# Acrylamide Hemoglobin Adducts

## Sources

Acrylamide is a chemical naturally found in starchy foods that are cooked at high temperatures (above 120°C) and in low-moisture conditions. Baking and frying are examples of these conditions. There are also several foods in which acrylamide appears to form in high-moisture conditions at lower temperatures, such as prune juice and black olives (Becalski 2011; Casado 2010). Acrylamide is formed in food mainly due to a reaction between the amino acid asparagine and reducing sugars, such as glucose and fructose (Stadler 2002; Mottram 2002). The formation of acrylamide is part of the Maillard reaction (Tamanna 2015), which leads to browning and flavor changes in cooked foods. Foods that are the greatest contributors of acrylamide levels include potato chips, crackers, snacks, and coffee (Quesada-Valverde 2022; Abt 2019; Dybing 2005). Most people consume foods containing acrylamide daily. Acrylamide is also present in tobacco smoke. The reported levels of acrylamide in filtered cigarettes range from 1100 to 2340 ng per cigarette (Çebi 2024; Kenwood 2022; Smith 2000). In addition, acrylamide is an industrial chemical found in products used for water purification, grouts, packaging, cosmetics, and scientific research (U.S. Department of Health and Human Services/Agency for Toxic Substances and Disease Registry 2012).

## Health Effects

High levels of acrylamide can be neurotoxic in both humans and animals and genotoxic and carcinogenic in animals (Kim 2017; Park 2021; Benford 2022; Çebi 2024). Acrylamide has been categorized by the International Agency for Research on Cancer (IARC) as a probable human carcinogen (IARC 1995). This categorization is subject to further evaluation (IARC 2014). In the National Toxicology Program Report on Carcinogens, acrylamide has been categorized as *"reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals" (U.S. National Toxicology Program 2021). The U.S. Environmental Protection Agency has characterized acrylamide as "likely to be carcinogenic to humans" (U.S. Environmental Protection Agency 2010). In the body, some acrylamide is metabolized to glycidamide, an epoxide of acrylamide, through action of cytochrome P450 2E1. In contrast to acrylamide, glycidamide reacts with DNA in the body and is therefore considered the

genotoxic agent. Acrylamide and glycidamide are cleared through the body mainly by formation of glutathione adducts and excretion in urine. Neither compound accumulates in the body.

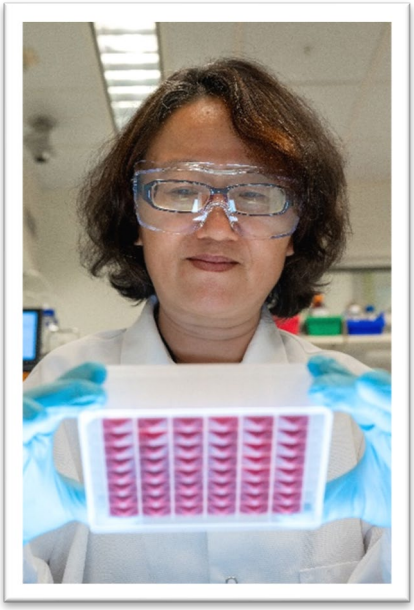
## Intake

The mean estimated intake of acrylamide from food in the general U.S. population (ages 2 years and older) based on 2011–2015 data were on average 0.36 microgram per kilogram bodyweight per day (µg/kg bw/day), comparable to the 0.44 µg/kg bw/day reported by FDA in 2006. The 90th percentile of intake was 0.86 µg/kg bw/day. Children less than 2 years of age had a mean estimated intake of 1.42 µg/kg bw/day, with a 90th percentile of 3.02 µg/kg bw/day (Abt 2019; Doerge 2008). The median dietary intake in the general population of 26 countries, including the U.S., was estimated to be 0.02–1.53 µg/kg bw/day (Timmermann 2021). These levels are about 100 times below those known to cause neurotoxic effects or cancer in animals. The lifelong exposure of most of the population through food and smoking has raised concerns about acrylamide's potential health effects, even at these low levels of intake. Initial studies used food intake questionnaires to investigate the relationships between acrylamide intake and various cancers. These studies did not find any consistent associations (Çebi 2024; Hogervorst 2010). The studies' authors suggested that future researchers obtain more information about actual acrylamide exposure in the body using biomarkers of acrylamide exposure.

