Aspartame and Cancer: What is the Evidence?

Aspartame is an artificial sweetener used in thousands of products worldwide. Questions about a possible link between aspartame and cancer have persisted for decades. However, compelling evidence now indicates that aspartame is a carcinogen. This fact sheet summarizes the evidence on aspartame and cancer, including important new evidence, and makes recommendations.

Animal Evidence

- The FDA relied on unpublished industry studies and others that reported no evidence of cancer\(^2\) when it approved aspartame in 1981.\(^4\) These studies used smaller numbers of animals than are now recommended by the FDA and other agencies, rendering them less able to detect cancers than larger studies.\(^5\) Furthermore, female animals given the highest dose of aspartame in one study had significantly lower survival rates than controls, making the study less likely to detect tumors induced by aspartame.\(^6\) Similarly, a very small 2005 government study piloting a new testing approach using transgenic mice\(^7\) reported no excess cancer in aspartame-treated animals, but the government acknowledged the study might lack the sensitivity to detect cancer.\(^8\)

- More recently, three independent, high-quality, peer-reviewed studies found that aspartame causes cancers in laboratory animals. That these cancers occur in multiple species, both sexes, and at multiple sites provides strong evidence that aspartame poses a cancer risk to humans. (The types of cancers reported in animal studies frequently vary depending on the conditions of the studies (e.g., timing of exposures, species, sex), including for known carcinogens).\(^9\)
  - A 2006 rat study\(^10\) reported that females treated with aspartame had statistically significant\(^11\) increases in lymphomas/leukemias (L/L) and a very rare type of urinary tract cancer (transitional cell carcinomas of the renal pelvis/ureter) and related precancerous changes compared to untreated controls; and statistically significant dose-response trends in incidence of these and other tumors (in peripheral nerves, and malignant tumors overall) in one or both sexes.
    - This “mega-experiment” was better at detecting tumors than previous studies because it used many more animals and exposed them for a longer portion of their lifespans.\(^12\)
    - Transitional cell carcinomas of the renal pelvis/ureter are so extremely rare in untreated rats of this strain, and thus highly unlikely to be due to chance.\(^13\) Such rare tumors in a single animal study can be enough to conclude that an agent is likely carcinogenic to humans.\(^14\)
  - A 2007 study\(^15\) in which rats were dosed starting before birth (prenatally) also reported statistically significant\(^16\) increases in L/L in treated males and females and in mammary (breast) cancers in females compared to untreated controls.
    - Exposures to aspartame begun prenatally produced much greater increases in L/L, and at earlier ages, than postnatal exposures only\(^17,18\); a finding raising special concerns for consumption of aspartame by pregnant women.
  - A 2010 study\(^19\) in which mice were administered aspartame beginning prenatally reported statistically significant\(^20\) increases in hepatocellular (liver) carcinomas and alveolar-bronchiolar (lung) carcinomas in treated males vs. controls.

- Diagnoses of L/L in the 2006 rat study were generally confirmed by pathologists\(^21\) convened by the National Institute of Environmental Health Sciences (NIEHS) to provide a “second opinion” about cancers in the 2006 rat study, at the request of the authors of the study.

- After questions were raised about the independent laboratory’s accuracy in diagnosing L/L in rats,\(^22\) a 2020 study using state-of-the-art diagnostic methods confirmed most (92%) L/L diagnoses in the 2007 prenatal rat study and the occurrence of the L/L remained statistically significant.\(^23,24\)
The Independent Laboratory Testing Aspartame Produces Valid Results
Although no stranger to controversy,23 the independent laboratory that conducted the 2006, 2007, and 2010 studies described above—the Ramazzini Institute (RI) based in Bologna, Italy—has been assessed by scientists at several US regulatory agencies. Chemicals tested for carcinogenicity by both RI and the U.S. National Toxicology Program NTP) produce “remarkably consistent” results, according to an analysis by an NTP scientist.26 A 2010 NTP review of RI found “very organized and clean facilities” and “meticulous detail to the necropsy record, collecting, and archiving of materials/tissues.” The review also found RI procedures and records “were within GLP [Good Laboratory Practice] expectations.”27 A 2011 NTP/Environmental Protection Agency (EPA)-sponsored review found “good agreement” between RI’s and its own diagnoses for several cancers, but it diagnosed fewer L/L than did RI.28 As previously noted, better diagnostic methods have now confirmed most of the L/L in the 2007 prenatal study.29 A review of RI studies by EPA scientists concluded that “aspects of the RI design, including gestational exposure, lifespan observation, and larger numbers of animals and dose groups, may impart advantages that provide chemical risk assessors with valuable insights … not obtained from other bioassays.”30

Human Evidence
• A 2012 prospective cohort study31 reported a statistically significant32 association between diet soda and total aspartame intake and risk of non-Hodgkin’s lymphoma (NHL) and multiple myeloma (MM) in men. These cancers are very similar to the most frequently observed cancers (L/L) in the RI rat studies—thus providing additional supportive evidence that aspartame is a carcinogen. This study is arguably the best of the human studies, since it was the largest prospective study that considered long-term exposure to aspartame (22 years), and the only one that assessed exposure to aspartame over time, although all cohort studies, by their nature, have important limitations.
• Two other prospective studies did not report an association between aspartame and cancer, but they had shortcomings compared to the 2012 study. A large 2006 study33 only evaluated older adults (ages 50 to 71), who could not have consumed aspartame until middle-age or older, given that aspartame was only approved in 1981. In addition, participants were followed for only five years and intakes of aspartame were modest (only about 16% consumed more than about one 12-ounce soda per day). A 2014 study34 was smaller and followed participants for less time (10 years) than the 2012 study. Both the 2006 and 2014 studies assessed exposure to aspartame only when people entered the study, so they did not capture changes in consumption over time.

