

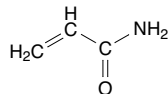
Acrylamide

CAS No. 79-06-1

Reasonably anticipated to be a human carcinogen

First listed in the *Sixth Annual Report on Carcinogens* (1991)

Also known as 2-propenamamide



Carcinogenicity

Acrylamide is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Acrylamide caused tumors in two rodent species, at several different tissue sites, and by several different routes of exposure. Administration of acrylamide in the drinking water caused benign thyroid-gland tumors (follicular-cell adenoma) in rats of both sexes. In male rats, it also caused tumors of the lining of the testes (mesothelioma of the tunica albuginea) and benign adrenal-gland tumors (pheochromocytoma). In female rats, it also caused cancer of the uterus (adenocarcinoma), benign and malignant tumors of the mammary gland (adenoma and adenocarcinoma), and benign tumors of the pituitary gland (adenoma), oral cavity (papilloma), and clitoral gland (adenoma). In strain A/J mice (a strain with a high spontaneous incidence of lung cancer), administration of acrylamide by stomach tube or by intraperitoneal injection increased both the incidence of benign lung tumors (adenoma) and number of tumors per animal in both sexes. In initiation-promotion studies, acrylamide administered dermally, by stomach tube, or by intraperitoneal injection followed by long-term dermal exposure to the tumor promoter 12-*O*-tetradecanoylphorbol-13-acetate induced benign and malignant skin tumors (squamous-cell papilloma and carcinoma) in female mice (IARC 1986).

Cancer Studies in Humans

Most of the available epidemiological studies of cancer and exposure to acrylamide have been published since acrylamide was listed in the *Sixth Annual Report on Carcinogens*. In a study of a multi-plant cohort consisting mostly of male workers, the incidence of pancreatic cancer was significantly higher among workers with the highest cumulative exposure to acrylamide than in the U.S. population. Among exposed workers, the incidence of pancreatic cancer was significantly associated with duration of exposure and time since first exposure (Marsh *et al.* 1999, Schulz *et al.* 2001). In a follow-up of this cohort, the relative risk of pancreatic cancer increased with increasing duration of exposure after adjustment for smoking, but the trend was not statistically significant, and no clear trends were observed for cumulative or average exposure (Marsh *et al.* 2007). A small cohort study of U.S. workers (mostly male) found statistically nonsignificant increases in the risks for cancers of the digestive system, including pancreatic cancer (Sobel *et al.* 1986, Swaen *et al.* 2007).

Several population-based studies that investigated the association between dietary intake of acrylamide and specific cancer outcomes were reviewed by Hogervorst *et al.* (2010). Several prospective cohort studies used case-cohort or nested case-control analyses to evaluate dietary exposure to acrylamide (based on a food-frequency questionnaire) and the risks of cancer at specific tissue sites; these include the Swedish Women's Lifestyle and Health Cohort, the Swedish

Mammography Cohort, the Netherlands Study on Diet and Cancer, a cohort of Swedish men, the U.S. Nurses' Health Study, and the Danish Diet, Cancer, and Health Study. In addition, several case-control studies (most of which used food-frequency questionnaires) assessed cancer and dietary exposure of Swedish, French, and U.S. populations to acrylamide. The tissue site studied most frequently was the breast. These studies found no overall association between breast cancer and dietary exposure to acrylamide; however, some, but not all, studies reported an association between acrylamide exposure and a specific type of breast cancer (sex-hormone-receptor-positive cancer in post-menopausal women). The Danish study used acrylamide-hemoglobin adducts to assess exposure; however, these adducts are not source-specific, but reflect both dietary exposure and exposure from other sources, such as smoking. Two of three prospective cohort studies reported increased risks of endometrial and ovarian cancer, but a case-control study found no increased risk of ovarian cancer. Most of the studies evaluating prostate and colorectal cancer did not find increased risks associated with dietary exposure to acrylamide. Findings were mixed for cancer of the kidney, head, and neck, and evaluation of cancer at other tissue sites was limited by the small numbers of studies.

