Naphthalene
CAS No. 91-20-3

Reasonably anticipated to be a human carcinogen
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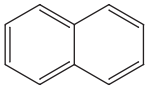

Carcinogenicity

Naphthalene is *reasonably anticipated to be a human carcinogen* based on sufficient evidence from studies in experimental animals. When administered to F344/N rats by inhalation, naphthalene caused olfactory epithelial neuroblastoma of the nose (a highly malignant and extremely rare tumor of the lining of the nose) and respiratory epithelial adenoma (an uncommon nasal tumor) (NTP 2000). The incidence of neuroblastoma of the olfactory epithelium increased with increasing naphthalene exposure in both male and female rats and was significantly increased at the highest exposure level in females. Some of the neuroblastomas also invaded the brain. The increase in the incidence of the respiratory epithelial adenoma was statistically significant in male rats, but not in females. In female $B6C3F_1$ mice, inhalation exposure to naphthalene significantly increased the incidence of lung tumors (NTP 1992). The International Agency for Research on Cancer (2002) concluded that there was sufficient evidence for the carcinogenicity of naphthalene in experimental animals.

The data on human exposure to naphthalene are inadequate for evaluating its carcinogenicity. Two case-series studies of cancer occurring in individuals exposed to naphthalene were identified in the literature. The first study reported the occurrence of laryngeal and other cancers among German workers occupationally exposed to naphthalene, and the second reported the occurrence of colorectal cancer among Africans who had used a naphthalene compound for medicinal purposes (Ajao *et al.* 1988, NTP 2000).

Additional Information Relevant to Carcinogenicity

Naphthalene caused mutations in insects, but not in bacteria or cultured human lymphoblastoid cells (immature white blood cells) (Sasaki *et al.* 1997, Grosovsky *et al.* 1999, NTP 2000). It caused other types of genetic damage in some but not all test systems. In newt larvae, naphthalene induced micronucleus formation (an indicator of chromosome damage or loss). In cultured mammalian cells, it caused chromosomal aberrations (changes in chromosome structure or number), sister chromatid exchange (CHO cells only), and formation of kinetochore-negative micronuclei (which indicate chromosome breakage), but did not cause DNA strand breaks, formation of kinetochore-positive micronuclei (which indicate chromosome loss), or cell transformation (a step in tumor formation). Inhalation exposure of rats to naphthalene caused oxidative stress and DNA damage in liver and brain tissue (IARC 2002, NTP 2002).

When administered to animals dermally, orally, or by inhalation, naphthalene is rapidly absorbed and metabolized (NTP 2000). Evidence suggesting that naphthalene is absorbed in humans comes from studies of workers in a coke plant, which found that concentrations of naphthalene metabolites in the urine were significantly correlated with concentrations of naphthalene in personal air samples (Bieniek 1994, 1997). The first step in the metabolism of naphthalene is formation of naphthalene-1,2-oxide (as two stereoisomers, 1*R*,2*S*-oxide and 1*S*,2*R*-oxide) through the action of cytochrome P-450 enzymes in the presence of the coenzyme NADPH. These oxides are metabolized further by three pathways: (1) hydration by epoxide hydrolases into dihydrodiols, (2) conjugation by glutathione transferases, and (3) spontaneous rearrangement into 1-naphthol and 2-naphthol, which are converted to naphthoquinones (Chichester *et al.* 1994, Shultz *et al.* 1999). Naphthalene is excreted in the urine as the unchanged parent compound or as metabolites, including 1-naphthol, 2-naphthol, naphthoquinones, dihydroxynaphthalenes, and conjugated forms, including glutathione, cysteine, glucuronic acid, and sulfate conjugates (NTP 2002).

The mechanism by which naphthalene causes cancer is unknown. A strong correlation has been observed between the rates of formation of the stereoisomer (1*R*,2*S*)-naphthalene oxide in various tissues and the selective toxicity of naphthalene to these tissues, suggesting that this metabolite may play a role in naphthalene's toxicity to the lung and other tissues (Buckpitt and Franklin 1989). Oxidative damage and DNA breakage, observed in rat liver and brain tissue, may contribute to naphthalene's toxicity and carcinogenicity.

Properties

Naphthalene is an aromatic hydrocarbon compound with a molecular weight of 128.2. It occurs as white monoclinic plates, scales, powder, balls, or cakes, with the distinctive odor usually associated with mothballs. Naphthalene melts at 80.2°C and boils at 217.9°C. It has low solubility in water (31.7 mg/L at 25°C), but is more soluble in organic solvents (e.g., alcohol, benzene, ether, and acetone). Naphthalene has a log octanol-water partition coefficient of 3.3. It may degrade some forms of plastics, rubber, and coatings. Naphthalene is sensitive to heat and volatilizes at room temperature, with a vapor pressure of about 0.09 mm Hg. The vapor is heavier than air, with a density of 4.42. Naphthalene sublimes at temperatures above its melting point (ATSDR 2003, HSDB 2003).

Use

The principal use of naphthalene in the United States is as an intermediate in the production of phthalic anhydride, which is an intermediate in the production of phthalate plasticizers, pharmaceuticals, insect repellents, and other materials. Naphthalene also has been used as an intermediate in the production of 1-naphthyl-*N*-methylcarbamate insecticides, beta-naphthol, synthetic leather tanning chemicals, surfactants (e.g., naphthalene sulfonates), moth repellents, and toilet bowl deodorants (ATSDR 2003, HSDB 2003). In 1999, 59% of naphthalene was used for production of phthalic anhydride, 21% for production of surfactant and dispersant chemicals, 11% for production of 1-naphthyl-*N*-methylcarbamate insecticides, and 9% in moth repellents and for other purposes (ChemExpo 1999). The Naphthalene Panel of the American Chemistry Council reported in 2002 that naphthalene was no longer used directly in tanneries, in the textile industry, or in the production of toilet bowl deodorizers and that beta naphthol was not manufactured in the United States (ACC 2002).

