Disperse Blue 1 CAS No. 2475-45-8

Reasonably anticipated to be a human carcinogen First listed in the *Eighth Report on Carcinogens* (1998) Also known as C.I. disperse blue 1, C.I. 64500, or 1,4,5,8-tetraaminoanthraquinone

Carcinogenicity

Disperse blue 1 is *reasonably anticipated to be a human carcinogen* based on (1) sufficient evidence of carcinogenicity from studies in experimental animals and (2) the fact that it belongs to a well-defined, structurally related class of anthraquinones whose members are listed in the Report on Carcinogens as *reasonably anticipated to be human carcinogens*.

Cancer Studies in Experimental Animals

Oral exposure of rats to disperse blue 1 caused tumors of a type that is rare in this species. Dietary administration of disperse blue 1 caused benign and malignant urinary-bladder tumors in rats of both sexes (Burnett and Squire 1986, NTP 1986). Incidences were significantly increased of benign and malignant transitional-cell tumors combined (papilloma and carcinoma) and malignant tumors of the smooth muscle and smooth-muscle connective tissue combined (leiomyoma and leiomyosarcoma) in both sexes, as well as benign and malignant squamous-cell tumors combined (papilloma and carcinoma) in females. No urinary-bladder tumors were observed in any of the concurrent control groups. The historical control incidence of urinary-bladder tumors was 0.3% in males (6 tumors in 2,189 animals) and 0.2% in females (5 tumors in 2,263 animals); the tumors included 6 transitional-cell papillomas, 2 transitional-cell carcinomas, 1 leiomyoma, and 2 papillomas not otherwise specified. The findings in mice orally exposed to disperse blue 1 were equivocal, based on marginally increased combined incidences of benign and malignant liver tumors (hepatocellular adenoma and carcinoma) and lung tumors (alveolar/ bronchiolar adenoma and carcinoma).

Studies on Mechanisms of Carcinogenesis

In genotoxocity studies of anthraquinone derivatives and related anthracene derivatives, 35% of the compounds tested have shown some mutagenic activity. Of the anthraquinone analogues tested, mutagenic activity was strongest for nitro-anthraquinones, followed by hydroxy-anthraquinones, and was weakest for amino-anthraquinones; all nitro-anthraquinones tested were mutagenic. Disperse blue 1 was weakly mutagenic in *Salmonella typhimurium* (Brown and Brown 1976). It also caused sister chromatid exchange and chromosomal aberrations in Chinese hamster ovary cells (Anderson *et al.* 1990), *tk* gene mutations in mouse lymphoma L5178Y cells (Myhr *et al.* 1990), and morphological transformation in Balb/c 3T3 mouse cells (Matthews *et al.* 1993).

A study of the relationship between chemical structure and the carcinogenic activity of anthraquinone and six anthraquinone derivatives tested in long-term bioassays found that changes in functional groups (i.e., amino-, alkyl-, nitro-, hydroxyl-, or halogen substitutions)

altered the tissue sites of carcinogenesis, which included liver, kidney, skin, intestine, and urinary bladder in rats, and liver, skin, forestomach, and lung in mice (Doi *et al.* 2005).

The occurrence of urinary-bladder tumors (transitional- and squamous-cell tumors) in rats exposed to disperse blue 1 was associated with the dose-dependent incidence of calculi, which were thought to cause chronic inflammation and cell proliferation (NTP 1986). Calculi and resulting inflammatory and proliferative lesions also occurred in the urinary bladder of mice of both sexes, although tumor incidences were not significantly increased. It has been suggested that urinary-bladder calculi do not appear to form in humans at normal levels of exposure to disperse blue 1 (CIR 1995). However, there is no compelling evidence for a causal relationship between urinary-bladder calculi and development of leiomyoma or leiomyosarcoma in rats to contradict the evidence that disperse blue 1 is *reasonably anticipated to be a human carcinogen*.

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to disperse blue 1.

Properties

Disperse blue 1 is an amino-anthraquinone-based dyestuff (NTP 1986) that exists at room temperature as a blue-black microcrystalline powder. It is practically insoluble in water, soluble in acetone, ethanol, and cellosolve (glycol ether), and slightly soluble in benzene and linseed oil. It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of disperse blue 1 are listed in the following table.

Property	Information
Molecular weight	268.3°
Melting point	332°C ^a
Log K _{ow}	-0.96 ^a
Water solubility	0.03 mg/L at 25°C ^b
Vapor pressure	1.8×10^{-8} mm Hg at 25° C ^a

Sources: ${}^a\text{HSDB}$ 2009, ${}^b\text{ChemIDplus}$ 2009.

Use

Disperse blue 1 has been used in hair-color formulations and to color fabrics and plastics. Commercial preparations of disperse blue 1 contain approximately equal amounts of dyestuff and lignosulfonate dispersants. In the mid 1980s, it was reported that semi-permanent hair-color formulations commonly contained disperse blue 1 at concentrations of less than 1% (NTP 1986). Disperse blue 1 is used as a fabric dye for nylon, cellulose acetate and triacetate, polyester, and acrylate fibers and for surface dyeing of thermoplastics, as a solvent dye in cellulose acetate plastics, and to dye fur and sheepskins (NTP 1986, IARC 1990, HSDB 2009). It is also used in some personal-care products, such as hair mousse and toothpaste (HPD 2009).