Properties

Acrylamide is an unsaturated amide that exists as a white, odorless crystalline solid at room temperature. It is soluble in water, methanol, ethanol, acetone, ethyl acetate, and chloroform, and insoluble in benzene and heptane. Acrylamide is stable under normal conditions but may decompose or polymerize when heated or exposed to ultraviolet light (Akron 2009). When heated to decomposition, acrylamide emits acrid fumes and nitrogen oxides (HSDB 2009). Commercial acrylamide monomer contains residual levels of acrylonitrile (1 to 100 mg/kg) (IARC 1986). Residual acrylamide monomer is present in the polymer at approximately 0.01% (Fujiki *et al.* 1984, IARC 1986). Physical and chemical properties of acrylamide are listed in the following table.

Property	Information
Molecular weight	71.1
Specific gravity	1.122 at 30°C/4°C
Melting point	84.5°C
Boiling point	192.6°C
Log K_{ow}	-0.67
Water solubility	371 g/L at 20°C
Vapor pressure	7×10^{-3} mm Hg at 25°C
Vapor density relative to air	2.5

Source: HSDB 2009.

Use

Acrylamide is a chemical intermediate used in the production and synthesis of polyacrylamides that can be modified to develop non-ionic, anionic, or cationic properties for specific uses. These water-soluble polymers can be used as additives for water treatment, enhanced oil recovery, flocculants, papermaking aids, thickeners, soil-conditioning agents, sewage and waste treatment, ore processing, and permanent-press fabrics (Habermann 2002). In 2001, 94% of acrylamide was used to produce polyacrylamide, of which 56% was used for water treatment, 24% for pulp and paper production, 10% for mineral processing, 4% for miscellaneous uses, and the remaining 6% for production of *N*-methylolacrylamide and other monomers (CMR 2002). Acrylamide is also used in the synthesis of dyes, in copolymers for contact lenses, and in the construction of dam foundations, tunnels, and sewers (Habermann 2002).

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The U.S. Food and Drug Administration has regulated the use of acrylamide and polyacrylamide in foods (IARC 1994). Acrylamide polymers containing less than 0.2% monomer may be used in food-packaging adhesives, paper, and paperboard; to wash or peel fruits and vegetables; and in gelatin capsules. In acrylamide polymers added to water for steam that will contact food, the monomer should not exceed 0.05% by weight.

Production

In 2002, four U.S. producers of acrylamide reported a production capacity of 301 million pounds (CMR 2002). In 2009, acrylamide was produced by 30 manufacturers worldwide, including 4 in the United States (SRI 2009), and was available from 55 suppliers, including 28 U.S. suppliers (ChemSources 2009). The demand for acrylamide increased from 191 million pounds in 2000 to 200 million pounds in 2001 (CMR 2002). In 1972, U.S. imports of acrylamide were considered negligible (HSDB 2009). Imports totaled 6.8 million kilograms (15 million pounds) in 1992, 2 million pounds in 2001, 2.9 million kilograms (6.4 million pounds) in 2007, and 2.6 million kilograms (5.8 million pounds) in 2008. U.S. exports of acrylamide were less than 0.9 million kilograms (2 million pounds) in 1992, 11 million pounds in 2000, and 8 million pounds in 2001; no more recent data on exports were found (EPA 1994, CMR 2002, USITC 2009). Reports filed from 1988 to 2006 under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of acrylamide totaled 100 million to 500 million pounds except in 1990, when the quantity was 50 million to 100 million pounds (EPA 2004, 2009).