## Biochemical Indicators

Hemoglobin adducts of acrylamide and glycidamide reliably reflect the internal dose of acrylamide during the preceding two to four months (Bergmark 1991; Törnqvist 2002). The measured hemoglobin adduct levels reflect a time-weighted average of exposure over the lifetime of the erythrocyte (Fennell 1992). Hemoglobin adducts show a high within-person correlation over time, suggesting that a single blood measurement is a relatively good indicator of long-term acrylamide intake (Wilson 2009). Hemoglobin adducts, however, are not specific with regard to the source of acrylamide intake or exposure. Therefore, studies using these biomarkers to investigate acrylamide intake from foods need to control for exposures from other sources, such as smoking. Persons who smoke tobacco products have higher acrylamide exposure than those who do not smoke (Vesper 2007; Mojska 2016; Kenwood 2022). In non-smokers, exposure to second-hand smoke seems to have a small but significant effect on hemoglobin adduct levels (Vesper 2010).

## Analytical Methods



Analytical methods measuring hemoglobin adducts of acrylamide determine the adducts at the N-terminal valine of the hemoglobin protein chains. Initial methods employed gas chromatography coupled with mass spectrometry. These methods were based on a modified Edman reaction, which was first described for measuring N-terminal hemoglobin adducts of ethylene oxide, propylene oxide, and styrene oxide (Mowrer 1986). These initial methods were further developed and optimized to measure hemoglobin adducts of acrylamide and glycidamide (Törnqvist 1986; Vesper 2006; Sabbioni 2022; Gauch 2022).

## Findings from NHANES

The National Health and Nutrition Examination Survey (NHANES) is the only source for nationally representative data on acrylamide hemoglobin adducts for the U.S. population (Pfeiffer 2026). No data on these compounds exist in NHANES prior to 2003. The acrylamide hemoglobin adducts data from NHANES 2003–2004 provide information both about acrylamide exposure and metabolism (Vesper 2010). Hemoglobin adduct concentrations were detectable in 98% of all blood samples measured. The glycidamide-to-acrylamide hemoglobin adduct ratio can be used as an indicator of the extent of acrylamide metabolism. This ratio indicates the formation of the genotoxic metabolite glycidamide in the body and its detoxification. Children had higher glycidamide-to-acrylamide hemoglobin adduct ratios compared to adolescents and adults, suggesting differences in acrylamide metabolism or metabolic rate among age groups. Non-Hispanic Black persons had lower hemoglobin adduct ratios compared to non-Hispanic White and Mexican-American persons, which may indicate differences in polymorphisms of the genes involved in phase II detoxification of acrylamide and glycidamide. Using data from NHANES 2003–2004, researchers showed that dietary acrylamide positively correlated with both acrylamide and glycidamide hemoglobin adducts but the correlation was low ($R^2$ <3.5%) (Tran 2010). Additional acrylamide hemoglobin adduct data are publicly available for the NHANES 2013–2014 and 2015–2016 cycles. Research on possible associations between acrylamide adduct levels and health is ongoing (Hogervorst 2021; Yin 2021; Cheang 2021; Lin 2023).

## Data in the 2026 tables

Data presented are from univariate analysis that was not adjusted for demographic variables (e.g., age, sex, race and Hispanic origin) or other blood concentration determinants (e.g., dietary intake, supplement use, smoking, BMI). Data for acrylamide hemoglobin adduct, glycidamide hemoglobin adduct, and the ratio between these two biomarkers were available for different population subgroups sampled in four NHANES cycles. All data were generated using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS; Vesper 2008). While different specimen types were used in 2003–2004 (whole blood) and 2005–2006 (washed erythrocytes), concentrations were comparable overall. Given that smoking rather than dietary supplement use is the more influential variable for the hemoglobin adduct biomarkers, we provide separate trend tables for adult smokers (serum cotinine >10 ng/mL) and nonsmokers.

| NHANES cycle | Matrix | Population subgroup |
|---|---|---|
| 2003–2004 | Whole blood | Persons ≥3 years of age |
| 2005–2006 | Washed erythrocytes | Persons ≥3 years of age |
| 2013–2014 | Washed erythrocytes | Persons ≥6 years of age (1/3 sample subset) |
| 2015–2016 | Washed erythrocytes | Persons ≥6 years of age (1/3 sample subset) |

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