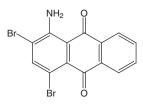
1-Amino-2,4-Dibromoanthraquinone CAS No. 81-49-2

Reasonably anticipated to be a human carcinogen First Listed in the *Eleventh Report on Carcinogens* (2004)



Carcinogenicity

1-Amino-2,4-dibromoanthraquinone (ADBAQ) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence from studies in experimental animals. Orally administered ADBAQ significantly increased the incidences of benign and/or malignant tumors at multiple tissue sites in two species of animals. ADBAQ caused benign and malignant liver tumors in rats and mice of both sexes; tumors of the large intestine, kidney, and urinary bladder in male and female rats; and tumors of the forestomach and lung in male and female mice (NTP 1996).

Two cohort studies evaluated the risk of cancer among workers in plants manufacturing anthraquinone dyes; however, it is not known whether workers were exposed specifically to ADBAQ (Gardiner *et al.* 1982, Delzell *et al.* 1989). Some evidence suggests that anthraquinone dye workers may have an increased risk of cancer. Significant excesses of esophageal and prostate cancer occurred among workers in some areas of a Scottish anthraquinone dyestuffs plant, and excesses of lung and central nervous system cancer occurred among workers at a New Jersey anthraquinone dye and epichlorohydrin plant (Barbone *et al.* 1992, 1994, Sathiakumar and Delzell 2000). Nevertheless, estimates of risk in all studies were based on small numbers of cancer deaths, and workers may have been exposed to other carcinogens.

Additional Information Relevant to Carcinogenicity

Evaluation of ADBAQ's genetic effects has been hindered by ADBAQ's limited solubility. ADBAQ caused mutations in some strains of bacteria but not in rodent cells, which were tested at lower concentrations (Haworth *et al.* 1983, NTP 1996). In mammalian cells, ADBAQ induced chromosomal aberrations (changes in chromosome structure or number) and sister chromatid exchange; however, the results varied between laboratories and between trials at the same laboratory (Loveday *et al.* 1990, NTP 1996). Point mutations in the *ras* proto-oncogene (a gene potentially associated with cancer) occurred at a higher frequency in forestomach and lung tumors from the two-year carcinogenicity study of ADBAQ-exposed mice than in spontaneous tumors from control mice not exposed to ADBAQ. The predominant types of mutations were A to T transversions and A to G transitions, suggesting that ADBAQ or its metabolites target adenine bases in the *ras* proto-oncogene (Hayashi *et al.* 2001).

ADBAQ is rapidly absorbed from the gastrointestinal tract and distributed to most soft tissues. The majority of ADBAQ is metabolized, and both ADBAQ and its metabolites are excreted in the feces and urine. However, the metabolites of ADBAQ have not been identified (NTP 1996).

The mechanism by which ADBAQ causes cancer is not known; however, there is no evidence to suggest that mechanisms of tumor induction observed in experimental animals would not occur in humans. Four other anthraquinones (2-aminoanthraquinone, 1-amino-2methylanthraquinone, danthron [1,8-dihydroxyanthraquinone], and disperse blue 1) are listed in the Report on Carcinogens as reasonably anticipated to be human carcinogens.

Properties

ADBAQ has a molecular weight of 381.0 and is a member of the class of aminoanthraquinones. It occurs as a reddish-brown to orange powder with a melting point of 221°C. ADBAQ is insoluble in water, has an estimated log octanol-water partition coefficient of 5.31, and a vapor pressure of 1.4×10^{-9} mm Hg at 25°C (NTP 1996, ChemFinder 2003, HSDB 2003).

Use

ADBAQ and other aminoanthraquinones are key intermediates for production of almost all anthraquinone dyes (HSDB 2003). Anthraquinones, including ADBAQ, are widely used as starting material for the manufacture of vat dyes. Vat dyes are a class of waterinsoluble dyes that can easily be reduced to a water-soluble and usually colorless form. In this form, they are readily impregnated into fibers and textiles. Oxidation then produces an insoluble colored form that is remarkably fast to washing, light, and chemicals. Vat dyes typically are used with cotton, wool, and cellulose acetate (NTP 1996).