Production

The last reported quantity for U.S. production of disperse blue 1 was over 350,500 lb in 1972 (IARC 1990); after 1972, production figures specifically for disperse blue 1 were no longer reported. Production in the United States, by one company, was last reported in 1992 (HSDB 2009). In 2009, no commercial manufacturers of disperse blue 1 were identified worldwide (SRI 2009), but disperse blue 1 was available from five suppliers, including three U.S. suppliers (ChemSources 2009). No data on U.S. imports or exports of disperse blue 1 were found.

Exposure

The routes of potential human exposure to disperse blue 1 are inhalation, ingestion, and dermal contact (HSDB 2009). Ingestion is a potential route of exposure because of the use of disperse blue 1 in toothpaste. More commonly, it is used in hair dyes or hair mousse, and individuals using, producing, or applying these products potentially could be exposed by inhalation and dermal contact (IARC 1990). In the mid 1980s, it was reported that over 3 million people in the United States used semipermanent hair-color preparations containing disperse blue 1, usually at concentrations of less than 1% (NTP 1986). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 43,522 workers (mostly in the Personal Services industry), including 32,059 women, potentially were exposed to disperse blue 1 (NIOSH 1990).

Environmental releases can occur from production or use of disperse blue 1. If released to air, disperse blue 1 will exist mainly as a particulate, and it is not expected to be volatile in soil or water. It is estimated to have low mobility in soil and will bind to soil and water sediments. Based on estimated bioconcentration factors, disperse blue 1 may bioaccumulate in aquatic organisms (HSDB 2009).

Regulations

Department of Transportation (DOT)

Toxic dyes and toxic dye intermediates are considered hazardous materials, and special requirements have been set for marking, labeling, and transporting these materials.

References

Akron. 2009. The Chemical Database. The Department of Chemistry at the University of Akron. http://ull. chemistry.uakron.edu/erd and search on CAS number. Last accessed: 5/11/09.

Anderson BE, Zeiger E, Shelby MD, Resnick MA, Gulati DK, Ivett JL, Loveday KS. 1990. Chromosome aberration and sister chromatid exchange test results with 42 chemicals. *Environ Mol Mutagen* 16(Suppl 18): 55-137.

Brown JP, Brown RJ. 1976. Mutagenesis by 9,10-anthraquinone derivatives and related compounds in *Salmonella typhimurium*. *Mutat Res* 40(3): 203-224.

Burnett CM, Squire RA. 1986. The effect of dietary administration of Disperse Blue 1 on the urinary system of the Fischer 344 rat. *Food Chem Toxicol* 24(4): 269-276.

ChemIDplus. 2009. ChemIDplus Advanced. National Library of Medicine. http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp and select Registry Number and search on CAS number. Last accessed: 3/22/09.

ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. http://www.chemsources.com/chemonline.html and search on disperse blue. Last accessed: 5/11/09.

CIR. 1995. Final report on the safety assessment of Disperse Blue 1. Cosmetic Ingredient Review Expert Panel. *J Am Coll Toxicol* 14(6): 431-451.

Doi AM, Irwin RD, Bucher JR. 2005. Influence of functional group substitutions on the carcinogenicity of anthraquinone in rats and mice: analysis of long-term bioassays by the National Cancer Institute and the National Toxicology Program. *J Toxicol Environ Health B Crit Rev* 8(2): 109-126.

HPD. 2009. Household Products Database. National Library of Medicine. http://hpd.nlm.nih.gov/ingredients.htm and search on CAS number. Last accessed: 3/22/09.

 $HSDB.\ 2009.\ Hazardous\ Substances\ Data\ Bank.\ National\ Library\ of\ Medicine.\ http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen? HSDB\ and\ search\ on\ CAS\ number.\ Last\ accessed:\ 3/22/09.$

IARC. 1990. Disperse blue 1. In *Some Flame Retardants and Textile Chemicals and Exposures in the Textile Manufacturing Industry*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 48. Lyon, France: International Agency for Research on Cancer. pp. 139-147.

Matthews EJ, Spalding JW, Tennant RW. 1993. Transformation of BALB/c-3T3 cells: V. Transformation responses of 168 chemicals compared with mutagenicity in *Salmonella* and carcinogenicity in rodent bioassays. *Environ Health Perspect* 101(Suppl 2): 347-482.

Myhr B, McGregor D, Bowers L, Riach C, Brown AG, Edwards I, McBride D, Martin R, Caspary WJ. 1990. L5178Y mouse lymphoma cell mutation assay results with 41 compounds. *Environ Mol Mutagen* 16(Suppl 18): 138-167.

 $NIOSH.\ 1990.\ National\ Occupational\ Exposure\ Survey\ (1981-83).\ National\ Institute\ for\ Occupational\ Safety\ and\ Health.\ Last\ updated:\ 7/1/90.\ http://www.cdc.gov/noes/noes/1t0840sic.html.$

NTP. 1986. *Toxicology and Carcinogenesis Studies of C.I. Disperse Blue 1 (CAS No. 2475-45-8) in F344/N Rats and B6C3F*, *Mice (Feed Studies)*. NTP Technical Report Series no. 299. Research Triangle Park, NC: National Toxicology Program. 241 pp.

SRI. 2009. Directory of Chemical Producers. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 5/11/09.