Acetaldehyde

CAS No. 75-07-0

Reasonably anticipated to be a human carcinogen
First listed in the Sixth Annual Report on Carcinogens (1991)
Also known as ethanol

Carcinogenicity

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

Cancer Studies in Experimental Animals

Exposure to acetaldehyde by inhalation caused tumors in two rodent species and at two different tissue sites. In rats of both sexes, it caused cancer of the nasal mucosa (squamous-cell carcinoma and adenocarcinoma), and in hamsters of both sexes, it caused cancer of the larynx (carcinoma) (IARC 1985, 1987). Inhalation of acetaldehyde also promoted the induction of respiratory-tract tumors by intratracheal instillation of the known carcinogen benzo[a]pyrene in hamsters of both sexes.

Since acetaldehyde was listed in the Sixth Annual Report on Carcinogens, an additional study in rats has been identified. Administration of acetaldehyde in drinking water increased the incidences of hemolymphoreticular cancer (leukemia and lymphoma combined), benign tumors of the pancreas (islet-cell adenoma), and cancer of the bone (osteosarcoma) and nasal cavity (carcinoma) in males and benign mammary-gland tumors (fibroma or fibroadenoma) in females (Soffritti et al. 2002). Increased incidences of tumors observed at other sites occurred only at one of the lower doses tested.

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to acetaldehyde. A survey of workers producing acetaldehyde and other aldehydes in Germany reported 9 cases of cancer, including 5 of lung cancer and 2 of oral-cavity cancer, among an unspecified number of workers; these incidences reportedly were higher than expected, but the observations were confounded by the fact that all cases of cancer occurred in tobacco smokers (IARC 1985, 1987).

Since acetaldehyde was listed in the Sixth Annual Report on Carcinogens, additional epidemiological studies have been identified, primarily case-control studies of populations exposed to acetaldehyde (the main initial metabolite of alcohol) following consumption of alcoholic beverages. Alcoholic beverage consumption is listed in the Report on Carcinogens as known to be a human carcinogen. In its 1999 review, the International Agency for Research on Cancer noted that three small case-control studies found increased risks of alcohol-related cancer (of the oral cavity, pharynx, larynx, and esophagus) among individuals with genetic variations (polymorphisms) that result in increased levels of acetaldehyde after alcohol consumption. However, IARC concluded that the data available were inadequate to evaluate the carcinogenicity of acetaldehyde (IARC 1999). Since then, a number of review articles and meta-analyses have summarized the results of subsequent studies that found dose-response relationships between alcohol consumption and cancer of the oral cavity, pharynx, larynx, and esophagus, and possibly the stomach and colorectum, among individuals with genetic polymorphisms that increase blood or salivary levels of acetaldehyde (Bagnardi et al. 2001, Zeka et al. 2003, Boffetta and Hashibe 2006, Baan et al. 2007, Boccia et al. 2009, Salaspuro 2009). In 2009, IARC concluded that acetaldehyde associated with alcohol consumption was carcinogenic to humans (Secretan et al. 2009). Few studies have been conducted on the association of these polymorphisms with cancer at other tissue sites, and the role of acetaldehyde in pancreatic, liver, bladder, or breast cancer is not clear (van Dijk et al. 2001, Terry et al. 2006, Seitz and Becker 2007, Visvanathan et al. 2007, Druesne-Pecollo et al. 2009).

Studies on Mechanisms of Carcinogenesis

Alcohol is metabolized to acetaldehyde by alcohol dehydrogenases (ADH), and acetaldehyde is metabolized to acetic acid by aldehyde dehydrogenases (ALDH). In some individuals, genetic polymorphisms in these enzymes can result in either higher rates of acetaldehyde production from alcohol or lower rates of acetaldehyde metabolism to acetic acid, resulting in higher blood acetaldehyde levels after a given level of alcohol intake than in individuals without these polymorphisms. Five ADH genes have been identified in humans, two of which have been shown to be polymorphic. The variant allele of the ALDH2 gene, which is prevalent in Asians, encodes an enzyme that has almost no ability to detoxify acetaldehyde (IARC 1999).

Properties

Acetaldehyde is an aliphatic aldehyde that exists at room temperature as a colorless gas with a fruity, pungent odor. It is miscible with water, ether, benzene, gasoline, solvent naphtha, toluene, xylene, turpentine, and acetone. It is very flammable and is unstable in air (Akron 2009, HSDB 2009). Physical and chemical properties of acetaldehyde are listed in the following table.

