

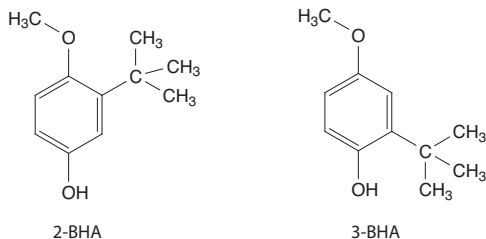
Butylated Hydroxyanisole

CAS No. 25013-16-5

Reasonably anticipated to be a human carcinogen

First listed in the *Sixth Annual Report on Carcinogens* (1991)

Also known as BHA or (1,1-dimethylethyl)-4-methoxyphenol



Carcinogenicity

Butylated hydroxyanisole (BHA) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Dietary exposure to BHA caused benign and malignant tumors of the forestomach (papilloma and squamous-cell carcinoma) in rats of both sexes and in male mice and hamsters (IARC 1986, Masui *et al.* 1986). Since BHA was listed in the *Sixth Annual Report on Carcinogens*, an additional study in experimental animals has been identified. Dietary administration of BHA to fish (hermaphroditic *Rivulus marmoratus*) as larvae caused liver cancer (hepatocellular carcinoma) in the adult fish (Park *et al.* 1990).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to BHA. Since BHA was listed in the *Sixth Annual Report on Carcinogens*, one epidemiological study of BHA has been identified. A population-based nested case-control study of stomach cancer in men and women within the Netherlands Cohort Study of dietary intake found no increase in risk at typical levels of dietary intake of BHA (Botterweck *et al.* 2000).

Properties

BHA is an antioxidant which exists at room temperature as a white or slightly yellow, waxy solid with a faint characteristic odor (IARC 1986). BHA in commercial use consists of a mixture of 3-*tert*-butyl-4-hydroxyanisole (3-BHA) and 2-*tert*-butyl-4-hydroxyanisole (2-BHA). BHA is insoluble in water, but is soluble in fats, oils, propylene glycol, petroleum ether, chloroform, and 50% alcohol. Physical and chemical properties of BHA are listed in the following table.

Property	Information
Molecular weight	180.2 ^a
Melting point	48°C to 55°C ^a
Boiling point	264°C to 270°C at 733 mm Hg ^a
Log K_{ow}	3.5 ^b
Water solubility	0.213 g/L at 25°C ^b
Vapor pressure	0.00248 mm Hg at 25°C ^a

Sources: ^aHSDB 2009, ^bChemIDplus 2009.

Use

BHA is used primarily as an antioxidant and preservative in food, food packaging, animal feed, and cosmetics, and in rubber and pe-

troleum products (IARC 1986). Food-grade BHA contains over 85% 3-BHA and less than 15% 2-BHA, while cosmetic-grade BHA contains 90% 3-BHA and 8% 2-BHA. Since 1947, BHA has been added to edible fats and fat-containing foods for its antioxidant properties. It is also used in foods cooked or fried in animal oils, because of its high thermal stability and its ability to remain active in baked and fried foods (HSDB 2009). BHA is added to butter, lard, meats, cereals, baked goods, sweets, beer, vegetable oils, potato chips, snack foods, nuts and nut products, dehydrated potatoes, and flavoring agents. It is used in sausage, poultry and meat products, dry mixes for beverages and desserts, glazed fruits, chewing gum, active dry yeast, defoaming agents for beet sugar and yeast, and emulsion stabilizers for shortening (IARC 1986). BHA stabilizes the petroleum wax coatings of food packaging (HSDB 2009). BHA is considered by the U.S. Food and Drug Administration (FDA) to be generally recognized as safe when the antioxidant content does not exceed 0.02% by weight of the food's total fat or oil content.

BHA is one of the primary antioxidants used in feeds, because it retards the oxidation of vitamin A, fats, and vegetable oils. It is an effective stabilizer for essential oils, paraffin, and polyethylenes (HSDB 2009). It is used as an antioxidizing agent in a biomaterial made from polyurethane and polyethylene oxide used to make mainline catheters (Silverstein *et al.* 1997). BHA is used as a preservative and antioxidant in pharmaceutical preparations and cosmetic formulations containing fats and oils. A 1981 FDA survey found that BHA was used in 3,217 of 21,279 cosmetic formulations; the majority (88%) of the reported concentrations did not exceed 0.1%. In that survey, use of BHA was highest in lipstick formulations (1,256 products), followed by eye-shadow products (410) (IARC 1986). For industrial use, BHA has largely been replaced by *tert*-butylhydroquinone.

Production

In 2009, no producers of BHA were identified worldwide (SRI 2009), but it was available from 46 suppliers, including 18 U.S. suppliers (ChemSources 2009). No recent data on U.S. imports or exports of BHA were found. Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of BHA totaled 10,000 to 500,000 lb in 1986 and 2000, 1 million to 10 million pounds in 1996, and less than 500,000 lb in 2006 (EPA 2004, 2009).

Exposure

Routes of human exposure to BHA are ingestion, inhalation, and dermal contact. In 1975, the estimated average daily intake of BHA in the diet was 4.3 mg (IARC 1986). Estimated annual U.S. use of BHA in food increased from 170,000 kg (374,000 lb) in 1960 to 300,000 kg (660,000 lb) between 1970 and 1982 (IARC 1986). Total reported annual use of BHA in the mid 1970s was 450 metric tons (990,000 lb) (Nicholas *et al.* 1978). The concentration of BHA in six samples of human adipose tissue ranged from 0.01 to 0.03 ppm (Conacher *et al.* 1986). Dermal exposure to BHA occurs from its use as an antioxidant in cosmetic products, especially lipstick and eye shadow (IARC 1986). BHA is also used as an antioxidant for some rubber and petroleum products, and it is a stabilizer for vitamin A (HSDB 2009).

Workers potentially are exposed to BHA in certain industries, including food producers, animal feed producers, livestock producers, cosmetic manufacturers, some petroleum workers, and rubber producers and those who handle the end products, such as tires. Fast-food service personnel who normally cook and serve fried and oily foods potentially are exposed to BHA at high levels; BHA is volatile at 150°C to 170°C (302°F to 338°F) and is readily lost from thermal processes that generate steam (Warner *et al.* 1986). The National

Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 89,673 workers, including 44,061 women, potentially were exposed to BHA. Most of these workers were in the Health Services (> 24,000 workers), Food (> 18,000 workers), and Chemical and Allied Products industries (> 13,000 workers) (NIOSH 1990).

Regulations

Food and Drug Administration (FDA)

BHA is generally recognized as safe for use in food when the total of antioxidants is not greater than 0.02% of fat or oil content.

BHA may be used as a food additive permitted for direct addition to food for human consumption as prescribed in 21 CFR 172 and 166.

BHA may be used in the manufacture of food packaging materials, with a limit of addition to food of 0.005%.

BHA may be used as an antioxidant in defoaming agents for processed foods, not to exceed 0.1% by weight of defoamer.

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