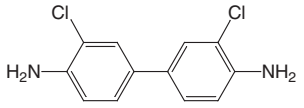
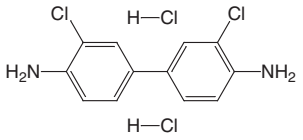
3,3′-Dichlorobenzidine and 3,3′-Dichlorobenzidine Dihydrochloride CAS Nos. 91-94-1 and 612-83-9

Reasonably anticipated to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)



3,3'-Dichlorobenzidine



3,3'-Dichlorobenzidine dihydrochloride

Carcinogenicity

3,3′-Dichlorobenzidine and 3,3′-dichlorobenzidine dihydrochloride are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1974, 1982a, b, 1987). The generic name 3,3′-dichlorobenzidine is used interchangeably with 3,3′-dichlorobenzidine dihydrochloride. Although only the dihydrochloride salt is believed to be available commercially, it was not always clear whether the salt or the free base was the compound under study. When administered in the diet, 3,3′-dichlorobenzidine induced hepatomas in male mice. When administered in the diet, the compound increased the incidences of granulocytic leukemia and Zymbal gland carcinomas in male rats and mammary adenocarcinomas in rats of both sexes. When administered in the diet, 3,3′-dichlorobenzidine induced transitional cell carcinomas of the urinary bladder in hamsters and female dogs and hepatocellular carcinomas in female dogs. When administered by transplacental exposure, the compound increased the incidences of lymphoid leukemia in mice.

No adequate data were available to evaluate the carcinogenicity of 3,3′-dichlorobenzidine or 3,3′-dichlorobenzidine dihydrochloride in humans (IARC 1982a, b, 1987). In three retrospective epidemiological studies, no urinary bladder tumors were reported in men occupationally exposed to 3,3′-dichlorobenzidine, but the studies were inadequate to evaluate carcinogenicity.

Properties

3,3′-Dichlorobenzidine occurs as a gray to purple crystalline solid. It is commercially available in the United States as the dihydrochloride salt with a 60% to 67% minimal purity measured as 3,3′-dichlorobenzidine. 3,3′-Dichlorobenzidine dihydrochloride occurs as moist, colorless or white needles or crystals with a mild odor of aromatic amines. 3,3′-Dichlorobenzidine and its dihydrochloride are essentially insoluble in cold water, but are soluble in ether, benzene, glacial acetic acid, and alcohol. 3,3′-Dichlorobenzidine degrades rapidly in sunlight. When heated to decomposition, these compounds emit toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (IARC 1974, 1982a, HSDB 2002).

Use

In the United States, 3,3′-dichlorobenzidine is used primarily in the manufacture of pigments for printing ink, textiles, paper, paint, rubber, and plastics and as a curing agent for isocyanate-containing polymers and solid urethane plastics (IARC 1974, ATSDR 1998). At least seven synthetic organic pigments, toners, and lakes were produced with 3,3′-dichlorobenzidine dihydrochloride (Kirk-Othmer 1981). The yellow pigments derived from the chemical and its salts can be used as substitutes for the lead chromate pigments (HSDB 2002). Use of 3,3′-dichlorobenzidine to synthesize dyes ended in 1986, with the introduction of better dyes from other sources (ATSDR 1998). Both compounds have also been reported to be used in a color test for the detection of gold (IARC 1982). 3,3′-Dichlorobenzidine has also found application in the production of tetraminobiphenol, which is used to produce polybenzimidazole. The thermally stable polymer is used in protective clothing, such as a firefighter's apparel and high-temperature gloves (ATSDR 1998).

Production

Current production volumes of 3,3′-dichlorobenzidine are considered confidential by individual companies, and therefore, were not available (ATSDR 1998). The 1998 *Chemical Buyers Directory* listed five U.S. suppliers of the dihydrochloride, whereas *Chemcyclopedia 98* only listed one supplier (Tilton 1997, Rodnan 1997). The 1997 Directory of Chemical Producers identified one producer of 3,3′-dichlorobenzidine hydrochloride (SRI 1997). The USITC has identified one U.S. manufacturer of 3,3′-dichlorobenzidine (base and salt) since 1988 producing an undisclosed quantity (USITC 1989-1991, 1993-1995). In 1986, two producers were named (USITC 1987). Ten U.S. suppliers of 3,3′-dichlorobenzidine or 3,3′-dichlorobenzidine dihydrochloride were listed in Chem Sources (2001). The compounds are imported, but no current data for the quantities imported were available. In 2000, 8.7 million lb of 3,3′-dichlorobenzidine dihydrochloride were imported (ITA 2001). The pigments derived from the chemical totaled approximately 129,000 lb in 1983 (ATSDR 1998). In 1980, approximately 324,000 lb of 3,3′-dichlorobenzidine and its salts were imported. Estimates from the USITC indicated that 208,000 lb of 3,3′-dichlorobenzidine were imported into the United States in 1979. The 1979 TSCA Inventory did not include 3,3′-dichlorobenzidine or its hydrochloride salt. EPA estimated that 1 million to 10 million lb of 3,3′-dichlorobenzidine dihydrochloride were produced in 1977. An estimated 5 million lb of 3,3′-dichlorobenzidine (base and salt) were produced in 1972. In 1971, the U.S. Tariff Commission reported that combined U.S. production of 3,3′-dichlorobenzidine and its salts by three companies amounted to 3.5 million lb. Commercial production of 3,3′-dichlorobenzidine in the United States began in 1938 (IARC 1974).

