Furan

CAS No. 110-00-9

Reasonably anticipated to be a human carcinogen

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

Carcinogenicity

Furan 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 furan caused tumors at several different tissue sites in mice and rats. Administration of furan by stomach tube for up to two years caused benign and/or malignant liver tumors (hepatocellular adenoma or carcinoma) in mice and rats of both sexes. It also caused bile-duct cancer (cholangiocarcinoma) and mononuclear-cell leukemia in rats of both sexes and benign adrenal-gland tumors (pheochromocytoma) in mice of both sexes (NTP 1993). Similar administration of furan to male rats for 9 to 13 weeks caused bile-duct cancer (cholangiocarcinoma) by 16 months after the end of exposure (Maronpot *et al.* 1991, Elmore and Sirica 1993). Since furan was listed in the *Eighth Report on Carcinogens,* an additional study in mice has been identified. Intraperitoneal injection of furan caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma) in newborn male mice (Johansson *et al.* 1997).

Cancer Studies in Humans

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

Studies on Mechanisms of Carcinogenesis

In bacteria, furan caused gene mutations in *Salmonella typhimurium* strain TA100 (Lee *et al.* 1994) and in *Escherichia coli* containing bacteriophage T7 (Ronto *et al.* 1992), but not in *S. typhimurium* strains TA98 (Lee *et al.* 1994), TA1535, or TA1537 (Mortelmans *et al.* 1986). It did not cause gene mutations in *Drosophila melanogaster* (Foureman *et al.* 1994). In mammalian *in vitro* systems, it caused gene mutations in mouse lymphoma cells (McGregor *et al.* 1988), DNA damage in Chinese hamster ovary (CHO) cells (NTP 1993), and chromosomal damage in CHO cells with mammalian metabolic activation (NTP 1993, IARC 1995), but it did not cause DNA damage in mouse or rat hepatocytes (Wilson *et al.* 1992, NTP 1993). In mammalian *in vivo* systems, furan caused chromosomal aberrations in bone marrow of mice (NTP 1993, Johansson 1997), but did not cause DNA damage in mouse bone marrow or hepatocytes or rat hepatocytes (Wilson *et al.* 1992, NTP 1993).

A current hypothesis for the mechanism of furan-induced carcinogenesis is metabolic activation of furan by cytochrome P450 to a reactive and cytotoxic intermediate that stimulates cell replication, increasing the likelihood of tumor induction (Kedderis *et al.* 1993, Chen *et al.* 1995). The postulated reactive metabolite is *cis*-2-butene-1,4-dial, which was characterized as a furan metabolite by Chen *et al.* (1995). This reactive metabolite probably explains furan's binding reactivity with proteins both *in vitro* (in uninduced and induced male rat liver microsomes) and *in vivo* (with male rat liver protein) (Burka *et al.* 1991, Parmar and Burka 1993). Furan metabolites may react with DNA, but no radiotracer was detected in DNA from livers of rats administered [^{14}C]furan (Burka *et al.* 1991).

Properties

Furan is a cyclic dienic ether that is a clear, colorless liquid with an ethereal odor (Akron 2009, HSDB 2009). It can turn brown upon standing (HSDB 2009). Furan is slightly soluble in water and is soluble at greater than 10% in acetone, benzene, ether, and ethanol. It is extremely flammable and may form explosive peroxides in the absence of inhibitors (Akron 2009). Physical and chemical properties of furan are listed in the following table.

Property	Information
Molecular weight	68.1[a]
Specific gravity	0.9371 at 19.4°C/4°C[a]
Melting point	–85.6°C[a]
Boiling point	31.4°C at 760 mm Hg[a]
Log K_{ow}	1.34[a]
Water solubility	10 g/L at 25°C[b]
Vapor pressure	600 mm Hg at 25°C[b]
Vapor density relative to air	2.3[a]

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

Use

Furan is used primarily as an intermediate in the synthesis and production of tetrahydrofuran, pyrrole, and thiophene. Hydrogenation of furan over a nickel catalyst produces high yields of tetrahydrofuran and is a source of commercial tetrahydrofuran (NTP 1993, IARC 1995). Furan is also used in the formation of lacquers, as a solvent for resins, and in the production of agricultural chemicals, stabilizers, and pharmaceuticals (IARC 1995, HSDB 2009).