Production

ADBAQ is prepared from 1-aminoanthraquinone by bromination in dilute mineral acids (HSDB 2003). ADBAQ is not produced in the United States, but is available from at least one supplier (ChemSources 2003, SRI 2003). U.S. production of all vat dyes totaled 14 million kilograms (31 million pounds) in 1991 (NTP 1996).

Exposure

ADBAQ is not known to be formed naturally in the environment, but may be released into the environment during its production or through its use in production of anthraquinone dyes (HSDB 2003). ADBAQ was detected in raw wastewater of a dye manufacturing plant (in four of eight samples, at concentrations of 92 to 170 ppb). However, it was not detected in the final effluent before its release into a nearby river, nor in sediments from the river. This finding suggests that ADBAQ may have been biodegraded or adsorbed to sludge during wastewater treatment (HSDB 2003).

Exposure to ADBAQ would be primarily through dermal contact. Because ADBAQ has a very low vapor pressure, inhalation exposure to vapor is unlikely; however, contaminated dust particles could be inhaled. No information was found on occupational exposure specifically to ADBAQ or to anthraquinone dyes in general, but epidemiological studies indicated occupational exposure to anthraquinone dyes in a New Jersey dye and resin manufacturing plant (Sathiakumar and Delzell 2000).

Regulations and Guidelines

No regulations or guidelines relevant to reduction of exposure specifically to ADBAQ were identified.

REFERENCES

- Barbone, F., E. Delzell, H. Austin and P. Cole. 1992. A case-control study of lung cancer at a dye and resin manufacturing plant. Am J Ind Med 22(6): 835-49.
- Barbone, F., E. Delzell, H. Austin and P. Cole. 1994. Exposure to epichlorohydrin and central nervous system neoplasms at a resin and dye manufacturing plant. Arch Environ Health 49(5): 355-8.
- Bolton, J. L., M. A. Trush, T. M. Penning, G. Dryhurst and T. J. Monks. 2000. Role of quinones in toxicology. Chem Res Toxicol 13(3): 135-60.
- ChemFinder. 2003. 1-Amino-2,4-Dibromoanthraquinone. CambridgeSoft Corporation. http://www.chemfinder.camsoft.com and search 81-49-2.
- ChemSources. 2003. 1-Amino-2,4-Dibromoanthraquinone. Chemical Sources International, Inc. http://www.chemsources.com and search CAS number 81-49-2.
- Delzell, E., M. Macaluso and P. Cole. 1989. A follow-up study of workers at a dye and resin manufacturing plant. J Occup Med 31(3): 273-8.
- Gardiner, J. S., S. A. Walker and A. J. MacLean. 1982. A retrospective mortality study of substituted anthraquinone dyestuffs workers. Br J Ind Med 39(4): 355-60.
- Haworth, S., T. Lawlor, K. Mortelmans, W. Speck and E. Zeiger. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ Mutagen 5 Suppl 1: 1-142.
- Hayashi, S., H. H. Hong, K. Toyoda, T. V. Ton, T. R. Devereux, R. R. Maronpot, J. Huff and R. C. Sills. 2001. High frequency of *ras* mutations in forestomach and lung tumors of B6C3F1 mice exposed to 1-amino-2,4-dibromoanthraquinone for 2 years. Toxicol Pathol 29(4): 422-9.
- HSDB. 2003. Hazardous Substances Database. 1-Amino-2,4-Dibromoanthraquinone. National Library of Medicine. Last reviewed: 1/31/96. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB and search

SUBSTANCE PROFILES

- CAS number. Last accessed: 12/15/03.
 Loveday, K. S., B. E. Anderson, M. A. Resnick and E. Zeiger. 1990. Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells *in vitro*. V: Results with 46 chemicals. Environ Mol Mutagen 16(4): 272-303.
 NTP. 1996. Toxicology and Carcinogenesis Studies of 1-Amino-2,4-Dibromoanthraquinone in F344/N Rats and B6C3F1 Mice (Feed Studies). Technical Report Series No 383. Research Triangle Park, NC: National Toxicology Program
- National Toxicology Program.
 Sathiakumar, N. and E. Delzell. 2000. An updated mortality study of workers at a dye and resin manufacturing plant. J Occup Environ Med 42(7): 762-71.
 SRI. 2003. Directory of Chemical Producers. http://dcp.sric.sri.com/Public/ (Visitor Search).