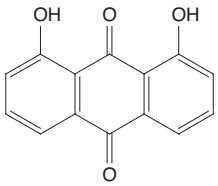
Danthron

CAS No. 117-10-2

Reasonably anticipated to be a human carcinogen

First listed in the *Eighth Report on Carcinogens* (1998)

Also known as 1,8-dihydroxyanthraquinone or chrysazin



Carcinogenicity

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

Cancer Studies in Experimental Animals

Oral exposure to danthron caused tumors in two rodent species and at several different tissue sites. Dietary administration of danthron caused liver cancer (hepatocellular carcinoma) in male mice and benign and malignant intestinal-tract tumors (adenoma and adenocarcinoma of the colon and adenoma of the cecum) in male rats (IARC 1990).

Cancer Studies in Humans

The data available from studies in humans are inadequate to evaluate the relationship between human cancer and exposure specifically to danthron. One case report was identified that described the occurrence of cancer of the small intestine (leiomyosarcoma) in an 18-year-old girl with a history of prolonged exposure to danthron (Patel *et al.* 1989).

Studies on Mechanisms of Carcinogenesis

Danthron has been evaluated for its ability to promote the induction of tumors by other chemicals. When danthron was fed to male mice that also received 1,2-dimethylhydrazine as a tumor initiator, the incidence and multiplicity of colon tumors (adenoma or adenocarcinoma) and liver tumors (adenoma) were significantly increased (Sugie *et al.* 1994). However, danthron did not promote the induction of tumors when either painted on the skin of mice pretreated with 7,12-dimethylbenz[*a*]anthracene or fed to rats pretreated with 1,2-dimethylhydrazine (IARC 1990). Danthron was found to cause genetic damage in a limited number of *in vitro* test systems, including *Salmonella typhimurium,* yeast, and mammalian cell cultures (IARC 1990).

Properties

Danthron is an anthraquinone that exists at room temperature as a reddish or orange crystalline powder. It is practically insoluble in water, soluble in acetone, chloroform, diethyl ether, and ethanol, and very soluble in alkaline hydroxide solutions (IARC 1990). It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of danthron are listed in the following table.

Property	Information
Molecular weight	240.2[a]
Specific gravity	1.54 g/cm^3[b]
Melting point	193°C[a]
Boiling point	sublimes[b]
Log K_{ow}	3.94[a]
Water solubility	9 mg/L[a]
Vapor pressure	7.6×10^{-11} mm Hg[a]
Vapor density relative to air	8.3[b]

Sources: [a]ChemIDplus 2009, [b]Akron 2009.

Use

Danthron has been used since the beginning of the twentieth century as a laxative (IARC 1990). In 1987, U.S. manufacturers voluntarily withdrew production of human drug products containing danthron, and in 1999, the U.S. Food and Drug Administration issued the final rule ordering the withdrawal of danthron-containing products from the U.S. market for use as laxatives (FDA 1999). However, danthron has continued to be used as a pharmaceutical in the United Kingdom (Bennett and Cresswell 2003). To a lesser extent, danthron has been used as an intermediate in the manufacture of alizarine and indanthrene dyes (Akron 2009).

Production

In the past, danthron was synthesized in Germany, India, Japan, Poland, the United Kingdom, and the United States (IARC 1990). In 2009, danthron was produced by one manufacturer in Europe and two manufacturers in China (SRI 2009) and was available from 24 suppliers, including 12 U.S. suppliers (ChemSources 2009). No data on U.S. imports or exports of danthron were found. A report filed in 1986 under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of danthron totaled 10,000 to 500,000 lb; no later reports were filed (EPA 2004).

Exposure

Historically, the primary route of potential human exposure to danthron has been oral administration of laxatives. Shortly before its withdrawal from the market, danthron was available from nine companies in over-the-counter products. The following products were voluntarily withdrawn from the market in the United States in 1987: Altan, Antrapurol, Bancon, Benno, DanSunate D, Danthron, Diaquone, Dionone, Dorban, Dorbane, Duolax, Fructines-Vichy, Istin, Istizin, Julax, Laxanorm, Laxans, Laxanthreen, Laxenta, Laxipur, Laxipurin, Modane, Neokutin S, Pastomin, Prugol, Roydan, Scatron D, Solven, Unilax, and Zwitsalax (NTP 1999). Danthron occurs naturally in several species of plants and insects. It has been isolated from dried leaves and stems of *Xyris semifuscata* harvested in Madagascar and forms the basic structure of the aglycones of naturally occurring laxative glycosides. Danthron has been identified in larvae of the elm-leaf beetle, *Pyrrhalta luteola;* it has been suggested that the insect biosynthesizes a mixture of anthraquinones and anthrones as protection from predators (IARC 1990).

Occupational exposure to danthron potentially could have occurred among health professionals during preparation and administration of the pharmaceutical and among workers involved in its formulation and packaging. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 357 workers (in the Health Services industry), including 187 women, potentially were exposed to danthron (NIOSH 1990).

Regulations

Food and Drug Administration (FDA)

Products containing danthron as a laxative are no longer generally recognized as safe and effective and may not be marketed in the United States.

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