Exposure

The potential routes of human exposure to acrylamide are ingestion, dermal contact, and inhalation (Manson *et al.* 2005). Acrylamide has been found in a number of food products. In 2002, a Swedish study reported that acrylamide was formed in heated foodstuffs, especially potato products and other baked or fried high-carbohydrate foodstuffs (Tareke *et al.* 2002). The acrylamide content of food items is directly related to the amount of reducing sugars and asparagine in the raw product and the cooking temperature used in the preparation (Pedreschi *et al.* 2004). Studies have quantified acrylamide content in foods such as potato chips (up to 3,700 $\mu\text{g}/\text{kg}$), French fries (up to 12,000 $\mu\text{g}/\text{kg}$), cereal (up to 1,346 $\mu\text{g}/\text{kg}$), bread (biscuits and crackers, up to 3,200 $\mu\text{g}/\text{kg}$), gingerbread (up to 1,660 $\mu\text{g}/\text{kg}$), nuts and nut butters (up to 457 $\mu\text{g}/\text{kg}$), and coffee (up to 16 $\mu\text{g}/\text{L}$) (Friedman 2003, Andrzejewski *et al.* 2004, Hoenicke *et al.* 2004, Aguas *et al.* 2006). Average U.S. daily dietary intake for all individuals over the age of two years was estimated at 0.43 $\mu\text{g}/\text{kg}$ of body weight; however, the estimated exposure of children aged two to five years was 1.06 $\mu\text{g}/\text{kg}$ (Manson *et al.* 2005).

Acrylamide may also be ingested in drinking water contaminated by polyacrylamide flocculants used in water treatment (Brown *et al.* 1980a, Howard 1989). Residual acrylamide concentrations in 32 polyacrylamide flocculants approved for water-treatment plants ranged from 0.5 to 600 ppm (Howard 1989). Acrylamide remains in water after flocculation with polyacrylamides because it is very water soluble and is not readily adsorbed by sediment (Brown *et al.* 1980b, Howard 1989).

Dermal exposure to acrylamide may result from trace quantities in cosmetic products, gardening products, paper and pulp products, coatings, and textiles resulting from the use of polyacrylamide in these products (Manson *et al.* 2005). Acrylamide has been measured in body and hand lotions, powders, and creams at concentrations of up to 1,200 $\mu\text{g}/\text{kg}$, and daily exposure to acrylamide through cosmetic

products was estimated at 0.95 $\mu\text{g}/\text{kg}$ of body weight per day. Acrylamide also has been measured in mainstream cigarette smoke at concentrations of up to 2.34 μg per cigarette, which would result in an average daily intake of 0.67 $\mu\text{g}/\text{kg}$ of body weight per day (based on a body weight of 70 kg) for a person smoking one pack a day.

Acrylamide may be released into the environment in waste from acrylamide production and the manufacture of polyacrylamides and other polymers (Howard 1989). The most important environmental contamination results from the use of acrylamide in soil grouting (IPCS 1985). Acrylamide is also released to water from acrylamide-based sewer grouting and wastepaper recycling (Brown *et al.* 1980a, 1982, Howard 1989). In 2005, EPA's Toxics Release Inventory reported environmental releases of 8,797,482 lb of acrylamide from 42 facilities, 99.9% of which was released to underground injection wells, and most of the rest to air (TRI 2009).

Because the vapor pressure of acrylamide is low, the monomer is not expected to occur in the vapor phase in air. Acrylamide biodegrades in surface water in approximately 8 to 12 days (Howard 1989). Acrylamide degradation in a secondary sewage plant would be complete in approximately 10 days; however, acrylamide has been detected in effluent from sewage treatment plants (HSDB 2009). Certain debris organisms that exist in anaerobic, light aerobic, or dark aerobic conditions in natural and polluted environments are able to degrade acrylamide (Brown *et al.* 1980b). Acrylamide is highly mobile in aqueous environments; it thus readily leaches into soil and is carried great distances in groundwater of deep rock aquifers, where it will not be biodegraded (IPCS 1985). Bioconcentration of acrylamide is unlikely, because it degrades easily in surface waters and is highly water soluble (Manson *et al.* 2005). In an EPA study of five industrial sites of acrylamide and polyacrylamide production and one site of polyacrylamide use, the highest concentration of acrylamide in water was found downstream from a polyacrylamide producer, at 1.5 mg/L (IPCS 1985, Howard 1989). In this study, the average acrylamide concentration was less than 0.2 $\mu\text{g}/\text{m}^3$ in air and less than 0.02 mg/kg in soil and sediment (IPCS 1985).

