

Aspartame and Formaldehyde

What does the science say?

Joshua DeWald - June 13, 2010

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Introduction

Aspartame, more commonly known as NutraSweet, is frequently claimed to have any number of ill effects in the body. This article will focus on the claim that aspartame contains formaldehyde, leading to toxic effects in the body (such as headaches), and will also touch on the claim that it is a carcinogen (cancer causing agent). There are additionally claims that aspartame leads to seizures, but this is a much less popular one (perhaps because the NutraSweet acknowledges the danger in the small amount of PKU sufferers for which it would affect). Hopefully the reader will be convinced it is true that one of the by-products of the breakdown of aspartame is formaldehyde, this does not represent any actual health hazard.

Just what is aspartame?

Aspartame is a low-caloric sweetener (i.e. alternative to sugar). Wikipedia [describes aspartame](#) as¹

a methyl ester of the dipeptide of the natural amino acids L-aspartic acid and L-phenylalanine. Under strongly acidic or alkaline conditions, aspartame may generate methanol by hydrolysis. Under more severe conditions, the peptide bonds are also hydrolyzed, resulting in the free amino acids

Claims and Discussion

A common claim is that aspartame contains formaldehyde which builds up in the body and creates all manner of ills. Others have claimed that it is a carcinogen (cancer causing agent) despite there being no studies that really demonstrate that.

Mark D. Gold and Ralph Walton are two of the more prolific writers on this topic out there. Gold's website has a section title "[Formaldehyde Poisoning from Aspartame](#)", which has the following:

1. <http://en.wikipedia.org/wiki/Aspartame> - Wikipedia page on aspartame. Used for general overview. Visited 3/5/2010

In 1997 there was an increase in aspartame users reporting severe toxicity reactions and damage such as **seizures, eye damage and vision loss, confusion, severe migraines, tremors, depression, anxiety attacks, insomnia, etc.** In the same years, Ralph Walton, MD, Chairman, The Center for Behavioral Medicine showed that **the only studies which didn't find problems with aspartame were those funded by the manufacturer (Monsanto).**

Given the agreement amongst independent scientists about the toxicity of aspartame, the only question was whether the formaldehyde exposure from aspartame caused the toxicity. That question has now been largely answered because of research in the late 1990s.

The following facts shown by recent scientific research:

1. Aspartame (nutrasweet) breaks down into methanol (wood alcohol).
2. Methanol quickly converts to formaldehyde in the body.
3. Formaldehyde causes gradual and eventually severe damage to the neurological system, immune system and causes permanent genetic damage at extremely low doses.
4. Methanol from alcoholic beverages and from fruit and juices does not convert to formaldehyde and cause damage because there are protective chemicals in these traditionally ingested beverages.
5. The most recent independent research in Europe demonstrates that ingestion of small amounts of aspartame leads to the accumulation of significant levels of formaldehyde (bound to protein) in organs (liver, kidneys, brain) and tissues.
6. Excitotoxic amino acids such as the one which is immediately released from aspartame likely increases the damage caused by the formaldehyde.

What the science says

While it is true that aspartame does break down into methanol then formaldehyde, it actually happens much more in fruit juices ([about 2x in a banana, or 6x in an 8oz glass of tomato juice²](#)). Gold attempts to address this in item 4, but simply waves his hand as an explanation for why it can be ignored. The fact is that it simply is not enough to do anything and your body easily disposes of it.

The above quoted article has one of the more untrue statements you can find. Not only do "non-independent" researchers find no problems, "independent" ones did not either. Instead what you will find are people making hypothetical claims which are not backed by anything. Gold and Walton are excellent at taking a statement by one scientist and using it as an explanation for **why** aspartame has been found to be bad, when in fact it has not. In other words, they start with the premise that aspartame is harmful then look for explanations for why it might be.

The Walton set of research is frequently cited, but let's break it down a bit. It actually was already [rebutted here](#):

2. Magnuson, B. "Straight facts on aspartame & health". The Beverage Institute. http://www.thebeverageinstitute.com/healthcare_professionals/pdf/Aspartame_Magnuson.pdf. Visited 6/13/2010. The actual numbers quoted come from the peer-reviewed paper by the same author, but I was unable to find a working full text link.

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.

Overwhelming indeed. My [own analysis is available here](#). What I found entertaining is how many of them (18 or 19) don't even find anything negative... yet Walton, either brazenly or unknowingly, still includes them in his number. All in all, Walton is quite sloppy.

