Hydrazine and Hydrazine Sulfate
CAS Nos. 302-01-2 and 10034-93-2

Reasonably anticipated to be human carcinogens

\[ \text{H}_2\text{N} \rightarrow \text{NH}_3 \]

Carcinogenicity

Hydrazine and hydrazine sulfate are reasonably anticipated to be human carcinogens based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to hydrazine or hydrazine sulfate caused tumors in two rodent species at several different tissue sites and by several different routes of administration. Most studies of oral exposure used hydrazine sulfate. Oral exposure to hydrazine sulfate (either in the drinking water or by stomach tube) caused benign and malignant lung tumors (adenoma and adenocarcinoma) in mice and rats of both sexes and liver cancer in mice of both sexes (hepatocellular carcinoma) and in male rats (spindle-cell sarcoma). Intraoperative injection of hydrazine caused lung tumors, myeloid leukemia, and lymphoma (reticulum-cell sarcoma) in mice of both sexes (IARC 1974).

Since hydrazine and hydrazine sulfate were listed in the Third Annual Report on Carcinogens, additional studies in rodents have been identified. Perinatal exposure to hydrazine sulfate caused lung cancer (adenocarcinoma) in mice as adults (IARC 1987). Exposure to hydrazine by inhalation caused benign or malignant nasal tumors (adenomatous or villous polyps, adenocarcinoma, or squamous-cell papilloma or carcinoma) in rats and benign tumors of the nasal cavity (adenomatous polyps) in male hamsters. A few tumors of the colon (adenocarcinoma, leiomyoma, and papilloma) and thyroid (parafollicular-cell adenoma) also were observed in male hamsters at the highest exposure level and may have been exposure-related (Vernot et al. 1985, IARC 1987). Administration of hydrazine sulfate in the drinking water caused liver cancer (hepatocellular carcinoma) in hamsters (IARC 1999).

Cancer Studies in Humans

No excess risk of cancer was found in a small cohort study of 423 men engaged in the manufacture of hydrazine (Roe 1978). Since hydrazine and hydrazine sulfate were listed in the Third Annual Report on Carcinogens, additional epidemiological studies have been identified. The International Agency for Research on Cancer concluded in 1999 that the evidence for the carcinogenicity of hydrazine from studies in humans was inadequate. No excess risk of cancer mortality was found in a follow-up of the Roe cohort (Wald et al. 1984, Wald 1985) or in a small retrospective cohort study of 427 workers in a hydrazine plant (Morris et al. 1995). Since the 1999 IARC review, studies of two additional cohorts have been identified. A significant dose-response relationship between hydrazine exposure and lung-cancer incidence and mortality and a significant increase in colorectal-cancer incidence were found among aerospace workers, of whom about one fourth potentially were exposed to hydrazine, 1-methylhydrazine, or 1,1-dimethylhydrazine in rocket fuel (Ritz et al. 1999, 2006). No association between smoking and hydrazine exposure was observed for a subset of these workers, and risk estimates were adjusted for potentially confounding occupational exposures. No significant association between cancer mortality and potential exposure to hydrazine was found in a retrospective cohort study of workers at a rocket engine testing facility, of whom 315 likely had been exposed to hydrazines (Boice Jr. et al. 2006).

Properties

At room temperature, hydrazine is a colorless oily liquid with a penetrating ammonia-like odor, and hydrazine sulfate is a white crystalline solid (HSDB 2009). Hydrazine is miscible with methyl, ethyl, propyl, and butyl alcohols, slightly miscible with hydrocarbons and halogenated hydrocarbons, and insoluble in chloroform and ether. Hydrazine sulfate is soluble in water but practically insoluble in ethanol. Both compounds are thermally unstable (Akron 2009). Physical and chemical properties of hydrazine and hydrazine sulfate are listed in the following table.

<table>
<thead>
<tr>
<th>Property</th>
<th>Hydrazine</th>
<th>Hydrazine Sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>32.1</td>
<td>130.1</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.0036 at 25°C/4°C</td>
<td>1.378</td>
</tr>
<tr>
<td>Melting point</td>
<td>2.0°C</td>
<td>254°C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>113.5°C at 760 mm Hg</td>
<td>NR</td>
</tr>
<tr>
<td>Log Kp</td>
<td>-2.07</td>
<td>NR</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>1,000 g/L</td>
<td>34.1 g/L</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>14.4 mm Hg at 25°C</td>
<td>NR</td>
</tr>
<tr>
<td>Dissociation constant (pKₐ)</td>
<td>7.96</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Source: HSDB 2009. NR = Not reported.

Use

Hydrazine is used primarily as a chemical intermediate to produce agricultural chemicals and chemical blowing agents, as a corrosion inhibitor and water-treatment chemical, and as a rocket propellant. In the early 1980s, 40% of hydrazine was used in agricultural chemicals, 33% in blowing agents, 15% as a corrosion inhibitor, and 5% as a rocket propellant (ATSDR 1997). It has been used for plating metals on glass and plastics, in fuel cells and solder fluxes, as a reducing agent in electrode-less nickel plating, as a chain extender in urethane polymerizations, and as a reducing agent in extraction of plutonium from nuclear reactor waste. It has also been used to produce photography chemicals, textile dyes, heat stabilizers, explosives, hydrazine sulfate, and antibacterials and other pharmaceuticals (Sax and Lewis 1987, ATSDR 1997, HSDB 2009).

