet n' Low), aspartame remains the most widely used sweetener in the world today [3].

Starting about 10-15 years after the FDA approval of aspartame, controversy over the safety of the sweetener began to rise [3]. A

famous study performed by the Ramazzini Institute raised concern that aspartame has many carcinogenic effects and could possibly be a toxic substance [2]. The institute performed three separate studies and each concluded that tumors such as lymphoreticular and liver tumors occurred spontaneously in rats given various amounts of aspartame [2]. These results were inconsistent with previous studies on aspartame toxicity that showed no potential for carcinogenic effects, which is what sparked this ongoing controversial debate [2].

Recent Progress

A meta-analysis study performed in 2013 aimed to collect information from many studies and compile the results to understand if aspartame really had the potential to cause tumors [1]. The researchers conducted a rigorous selection process to find ten randomized control trials that looked specifically at the carcinogenic effects of aspartame on rodents, with several other criteria involved to ensure that each study contained valid results [1]. They looked for the same outcome variable in each study – the number of rodents that had malignant tumors [1]. The results of the meta-analysis revealed that aspartame did not cause the presence of malignant tumors in rodents, regardless of dosage [1].

Some studies, however, have contrasting results, such as a study performed in 2021 that conducted the immunohistochemical analyses of rodents with particular types of tumors [3]. This was another study done at the Razzamini Institute, examining the lesions of previously diagnosed rodents that had tumors in the hematopoietic and lymphoid tissues [3]. They found that with each increased dose of aspartame, the incidence of tumors increased [3]. They sought to confirm again that their previously diagnosed tumors were indeed malignant through the different technology of immunohistochemical analysis, and that risk increased with higher dosage [3].

Discussion

Though these are only two prominent papers researching aspartame and cancer incidence, they represent the larger controversial discussion taking place in the scientific community. When analyzing these studies, it is important to consider the strength of the study design. A meta-analysis or systematic review, if performed correctly, will generally be a stronger study than a randomized control trial. That being said, the 2013 meta-analysis finding no correlation between aspartame and malignant tumors has some significant strength [1]. Mallikarjun, and Sieburth acknowledge some relevant limitations including a relatively small analysis size of ten control trials and consideration of only one outcome variable, but still believe their findings to be very comprehensive of accurate scientific data on the subject [3]. The 2021 randomized control trial, while more recent, has some larger points of concern. By nature of the study design, the control trial likely holds less significance. It is also only re-examining previous diagnoses using a different technology, rather than having an entirely new design or subjects [3]. In addition, it was conducted by the same institute that published the main studies in the early 2000s that caused the initial controversy with the safety of aspartame, which is an interesting aspect to consider [3]. Though it is a helpful addition to an older study that can add to previously found results, this study alone cannot compare to the strength of many studies finding the opposite results.

To add to the validity of the 2013 meta-analysis, a systematic review was conducted in 2019 which also considered ten prominent studies relating aspartame to possible carcinogenic effects [2]. Like many other scientists, the authors questioned the results of the Razzimi Institute trials and sought to understand the truth about aspartame [2]. After a thorough analysis of these

studies considering all relevant strengths and limitations, they concluded that there is no valid evidence connecting aspartame to carcinogenic effects [2]. The researchers of this systematic review closely investigated each study but paid even closer attention to the studies of the Ramazzini Institute [2]. They found many problems with the studies, including the use of dead or nearly dead mice and the creation of their own design and questions to interpret other aspartame studies [2]. They also point out that the Ramazzini Institute has published additional papers finding connections between other sweeteners to carcinogenic effects, yet again against the contrasting results of most of the scientific community [2]. This systematic review both adds credibility to some strong studies showing no positive correlation of aspartame to cancer and removes significant credibility from the prominent studies showing a strong positive correlation [2].

Though there are continuing discussions and further studies being performed on the safety of aspartame, the general consensus of the scientific community is that there is not enough evidence to conclude that aspartame causes the presence of malignant tumors. Many researchers do encourage the need for additional studies to be performed for greater certainty. The 2013 meta-analysis calls for additional studies with a standardized control trial design assessing the carcinogenic potential of aspartame [1]. Mallikarjun and Sieburth explain that additional studies with valid controls and variables will contribute to other meta-analyses and systematic reviews to form clearer conclusions [1]. Haighton et al. found no correlation between aspartame and tumor growth, but also call for additional research, especially concerning exposure to children during pregnancy [3]. Due to the nature of their results, they also call for reconsideration of the current Acceptable Daily Intake of aspartame because they believe it is too close to toxicity levels [3]. It would also be helpful for scientists to conduct additional research on other possible negative effects of aspartame on human health apart from carcinogenic effects. The early 2000s studies sparked a large interest in how aspartame relates to cancer, but it is possible there could be other dangers of aspartame with respect to other diseases or conditions.

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