The only reasonable study (which I believe is also the one being referenced in #5 above), but still frequently questioned is:

1. Trocho, C., et al., 1998. "[Formaldehyde Derived From Dietary Aspartame Vinds\(sic\) to Tissue Components in vivo](#)," Life Sciences, Vol. 63, No. 5, pp. 337+, 1998

Note the misspelling as "Vinds"... when it should be "Binds". It's generally cited as "Vinds" though.. a good indication that most of the sites claiming to do research are simply copy/pasting from this one guy.

...The administration of labelled aspartame to a group of cirrhotic rats resulted in comparable label retention by tissue components, which suggests that liver function (or its defect) has little effect on formaldehyde formation from aspartame and binding to biological components. The chronic treatment of a series of rats with 200 mg/kg of non-labelled aspartame during 10 days resulted in the accumulation of even more label when given the radioactive bolus, suggesting that the amount of formaldehyde adducts coming from aspartame in tissue proteins and nucleic acids may be cumulative. It is concluded that aspartame consumption may constitute a hazard because of its contribution to the formation of formaldehyde adducts.

One of the primary responses is from Tephyl, [quoted](#) by Butchko et al³:

However, according to Tephly (1999), the dose of aspartame used in the study (20 mg/kg body wt=2mg of methanol/kg body wt) would not yield blood methanol concentrations

3. Butchko, HH., Stargel, WW., Comer, CP., Mayhew, DA. "Aspartame: Review of Safety". Regulatory Toxicology and Pharmacology 35, S1-S93 (2002)

outside control values. Further, the administration of aspartame at 200 mg/kg body wt (equal to that in a single bolus of about 25 liters of beverage sweetened 100% with aspartame) to adult humans results in no detectable increase in blood formate concentrations (Stegink et al., 1981). Administration of [14C]methanol itself at 3000 mg/kg body wt to monkeys produces no detectable [14C]formaldehyde in body fluids and tissues (McMartin et al., 1979)...The lack of formaldehyde accumulation at very high doses of methanol question considerably the conclusion that formaldehyde adducts are forming from low doses of methanol (derived from high doses aspartame). Thus, Tephly (1999) concluded, "the normal flux of one-carbon moieties whether derived from pectin, aspartame, or fruit juices is a physiologic phenomenon and not a toxic event."

To break it down:

1. Formaldehyde build-up has not in fact been detected even when 200mg/kg is given to humans (which is a huge amount)
2. Even when large doses of direct methanol (which is what breaks down into formaldehyde) were given to monkeys, it did not produce formaldehyde build-up
3. There are other explanations for the labelled-carbon staying in the body, aside from formaldehyde build-up which will also occur with other substances (such as fruit pectin).

Going back to the original comments about Gold and Walton, we have a situation of someone trying to explain the build-up for formaldehyde, when no other scientists are able to actually see a build-up in the first place. Instead it seems that the labelled molecules are making their way through the basic chemistry of the process, but the full molecule is not.

Systematic Reviews

Let's continue one with some of the large overviews which discuss the overall safety of aspartame in the broader scope, and occasionally look at studies purporting to show harm.

US Food and Drug Administration (FDA)

Both the FDA and the European Commission have determined that aspartame is safe. However they kicked off additional reviews in response to a study done by the European Ramazzini Foundation ([linked here](#)⁴) that claimed to demonstrate that aspartame was a carcinogen. The European review found this to not at all be supported by the data. The US FDA decided to do its own [separate review](#) of the study and had similar findings⁵:

4. Soffritti, M., Belpoggi F. et al. "First Experimental Demonstration of the Multipotential Carcinogenic Effects of Aspartame Administered in the Feed to Sprague-Dawley Rats". *Environ Health Perspect.* 2006 March; 114(3): 379–385.

5. US Food and Drug Administration. "FDA Statement on European Aspartame Study". CFSAN/Office of Food Additive Safety. April 20, 2007. <http://www.fda.gov/Food/FoodIngredientsPackaging/FoodAdditives/ucm208580.htm>. Accessed 6/13/2010

FDA has completed its review concerning the long-term carcinogenicity study of aspartame entitled, "Long-Term Carcinogenicity Bioassays to Evaluate the Potential Biological Effects, in Particular Carcinogenic, of Aspartame Administered in Feed to Sprague-Dawley Rats," conducted by the European Ramazzini Foundation (ERF), located in Bologna, Italy. FDA reviewed the study data made available to them by ERF and finds that it does not support ERF's conclusion that aspartame is a carcinogen. Additionally, these data do not provide evidence to alter FDA's conclusion that the use of aspartame is safe.

....