Production

Naphthalene is produced from either coal tar (which contains approximately 10% naphthalene) or petroleum. It is produced by condensation and separation of coal tar from coke-oven gases, or from petroleum by dealkylation of methylnaphthalenes. In the United States, most naphthalene was produced from petroleum through the 1980s. U.S. production of naphthalene peaked in 1968, at 900 million pounds (408,000 metric tons); by 1994, production had decreased substantially, to 222 million pounds (101,000 metric tons) (ATSDR 2003). In 2000, production was 235 million pounds (107,000 metric tons), over 90% of which (219 million pounds [99,000 metric tons]) was from coal tar (CEH 2000). Estimated consumption in 2000 was 241 million pounds (109,000 metric tons). Production capacity for naphthalene in the United States has remained relatively stable in recent years, with an estimated capacity for 2002 of 215 million pounds (98,000 metric tons) (ATSDR 2003). In 2004, two producers of naphthalene in the United States were identified (SRI 2004)).

From 1989 to 1998, U.S. demand for naphthalene grew 0.5% per year. Demand was 246 million pounds (112,000 metric tons) in 1998 and 248 million pounds (112,500 metric tons) in 1999 (ChemExpo 1999). Demand for naphthalene sulfonates, used primarily as superplasticizer additives to increase the flowability of concrete, grew steadily in the late 1990s. In 2004, 27 suppliers of naphthalene in the United States were identified (ChemSources 2004).

U.S. imports of naphthalene totaled 6.9 million kilograms (15.2 million pounds) in 2003 (USITC 2004). Between 1989 and 2003, the largest amount imported was reported in 1989 at 18.5 million kilograms (40.9 million pounds) and the smallest amount in 1999 at 1.1 million kilograms (2.5 million pounds). Exports also fluctuated during the period of 1989 to 2003, with 14.1 million liters exported in 2003 compared to a high of 64.9 million liters in 1998 and a low of 2.5 million liters in 1993.

Exposure

The general public is potentially exposed to naphthalene through inhalation of ambient and indoor air. The average daily intake of naphthalene from ambient air has been estimated to be 19 µg, based on an average naphthalene concentration of 0.95 µg/m^3 in urban and suburban air and an inhalation rate of 20 m^3/day. Accidental ingestion of household products containing naphthalene, mainly by children, has been reported. Dermal exposure to naphthalene may occur through handling or wearing of clothing stored with moth repellents containing naphthalene (ATSDR 2003).

The National Occupational Exposure Survey, conducted from 1981 to 1983, estimated that about 112,700 workers potentially were exposed to naphthalene (NIOSH 1984). Workers identified by the U.S. Environmental Protection Agency as potentially exposed to naphthalene include beta-naphthol makers, celluloid makers, coal tar workers, dye chemical makers, fungicide makers, hydronaphthalene makers, moth repellent workers, phthalic anhydride makers, smokeless powder makers, tannery workers, textile chemical workers, and aluminum reduction plant workers (EPA 1980). More recent occupational surveys were not identified in the published literature. However, recent industry estimates indicate that approximately 1,000 workers were employed by the largest tar distillation and wood preservation company in the United States in 2002 and that fewer than 50 workers with potential exposure to naphthalene were employed in the moth repellent industry (ACC 2002). These estimates do not include workers potentially exposed to naphthalene in production of phthalic anhydride and other uses.

Workplace air concentrations of naphthalene have been measured in many studies and vary with the type of industry. A survey by the National Institute for Occupational Safety and Health in 1980 reported air concentrations of naphthalene as high as 10.2 µg/m^3 in an area sample and 19.3 µg/m^3 in a personal sample (ATSDR 2003). EPA's Toxics Release Inventory (TRI) for 2001 (TRI01 2003) includes 763 facilities reporting total on- and off-site releases of naphthalene. These facilities reported releasing more than 2.6 million pounds (1,200 metric tons) of naphthalene, of which more than 75% was released to the air. Releases of naphthalene had decreased annually since 1998 when the total was almost 6 million pounds (2,700 metric tons).

Regulations

DOT

Naphthalene is considered a hazardous material and requirements have been prescribed for shipping papers, package marking, labeling, and transport vehicle placarding for shipping and transporting the substance

EPA

Clean Air Act
- Mobile Source Air Toxics: Listed as a Mobile Source Air Toxic for which regulations are to be developed
- NESHAP: Listed as a Hazardous Air Pollutant (HAP)
- NSPS: Manufacture of substance is subject to certain provisions for the control of Volatile Organic Compound (VOC) emissions

Clean Water Act
- Effluent Guidelines: Listed as a Toxic Pollutant

Comprehensive Environmental Response, Compensation, and Liability Act
- Reportable Quantity (RQ) = 100 lb

Emergency Planning and Community Right-to-Know Act
- Toxics Release Inventory: Listed substance subject to reporting requirements

Resource Conservation and Recovery Act
- Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U165, F034, K001, K035
- Listed as a Hazardous Constituent of Waste

OSHA

Permissible Exposure Limit (PEL) = 10 ppm (50 mg/m^3)

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 10 ppm (50 mg/m^3)
Threshold Limit Value - Short Term Exposure Limit (TLV-STEL) = 15 ppm (75 mg/m^3)

NIOSH

Recommended Exposure Limit (REL) = 10 ppm (50 mg/m^3)
Short-Term Exposure Limit (STEL) = 15 ppm (75 mg/m^3)
Immediately Dangerous to Life and Health (IDLH) = 250 ppm (1,250 mg/m^3)

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