Production

Commercial production of furan involves decarbonylation of furfural over a palladium-charcoal catalyst. The commercial product is at least 99% pure (IARC 1995). U.S. production of furan was between 10 and 50 million pounds from 1986 to 1998 (EPA 2004), but combined production and imports had fallen to between 1 million and 10 million pounds by 2014 (EPA 2016). In 1986, U.S. imports of furan resins totaled about 9.7 million pounds (HSDB 2009). No information on U.S. imports and exports of furan was found. In 2009, furan was available from 20 suppliers worldwide, including 11 U.S. suppliers (ChemSources 2009).

Exposure

Evidence that the U.S. general population is exposed to furan comes findings of furan in human blood and exhaled breath. The 2013–2014 National Health and Nutrition Examination Survey (NHANES) found that the 95th-percentile concentration of furan in whole blood was 0.091 ng/mL, based on a sample of 3,203 individuals of all ages, both genders, and all race and ethnicity groups (CDC 2018a). People are exposed to furan primarily through ingestion of food, inhalation of contaminated air, and tobacco smoking. The pattern of commercial use suggests that minimal exposure to the general population would be expected through contact with products contaminated with furan (NTP 1993). However, furan can be formed in foods during processing.

Furan was measured by the U.S. Food and Drug Administration in various foods and beverages, including infant formulas, baby foods, soups and sauces, fruits and vegetables, bread, and meat products. The maximum concentration found was 125 ppb (µg/kg) in canned soup (FDA 2005). A second study confirmed that heat-treated foods, such as canned and jarred foods, contained measurable quantities of furan (up to 240 µg/kg in canned chili) (Becalski *et al.* 2005). Furan was measured in fruit juice at concentrations near 1 µg/kg (Goldmann

et al. 2005). In several brands of brewed coffee, the highest furan concentration found was 84.2 ppb (FDA 2005, Ho *et al.* 2005). Furan was also identified as a component of coffee aroma that has antioxidant activity (Fuster *et al.* 2000). Furan was also detected at a concentration of 110 µg/kg in jarred baby food containing cooked vegetables (Goldmann *et al.* 2005). However, furan concentrations decreased after the jar was opened and the contents were heated. When food is heated in a container, furan concentrations increase if the container remains closed, but not if it is open (Hasnip *et al.* 2006). Furan does not appear to be transferred from the packaging or gasket of the can or jar. Furan is formed from ascorbic acid, fructose, sucrose, and glucose when foods are heated or irradiated (Fan 2005). Furan production increases greatly with decreasing pH of the medium; 1,600 times as much furan is formed at pH 3 as is formed at pH 8.

Furan is found at higher levels in the blood and exhaled breath of smokers than in the general population. The 2013–2014 NHANES found that in a sample of 951 cigarette smokers of all ages and both genders, the 95th-percentile concentration in whole blood was 0.172 ng/mL (CDC 2018b). In one study in Texas, furan was detected in the exhaled breath of two of three male smokers and four of five male nonsmokers (HSDB 2009). Smokers exhaled between 0.25 and 98 µg of furan per hour, and nonsmokers exhaled between 0.33 and 28 µg/h. In a study in Chicago, 15 of 387 breath samples collected from 54 male and female nonsmokers had detectable levels of furan, with a mean concentration of 0.55 ng/L. Furan was also detected in the indoor air of homes in the Chicago, Illinois, and Washington, D.C., metropolitan areas (NTP 1999). Furan also occurs naturally in pine rosin and in volatile emissions from sorb trees (HSDB 2009).

The primary route of occupational exposure to furan is inhalation. The industrial processes in which furan is used are conducted in closed systems, and its volatility requires that furan be handled in closed containers; therefore, occupational exposure is limited (NTP 1993). The National Occupational Hazard Survey (conducted from 1972 to 1974) estimated that 244 workers potentially were exposed to furan (NIOSH 1976). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 35 workers (mostly in the Business Services industry), including 7 women, potentially were exposed to furan (NIOSH 1990).

Regulations

Department of Transportation (DOT)

Furan is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Clean Air Act

Listed as a mobile source air toxic.
Prevention of Accidental Release: Threshold quantity (TQ) = 5,000 lb.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 100 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.
Reportable quantity (RQ) = 100 lb.
Threshold planning quantity (TPQ) = 500 lb.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of furan = U124.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

Considered a highly hazardous chemical; threshold quantity (TQ) = 500 lb.

Guidelines

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Immediately dangerous to life and health (IDLH) limit = 13 ppm (35.1 mg/m^3).

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