Hydrazine sulfate has been used in refining rare metals, as an antioxidant in soldering flux for light metals, in analytical tests for blood, as a reducing agent in the analysis of minerals and slag, in the preparation of hydrazine hydrate, in the manufacture of chemicals, in condensation reactions, as a catalyst in making acetate fibers, as a fungicide and germicide, in the analysis of minerals, and in the determination of arsenic in metals (HSDB 2009).

Production

U.S. production capacity for hydrazine hydrate was estimated at 55 million pounds in 1988, and production capacity for hydrazine solutions was 36.3 million pounds in 1992 (IARC 1999). In 2009, hydrazine was produced by three manufacturers worldwide, including one in the United States, and hydrazine sulfate by 14 manufacturers, including one in the United States (SRI 2009). Hydrazine was available from 27 suppliers, including 19 U.S. suppliers, and hydrazine sulfate from 34 suppliers, including 20 U.S. suppliers (ChemSources 2009). U.S. imports in the category “hydrazine and hydroxyamine and their salts” generally increased from 1989 to 2008, reaching a low of 2 million kilograms (4.4 million pounds) in 1993 and a high of 23.5 million kilograms (51.8 million pounds) in 1999 (USITC 2009). During this period, U.S. exports in this category fluctuated but generally declined, from a high of 20.3 million kilograms (44.7 million pounds) in 1997 to a low of 2.4 million kilograms (5.3 million pounds).
in 2008. Reports filed in 1986 and 1990 under the U.S. Environmental Protection Agency’s Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of hydrazine totaled 10,000 to 500,000 lb. No reports for hydrazine were filed in 1994 or 1998, but reports filed in 2002 and 2006 indicated quantities of 1 million to 10 million pounds (EPA 2004, 2009). Inventory updates were filed for hydrazine sulfate only in 1990, indicating a total quantity of 10,000 to 500,000 lb (EPA 2004).

**Exposure**

The primary routes of potential human exposure to hydrazine are ingestion, inhalation, and dermal contact (HSDB 2009). The exposure potential for the general population is low, but exposure may occur through inhalation of cigarette smoke or ingestion of trace amounts in processed foods. Hydrazine has been detected in cigarette smoke at a concentration of 32 μg per cigarette (PHS 1982). Hydrazine sulfate may be ingested intentionally, as it has been studied as a treatment for cancer (NCI 2008).

Hydrazine and hydrazine sulfate may be released to the environment through production, use, and waste disposal (ATSDR 1997, HSDB 2009). EPA’s Toxics Release Inventory reported that in 2007, environmental releases of hydrazine from 23 facilities totaled 16,759 lb, 14,570 lb of which was released by one facility to underground injection wells. Releases of hydrazine sulfate between 1988 and 2003 ranged from 24,000 lb (in 2001) to 356,172 lb (in 1988), with no major long-term trend. Almost all hydrazine sulfate was released to underground injection wells; a small amount was released to air. No releases of hydrazine sulfate were reported after 2003 (TRI 2009).

In most environmental media, hydrazine is rapidly degraded by oxidation. High concentrations of hydrazine are toxic to microorganisms, but at low concentrations, biodegradation may occur. Use of hydrazine in boiler water treatment may result in its brief occurrence in discharged waste, where it will be oxidized (ATSDR 1997, HSDB 2009).

Occupational exposure is most likely to occur by inhalation or dermal contact where hydrazine or hydrazine sulfate is produced or used (HSDB 2009). Hydrazine exposure has been documented in the paper, tire-manufacturing, military, and aerospace industries (Helmers et al. 2004, Korhonen et al. 2004, Ritz et al. 2006, Durmusoglu et al. 2007). In the vulcanization step of tire manufacturing, hydrazine was measured at concentrations of up to 8.0 mg/m³, resulting in an estimated daily intake of 0.0031 mg/kg of body weight (Durmusoglu 2007). Hydrazine fuels are used for rockets and high-performance military jet aircraft; exposure of workers refueling these planes has been reported (Helmers 2004). The National Aeronautics and Space Administration reported developing a reusable propellant-handler’s suit that was expected to be the world’s most advanced garment for exposure to chemical agents in the paper industry.

**Regulations**

**Department of Transportation (DOT)**

Hydrazine 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 Emission Standards for Hazardous Air Pollutants:** Hydrazine is listed as a hazardous air pollutant. Prevention of Accidental Release: Threshold quantity (TQ) = 15,000 lb for hydrazine.

**Urban Air Toxics Strategy:** Hydrazine is identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

**Comprehensive Environmental Response, Compensation, and Liability Act**

Reportable quantity (RQ) = 1 lb for hydrazine.

**Emergency Planning and Community Right-To-Know Act**

Toxic Release Inventory: Listed substance subject to reporting requirements. Reportable quantity (RQ) = 1 lb for hydrazine.

**Resource Conservation and Recovery Act**

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of hydrazine = U133.

Hydrazine is listed as a hazardous constituent of waste.

**Food and Drug Administration (FDA)**

Hydrazine is not permitted in steam in food-treatment processes.

**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) = 1 ppm (1.3 mg/m³) for hydrazine.

**Potential for dermal absorption.**

**Guidelines**

**American Conference of Governmental Industrial Hygienists (ACGIH)**

Threshold limit value – time-weighted average (TLV-TWA) = 0.01 ppm for hydrazine.

**National Institute for Occupational Safety and Health (NIOSH)**

Immediately dangerous to life and health (IDLH) limit = 50 ppm for hydrazine.

Ceiling recommended exposure limit = 0.03 ppm (0.04 mg/m³) (2-h exposure) for hydrazine. Hydrazine is listed as a potential occupational carcinogen.

**References**


**Report on Carcinogens, Fourteenth Edition**
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