<table>
<thead>
<tr>
<th>Property</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>44.0 g/mol</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>0.79 at 16°C/4°C</td>
</tr>
<tr>
<td>Melting point</td>
<td>–124°C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>21°C</td>
</tr>
<tr>
<td>Log K&lt;sub&gt;a&lt;/sub&gt;</td>
<td>–0.34</td>
</tr>
<tr>
<td>Water solubility</td>
<td>1,000 g/L at 25°C</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>902 mm Hg at 25°C</td>
</tr>
<tr>
<td>Vapor density relative to air</td>
<td>1.5 g/L</td>
</tr>
<tr>
<td>Dissociation constant (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
<td>13.6 at 25°C</td>
</tr>
</tbody>
</table>

Sources: *HSDB 2009,* ChemIDplus 2009.

Use

Acetaldehyde is used primarily as a chemical intermediate in the production of acetic acid, pyridine and pyridine bases, peracetic acid, pentaerythritol, butylene glycol, and chloral. It is also used in the synthesis of crotonaldehyde, flavor and fragrance acetal, acetaldehyde 1,1-dimethylhydrazone, acetaldehyde cyanohydrin, acetaldehyde oxime, various acetic acid esters, paraaldehyde, metaldehyde (a molluscicide widely used to kill slugs and snails), polymers, and various halogenated derivatives (IARC 1985, 1999). Acetaldehyde has been used in the manufacture of aniline dyes, plastics, and synthetic rubber, to silver mirrors, and to harden gelatin fibers. It has also been used in the production of polyvinyl acetal resins, in fuel compositions, to inhibit mold growth on leather, and in the manufacture of disinfectants, pesticides, drugs, explosives, lacquers and varnishes, photographic chemicals, phenolic and urea resins, and rubber accelerators and antioxidants (EPA 1994).

Acetaldehyde is considered by the U.S. Food and Drug Administration to be generally recognized as safe for use as a flavoring agent and adjuvant (Furia and Bellanca 1975, HSDB 2009). It is an important component of food flavorings and is added to milk products, baked
Acetaldehyde was first produced commercially in 1916 (IARC 1985). U.S. production was 63.5 million kilograms (140 million pounds) in 1940 and 408 million kilograms (899 million pounds) in 1960. Production peaked in 1969 at 748 million kilograms (1.65 billion pounds), decreasing to 281 million kilograms (619 million pounds) in 1982. In 2009, acetaldehyde was produced by 50 manufacturers worldwide (17 in China, 12 in India, 6 in East Asia, 5 in Europe, 5 in Central and South America, 2 in Mexico, 2 in the Middle East, and 1 in the United States) (SRI 2009) and was available from 49 suppliers, including 21 U.S. suppliers (ChemSources 2009). U.S. imports of acetaldehyde increased from 1,000 kg (2,200 lb) in 1989 to 414,000 kg (913,000 lb) in 2006 (USITC 2009). U.S. exports of acetaldehyde were 19 million kilograms (42.6 million pounds) in 1989, decreasing to 1.6 million kilograms (3.5 million pounds) in 2003 and remaining near this level from 2004 through 2008 (USITC 2009). Reports filed under the U.S. Environmental Protection Agency’s Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of acetaldehyde totaled 500 million to 1 billion pounds in 1986 and 1990 and 100 million to 500 million pounds in 1994, 1998, and 2002 (EPA 2004).

Exposure

There is high potential for exposure of the general population to acetaldehyde through ingestion, inhalation, and dermal contact and of workers through inhalation and dermal contact. The main source of exposure of the general population is through consumption of alcoholic beverages and the subsequent metabolism of alcohol to form acetaldehyde (HSDB 2009). Because acetaldehyde may form in wine and other alcoholic beverages after exposure to air (Hagemeyer 2002), alcoholic beverages (including wines, beer, and spirits) also frequently contain acetaldehyde as a volatile component (HSDB 2009).