Considering results from the large number of studies on aspartame's safety, including five previously conducted negative chronic carcinogenicity studies, a recently reported large epidemiology study with negative associations between the use of aspartame and the occurrence of tumors, and negative findings from a series of three transgenic mouse assays, FDA finds no reason to alter its previous conclusion that aspartame is safe as a general purpose sweetener in food.

Kind of interesting that the folks doing the study were not willing to actually submit it to a full review. If you take a look at the study's tables ([here](#) and [here](#)), the bit that stands out to me is the lack of a consistent dose-response effect as you get higher doses of aspartame. They had to get up to an insane amount (2500mg/kg... or the equivalent of 500mg/kg for humans) to get a statistically significant effect.

European Commission - Scientific Committee on Food

For reasons unknown, people against Aspartame link to to the "[European Commission updates their opinion](#)" study as if the EC had determined that aspartame was now unsafe. The update was kicked off because of the Ramazzini Foundation study claiming carcinogenicity. If you actually read the update, it is quite clear that they very much still find it to be safe.

Some important bits from the [text](#) (in all cases emphasis is my own)⁶:

The estimates of intake by mean and high level consumers are fairly consistent between European countries even though slightly different approaches were used. High level consumers, both adults and children, are unlikely to exceed the ADI of 40 mg/kg bw for aspartame. Special groups such as diabetics that are likely to be high consumers of foods containing aspartame are also well below the ADI. Therefore, from the available data it appears that no group is likely to exceed the ADI for aspartame on a regular basis.

6. European Commission Scientific Committee on Food. "Opinion of the Scientific Committee on Food: Update on the Safety of Aspartame". December 4, 2002. http://ec.europa.eu/food/fs/sc/scf/out155_en.pdf. Accessed 6/13/2010.

All this is really saying is that the actual amount that most people would consume is well below the worldwide maximum level allowed (40-50 mg/kg).

If you view the table in the document, you can see that the mean is in the 2-3mg/kg bw/d, with high levels around 6-10.

Animal studies have demonstrated that the metabolic breakdown products of aspartame are absorbed and metabolised similarly whether they are given alone or derived from aspartame. The extensive presystemic metabolism of aspartame results in little or no parent compound reaching the general circulation.

This is in alignment to the Butchko/Tepyl comments above: aspartame by-products (methanol, then formaldehyde) to not make it into the bloodstream.

And the key parts:

The aspartate component is rapidly metabolised and thus the plasma aspartate concentrations are not significantly elevated following aspartame doses of 34 to 50 mg/kg bw, whereas plasma Phe concentrations may increase depending on dose (Stegink, 1984). **Methanol is also rapidly metabolised and blood levels are usually not detectable unless large bolus doses of aspartame (>50 mg/kg bw) are administered.**

Trocho is discussed:

...Besides the fact that aspartame at high doses has never induced liver cancer in rats, Trocho's studies did not identify the radioactivity found in the proteins and DNA. Consequently, the formation of adducts of formaldehyde on the proteins and nucleic acids from aspartame, in vivo, remains to be proved

French Food Safety Agency (AFSSA)

The AFSSA published its own [systematic review](#) (here hosted on the UK Food standards agency... FDA equivalent). They go over much of the same material as those above. On the subject of the aspartame leading to headaches, they have to say⁷:

Another study...was also a randomised double-blind placebo-controlled cross-over trial, concluded that aspartame was no more likely than placebo to trigger headaches (Schiffman et al., 1987). This study consisted of 40 subjects who complained of aspartame-related headaches... While 35% of subjects developed headaches while on aspartame, 45% developed headaches while on placebo.

7. French Food Safety Agency (AFSSA). "Opinion on a possible link between the exposition to aspartame and the incidence of brain tumours in humans". May 7, 2002. <http://www.food.gov.uk/multimedia/pdfs/afssaeng.pdf>. Accessed 6/13/2010.

I found it interesting that the Shiffman study actually used people who were already pre-disposed to believe that they got headaches from aspartame, and even then it could not be demonstrated.

Conclusion

The fact of the matter is there is not a convincing body of evidence (or none at all depending on how you look at it) to indicate that there is any reason to be concerned with normal intake of foods and beverages containing aspartame--unless you somehow manage to consume 12 liters of soda in a single sitting, in which case you have worse things to worry about. If there is interest, another article could focus on the supposed "excitotoxin" aspects of aspartame and some of the other proposed effects. The problem with these claims is that there is a large amount of urban myth around aspartame which do not have any studies (or reproduced studies) to back them up. They are essentially made up from whole cloth, which actually makes them more difficult to disprove. If there are specific studies that you have found convincing, then they could serve as a new jumping off point for another essay. Until then, there seems no reason to not consume diet beverages and other "light" foods.