Exposure

The primary routes of potential human exposure to 3,3′-dichlorobenzidine and its dihydrochloride are inhalation of airborne dust, ingestion of contaminated well water by those living near hazardous waste sites, and dermal contact, primarily during industrial operations. Occupational exposure to the dihydrochloride has and probably continues to occur during its manufacture and conversion to derived pigments (HSDB 2002). Recent occupational studies, however, have shown that exposure from the use of benzidine-based dyes and pigments may be insignificant. For example, in 1989, no adverse health effects were found among 20 workers in a Japanese facility manufacturing and handling 3,3′-dichlorobenzidine alone (ATSDR 1998). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 1,100 workers were possibly exposed to 3,3′-dichlorobenzidine in the workplace (NIOSH 1976). No data were available on the number of workers potentially exposed to the dihydrochloride.

For the general population the chance of exposure to 3,3′-dichlorobenzidine and its dichloride salt is probably insignificant. Exposure via air, soil, or water is expected to be negligible. In the past, exposure may have occurred during the use of pressurized spray containers of paints, lacquers, and enamels containing traces of benzidine yellow, an azo dye derived from 3,3′-dichlorobenzidine. However, the greatest chance of exposure is from the improper land disposal of the compounds (ATSDR 1998).

EPA reported in 1980 that data on the presence of 3,3′-dichlorobenzidine dihydrochloride in the environment were limited; one survey detected 3,3′-dichlorobenzidine dihydrochloride at

concentrations of 0.13 to 3.0 mg/L at one 3,3′-dichlorobenzidine production waste disposal site (IARC 1982). 3,3′-Dichlorobenzidine and its dihydrochloride salt may be released as emissions or in wastewater during their production or use as dye intermediates. Atmospheric emissions of the compound most likely have been reduced as a result of closed-system operations. EPA's Toxic Chemical Release Inventory (TRI) listed 14 industrial facilities that produced, processed or otherwise used 3,3′-dichlorobenzidine in 1988 (TRI88 1990). The facilities reported releases of 3,3′-dichlorobenzidine to the environment which were estimated to total 1,000 lb. In 1994 the estimated releases were only 10 lb to air from one large processing facility, which accounted for all of the total reported environmental releases (ATSDR 1998). In 1999, total on-site releases of 3,3′-dichlorobenzidine and 3,3′-dichlorobenzidine dihydrochloride were reported to be 32 lb (TRI99 2001).

3,3′-Dichlorobenzidine may undergo photolysis in water exposed to sunlight. It has a strong tendency to partition to soils and sediments, reducing the potential for human exposure (ATSDR 1998). If released into water, the free base will rapidly adsorb to sediment and particulate matter, where it is bound. When released on land, it will bind to soil and possibly react with soil components. If released into the atmosphere, it will probably adsorb to particulate matter and photodegrade. Concentrations of 3,3′-dichlorobenzidine in wastewaters have been estimated to be 10 ppb (maximum) from metal finishing, 2 ppb (maximum, 0.3 ppb average) from nonferrous metals manufacture, 10 ppb (maximum) from paint and ink manufacture, and 3 ppb (maximum) from coal mining (HSDB 2002). According to the Consumer Product safety Commission (CPSC), residual levels or trace impurities of 3,3′-dichlorobenzidine dihydrochloride may be present both in 3,3′-dichlorobenzidine-based dyes and pigments and in the final consumer products; presence of this potential carcinogen, even as a trace contaminant, is cause for concern. However, no data are available on the actual levels of impurities in the final products, the potential for consumer exposure, and the potential uptake.

Regulations

EPA

Clean Air Act

NESHAP: 3,3′-Dichlorobenzidine listed as a Hazardous Air Pollutant (HAP)

Clean Water Act

Effluent Guidelines: Listed as a Toxic Pollutant (3,3′-dichlorobenzidine)

Water Quality Criteria: Based on fish/shellfish and water consumption = 0.021 ug/L (3,3′-Dichlorobenzidine); based on fish/shellfish consumption only = 0.028 ug/L (3,3′-Dichlorobenzidine)

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 1 lb (3,3′-Dichlorobenzidine)

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substances subject to reporting requirements

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U073 (3,3′-Dichlorobenzidine)

3,3′-Dichlorobenzidine listed as a Hazardous Constituent of Waste

OSHA

Potential occupational carcinogen: Engineering controls, work practices, and personal protective equipment required (3,3′-Dichlorobenzidine)

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = as low as possible (3,3′-Dichlorobenzidine)

NIOSH

3,3′-Dichlorobenzidine and its salts listed as potential occupational carcinogens

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