Acetaldehyde is a product of most hydrocarbon oxidation reactions and is a normal intermediate in the respiration of most higher plants. It is found in trace amounts in many plant products, including apples, broccoli, coffee, grapefruit, grapes, lemons, mushrooms, onions, oranges, peaches, nectarines, pears, pineapples, raspberries, strawberries, cranberries, sour cherries, and mango. It has been detected in the essential oils of alfalfa, rosemary, balm, clary sage, daffodil, bitter orange, camphor, angelica, fennel, mustard, peppermint, and lychee, and in oak and tobacco leaves and cotton leaves and blossoms (IARC 1985, Burdon et al. 1996, Gorny et al. 1999, Gunes et al. 2002, Bonerz et al. 2007, Mahattanatawee et al. 2007). Acetaldehyde has also been detected in breast milk. Consumers may be exposed to acetaldehyde in many milk products, including all types of cheese, yogurt, and milk of varying fat content (Mistry and Hassan 1992, Barbieri et al. 1994, Jandal 1996, Beshkova et al. 1998, Van Aardt et al. 2001, Kondylj et al. 2002, Boscaini et al. 2003, Di Cagno et al. 2004, Fernandez-Garcia et al. 2004, Blagden and Gilliland 2005, Gadaga et al. 2007, Kaminarides et al. 2007). Acetaldehyde has also been detected in cooked beef, chicken, and fish (HSDB 2009, Yasuhara and Shibamoto 1995) and is used as a synthetic flavoring ingredient in processed foods, especially margarine (HSDB 2009).

According to EPA’s Toxics Release Inventory, environmental releases of acetaldehyde have increased slightly since 1988, when 9.5 million pounds was released, 73% to air, 23% to underground injection wells, and the remainder to surface water and landfills. Since then, releases to underground injection wells have decreased, and releases to surface water have increased. In 2007, 11.4 million pounds of acetaldehyde was released from 336 facilities that processed, produced, or used the chemical; 29 facilities each released more than 100,000 lb. Of the total amount, 94% was released to air, 3.1% to underground injection wells, and 2.8% to water (TRI 2009). Acetaldehyde will volatilize rapidly from water or land, and it will leach into the ground, where it will biodegrade (HSDB 2009). Acetaldehyde is also degraded readily in soil, sewage, and natural waters by microorganisms (EPA 1987).

Acetaldehyde is a natural product of photooxidation of hydrocarbons commonly found in the atmosphere and occurs naturally as emissions from forest fires, volcanoes, and animal wastes. In the 1990s, annual emissions of acetaldehyde from all sources in the United States were estimated at 12.1 million kilograms (27 million pounds) (IPCS 1995). Burning wood produces acetaldehyde at approximately 0.7 g/kg of wood, and fireplace emissions range from 0.083 to 0.20 g/kg of wood burned (HSDB 2009). In the 1990s, annual emissions from residential burning in the United States were estimated at 5,000 metric tons (11 million pounds) (IPCS 1995). Acetaldehyde is also a combustion product of some plastics (e.g., polycarbonate) and some hard and soft polyurethane foams. It also occurs in gasoline exhaust (1.4 to 8.8 mg/m³) and diesel exhaust (0.05 to 6.4 mg/m³); however, very little is emitted from small engines such as lawn mowers or leaf blowers (IARC 1985, Baldauf et al. 2006).

Many individuals are exposed to acetaldehyde by inhalation. The highest ambient-air concentrations of acetaldehyde were reported for urban or suburban areas or near sources of combustion (HSDB 2009). In ambient air, concentrations of acetaldehyde generally averaged 5 µg/m³. Indoor air concentrations were higher than ambient concentrations in all locations where acetaldehyde air concentrations were measured, both in the United States and in other countries (Miguel et al. 1995, Mukund et al. 1996, Brickus et al. 1998, MacIntosh et al. 2000, Possanzini et al. 2002, Baez et al. 2003, Hellen et al. 2004, Hodgson et al. 2004, Park and Ikeda 2004, Saijo et al. 2004, Sax et al. 2004, Shendell et al. 2004, Gilbert et al. 2005, Cavalcante et al. 2006, Ohura et al. 2006, Pang and Mu 2006, Sax et al. 2006, Hodgson et al. 2007, Possanzini et al. 2007). Acetaldehyde is also found in tobacco and marijuana cigarette smoke (1,220 µg per cigarette) and tobacco cigarettes (980 to 1,370 µg per cigarette).

In 1988–89, acetaldehyde was detected in 4 of 10 surveyed water supplies (EPA 1987). In surface water, concentrations generally are less than 0.1 µg/L, and the contribution from drinking water to human exposure is considered negligible (IPCS 1995).

The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 216,533 workers, including 97,770 women, potentially were exposed to acetaldehyde (NIOSH 1990). Workers potentially exposed include those involved in the manufacture or use of industrial organic chemicals, dyes, fabricated rubber, plastics, urea-formaldehyde foam insulation, fuels, drugs, explosives, varnishes, pesticides, food additives, leather goods, and mirrors (IARC 1985, EPA 1994).

Regulations

Coast Guard, Department of Homeland Security

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

National Toxicology Program, Department of Health and Human Services
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Acetaldehyde is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

National Toxicology Program, Department of Health and Human Services