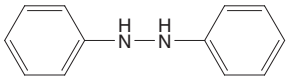
Hydrazobenzene

CAS No. 122-66-7

Reasonably anticipated to be a human carcinogen

First listed in the *Second Annual Report on Carcinogens* (1981)

Also known as 1,2-diphenylhydrazine



Carcinogenicity

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

Cancer Studies in Experimental Animals

Dietary exposure to hydrazobenzene caused tumors in two rodent species and at several different tissue sites. It caused liver cancer (hepatocellular carcinoma) in female mice and male rats and benign liver tumors (hepatocellular adenoma) in female rats. In rats, it also caused mammary-gland cancer (adenocarcinoma) in females and increased the combined incidence of benign and malignant Zymbal-gland tumors (squamous-cell papilloma and carcinoma) in males (NCI 1978). Since hydrazobenzene was listed in the *Second Annual Report on Carcinogens,* an additional study in mice has been identified. Hydrazobenzene administered by intraperitoneal injection to strain A mice (a strain with a high spontaneous incidence of lung cancer) caused benign lung tumors (alveolar-bronchial adenoma) in males, but not in females (Maronpot *et al.* 1986).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to hydrazobenzene. A number of historical occupational cohort studies of workers in the benzidine-based-dye industry, who may be exposed to hydrazobenzene (a precursor of benzidine), found significantly increased risks of urinary-bladder cancer (de Braud *et al.* 2002). Two case-control studies reported increased risks of urinary-bladder cancer among workers with potential exposure to chemical dyes, after controlling for smoking and other variables (Wynder *et al.* 1963, Anthony and Thomas 1970), prompting the National Cancer Institute to evaluate the carcinogenicity of hydrazobenzene in rodents (NCI 1978). In the studies of dye workers, hydrazobenzene exposure was not quantified and could not be distinguished from exposure to other chemicals, including benzidine, 2-naphthylamine, and 4-aminodiphenyl, which are known human carcinogens associated with urinary-bladder-cancer risk.

Properties

Hydrazobenzene is a hydrazine derivative that is a colorless crystal or tablet at room temperature. It is very soluble in ethanol, slightly soluble in benzene and deuterated dimethyl sulfoxide, insoluble in acetic acid, and practically insoluble in water (HSDB 2009). Hydrazobenzene is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of hydrazobenzene are listed in the following table.

Property	Information
Molecular weight	184.2
Specific gravity	1.158 at 16°C/4°C
Melting point	131°C (decomposes)
Boiling point	293°C at 760 mm Hg
Log K_{ow}	2.94
Water solubility	221 mg/L at 25°C
Vapor pressure	0.00044 mm Hg at 25°C
Dissociation constant (pK_a)	–0.65

Source: HSDB 2009.

Use

Hydrazobenzene has been used primarily in the dye manufacturing industry as the precursor of the dye intermediate benzidine (HSDB 2009). It is also used as an intermediate in the manufacture of pharmaceuticals such as sulfinpyrazone and phenylbutazone, which have been used to treat gout (Roberts and Morrow 2001, HSDB 2009). Some minor direct uses of hydrazobenzene are in polymerization reactions and as an anti-sludging additive to motor oil, desuckering agent for tobacco plants, reductant in the reclamation of rubber, component of experimental organometallic polymers, and component in photochromic resin compositions (HSDB 2009). It is also used in the manufacture of hydrogen peroxide and has been evaluated for insecticidal activity.

Production

Production of at least 450,000 kg (992,000 lb) of hydrazobenzene was reported in 1977 (HSDB 2009). Dye-manufacturing facilities produced additional unknown quantities of hydrazobenzene as an intermediate in the production of benzidine, which is formed by the reduction of nitrobenzene to hydrazobenzene followed by the rearrangement of hydrazobenzene to benzidine (NCI 1978). Manufacturing of benzidine-based dyes ceased in 1988 (ATSDR 1990). In 2009, hydrazobenzene was produced by three manufacturers in India (SRI 2009) and was available from 26 suppliers worldwide, including 15 U.S. suppliers (ChemSources 2009). U.S. imports of hydrazobenzene were 72,100 kg (158,600 lb) in 1977 and 23,200 kg (51,000 lb) in 1982.

Exposure

The routes of potential human exposure to hydrazobenzene are inhalation, ingestion, and dermal contact. The potential for exposure to hydrazobenzene formerly was greatest in the benzidine-based-dye industry (NCI 1978, ATSDR 1990). The greatest potential for exposure now is due to its use as an intermediate in the manufacture of certain pharmaceutical products. Because phenylbutazone and sulfinpyrazone can hydrolyze to hydrazobenzene, people who take these drugs to prevent gout attacks may be exposed to hydrazobenzene (ATSDR 1990). These drugs are used primarily in veterinary medicine; the extent of their current use in humans is unknown. In 2009, seven products approved by the U.S. Food and Drug Administration for use in humans contained sulfinpyrazone as an active ingredient, but all eleven pharmaceutical products containing phenylbutazone were listed as discontinued (FDA 2009).

According to the U.S. Environmental Protection Agency's Toxics Release Inventory, small quantities of hydrazobenzene have been released to air, surface water, and landfills. Annual releases of hydrazobenzene since 1998 have not exceeded 12 lb except in 2001, when 260 lb was released to an off-site nonhazardous-waste landfill. In 2007, one U.S. facility released 10 lb of hydrazobenzene to a hazardous-waste landfill (TRI 2009). Hydrazobenzene can exist in both particulate and vapor phases in the atmosphere. In the vapor phase, it degrades by reaction with photochemically produced hydroxyl rad-

icals, with a half-life of 5 hours. In the particle phase, it can be removed by wet and dry deposition. If released to soil or water, it is expected to bind to soil, suspended solids, and sediment and have low soil mobility. It is not expected to volatize readily from water or soil or to bioaccumulate to a large extent in aquatic organisms. Degradation of hydrazobenzene is reversible; hydrazobenzene undergoes oxidation to azobenzene under aerobic solutions, catalyzed by common environmental cations such as copper(II) and iron(III). In a municipal sewage effluent, the half-life for the decomposition of 100 µg of hydrazobenzene per liter was 60 minutes if oxygen was removed from the sewage, but only 15 minutes if the oxygen was not removed (ATSDR 1990). Hydrazobenzene was detected in 1.2% of 1,205 effluent samples collected from wastewater treatment plants in a national survey, at a median concentration of 10 µg/L (HSDB 2009). Hydrazobenzene was also found in drinking water at a concentration of 1 µg/L and was detected in fish taken from the Great Lakes.

The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 977 U.S. workers, including 154 women, potentially were exposed to hydrazobenzene (NIOSH 1990).

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.

Clean Water Act

Water Quality Criteria: Based on fish or shellfish and water consumption = 0.03 µg/L; based on fish or shellfish consumption only = 0.2 µg/L.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 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 code for which the listing is based wholly or partly on the presence of hydrazobenzene = U109.
Listed as a hazardous constituent of waste.

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