Biological Plausibility35
• Methanol, a breakdown product of aspartame, is metabolized in humans and rats to formaldehyde.36 Formaldehyde is listed in the U.S. Report on Carcinogens as “known to be a human carcinogen,”37 in part because it causes leukemia in humans.38
• Other chemicals that break down in the body to formaldehyde, including methanol and methyl tert-butyl ether (MTBE), are also linked to L/L.39,40
• An association between aspartame and L/L has been observed in female rats and male humans, as previously noted. Both have higher levels of an enzyme that converts methanol (a breakdown product of aspartame) to formaldehyde than do male rats and female humans.41,42,43
• Ingestion of alcoholic beverages inhibits the metabolism of methanol to formaldehyde. In the 2012 human study (above), in men consuming at least 2 diet sodas a day, those consuming less alcohol had a significantly higher risk of non-Hodgkin lymphoma than those with higher alcohol consumption.

Conclusions and Recommendations
The evidence that aspartame causes cancer is compelling. The U.S. Report on Carcinogens considers an agent “Reasonably Anticipated To Be a Human Carcinogen” in several circumstances, including when “there is sufficient evidence of carcinogenicity from studies in experimental animals which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors … in multiple species or at multiple tissue sites … or … to an unusual degree.” Aspartame meets those criteria (but has not been reviewed in the Report). It causes statistically significant increases in tumors in multiple species and at multiple tissue sites and to an unusual degree (e.g., extremely rare urinary tract cancers). Limited human and mechanistic data support that conclusion.

Aspartame is potent (it caused a high incidence of tumors at both high and low dosages).

By law, the Food and Drug Administration (FDA) cannot approve a food additive if it is found to induce cancer in animals or humans.

The Center for Science in the Public Interest therefore recommends that:

- the FDA and authorities in other nations take immediate steps to withdraw approval of aspartame.
- all consumers avoid aspartame, especially pregnant women and children.
- the International Agency for Research on Cancer (IARC) review the cancer evidence on aspartame as soon as possible. (IARC has already designated aspartame a “high priority” for review, following CSP’s nomination.)
- companies reformulate their products to eliminate aspartame and use available, safer alternatives.

For more information, please contact the Center for Science in the Public Interest at policy@cspinet.org.

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5 U.S. Food and Drug Administration. Redbook 2000: IVC.C. Carcinogenicity Studies with Rodents. 2006. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/redbook-3-ivc-carcinogenicity-studies-rodents. The Redbook states, “It is recommended that carcinogenicity studies begin with at least 50 animals per sex per dose group in each of three treatment groups and in a concurrent control group.” This minimizes the likelihood of detecting a weak carcinogenic effect.

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Typically, carcinogenicity studies with rats use a control group plus three (occasionally five) groups, 50 animals/sex group, and are terminated after two years.

Transitional cell carcinomas of renal pelvis/ureter were found in 21/1500 aspartame treated animals vs. 0 in the concurrent controls (Soffritti et al. 2006). They were found in 0 historical controls for this laboratory (of 1,934 males and 1,945 females). In 17 studies using 2,669 control Sprague-Dawley rats, there were found in only 1 male and 1 female (Toxicol Pathol. 1991;19(3):287-289).


14. Lymphomas/leukemias: positive trend in females (p < 0.01); increases compared with controls at 2,000 ppm in females (p < 0.01) and males (p < 0.05). Mammary carcinomas: positive trend in females (p < 0.05); increases compared with controls at 2,000 ppm in females (p < 0.05).


23. Most authorities assume that chemicals that cause cancer in animals cause cancer in humans, unless there is strong evidence otherwise. The U.S. Environmental Protection Agency states in its Guidelines for Carcinogen Risk Assessment (2006, p. 2-22) that “tumors observed in animals are generally assumed to indicate that an agent may produce tumors in humans.” The International Agency for Research on Cancer states in its Preamble to the IARC Monographs on the Identification of Carcinogenic Hazards to Humans (2019), “it is biologically plausible that agents for which there is sufficient evidence of carcinogenicity in experimental animals … present a carcinogenic hazard to humans. Accordingly, in the absence of additional scientific information, such as strong evidence that a given agent causes cancer in experimental animals through a species-specific mechanism that does not operate in humans … these agents are considered to pose a potential carcinogenic hazard to humans. The inference of potential carcinogenic hazard to humans does not imply tumour site concordance across species …”