Occupational exposure to acrylamide is primarily from dermal contact with the solid monomer and inhalation of dust and vapor during acrylamide and polyacrylamide production. The highest exposure occurs during the handling of the monomer. In two acrylamide manufacturing plants, breathing-zone concentrations were 0.1 to 3.6 mg/m³. During normal operations, workers at another plant were exposed to concentrations of up to 0.3 mg/m³ (IARC 1986). At U.S. acrylamide production facilities, the mean concentration of acrylamide in air was 640 $\mu\text{g}/\text{m}^3$ in packing areas (Manson *et al.* 2005). In other parts of the world, acrylamide-hemoglobin adducts were used to estimate occupational exposure. In China, the highest acrylamide adduct concentration was 34,000 pmol/g of globin, found in the blood of workers in an acrylamide and polyacrylamide manufacturing plant. Occupationally exposed German smokers had adduct concentrations of up to 85 pmol/g of hemoglobin. In tunnel workers exposed to polyacrylamide in grout, acrylamide adducts were found at concentrations of up to almost 17,000 pmol/g (IARC 1986). Occupational exposure to acrylamide in aqueous form occurs mainly during maintenance and repair operations and connection and disconnection of equipment for transport. Routine exposure is minimal in captive production operations (Klaassen 1986). Improvements in the polymerization process have reduced the monomer content of the non-potable-water-grade polymers from 5% to 0.3% (Brown *et al.* 1982).

Workers in the paper and pulp, construction, foundry, oil-drilling, textiles, cosmetics, food-processing, plastics, mining, and agricultural industries also are potentially exposed to acrylamide (Manson 2005). The potential for exposure is higher among grouters than other work-

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ers, because of the uncontrolled nature of the exposure; however, exposure levels have not been reported for grouters (IPCS 1985). The National Institute for Occupational Safety and Health estimated in 1976 that about 20,000 workers potentially were exposed to acrylamide (IARC 1986), and the National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 10,651 workers potentially were exposed (NIOSH 1990).

Regulations

Coast Guard, Department of Homeland Security

Minimum requirements have been established for safe transport of acrylamide solution on ships and barges.

Department of Transportation (DOT)

Acrylamide is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Clean Air Act

National Emissions Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.
New Source Performance Standards: Manufacture of acrylamide is subject to certain provisions for the control of volatile organic compound emissions.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 5,000 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.
Reportable quantity (RQ) = 5,000 lb.
Threshold planning quantity (TPQ) = 1,000 lb for solids in powder form with particle size < 100 µm or solution or molten form; = 10,000 lb for all other forms.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of acrylamide = U007, K014.
Listed as a hazardous constituent of waste.

Safe Drinking Water Act

Each public water system must certify annually that when acrylamide is used in drinking-water systems, the level does not exceed 0.05% dosed at 1 mg/L (or equivalent).

Food and Drug Administration (FDA)

Acrylamide and various acrylamide copolymers may be used as food additives permitted for direct addition to food for human consumption, indirect food additives, secondary direct food additives, and food additives permitted in feed and drinking water of animals, as prescribed in 21 CFR parts 172, 173, 175, 176, 177, 178, and 573.

Occupational Safety and Health Administration (OSHA)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2010, specific PELs may not reflect the more current studies and may not adequately protect workers.
Permissible exposure limit (PEL) = 0.3 mg/m³.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted-average (TLV-TWA) = 0.03 mg/m³.

National Institute for Occupational Safety and Health (NIOSH)

Recommended exposure limit (time-weighted-average workday) = 0.03 mg/m³.
Immediately dangerous to life and health (IDLH) limit = 60 mg/m³.
Listed as a potential occupational carcinogen.

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