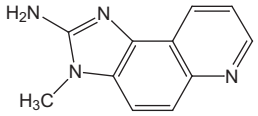
2-AMINO-3-METHYLIMIDAZO[4,5-f]QUINOLINE (IQ)
CAS No. 76180-96-6
First listed in the *Tenth Report on Carcinogens*



CARCINOGENICITY

2-Amino-3-methylimidazo[4,5-*f*]quinoline (IQ) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of benign and malignant tumor formation at multiple tissue sites in multiple species of experimental animals (IARC 1993). Oral exposure of rats to IQ induces neoplasms of the mammary gland, liver, small intestine, clitoral gland, oral cavity, and Zymbal gland in females and neoplasms of the liver, skin, colon, small intestine, oral cavity, and Zymbal gland in males. Oral exposure of mice to IQ induces neoplasms of the lung, liver, and forestomach in males and females. Intraperitoneal injection of IQ in mice and oral exposure in cynomologus monkeys causes liver tumors.

No adequate epidemiology studies have been reported that would indicate a human cancer risk specifically associated with exposure to IQ or other heterocyclic amines (HCAs). However, published epidemiology studies provide some indication that human cancer risk is related to consumption of broiled or fried foods that may contain IQ and/or other HCAs.

OTHER INFORMATION RELATING TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Studies have uniformly shown that IQ is genotoxic in a wide variety of bacterial, plant, and mammalian test systems, mainly with metabolic activation, and in animals *in vivo* (IARC 1993). IQ induces DNA and chromosomal damage in various cultured human cells, including mutations, chromosomal aberrations, sister chromatid exchange, micronuclei, and unscheduled DNA synthesis. IQ is metabolized to reactive intermediates via acetylation and hydroxylation. *N*-acetoxy-IQ degrades to an unstable nitrenium ion that can bind to DNA. In animals given IQ, DNA adducts have been found in many tissues, including those where IQ-induced tumors occur. All animal species studied have been found to metabolize IQ to products that react with DNA, as do human mammary gland cells and liver microsomes *in vitro.*

No available data suggest that mechanisms thought to account for IQ's induction of tumors in experimental animals would not also operate in humans.

PROPERTIES

IQ is a light tan crystalline solid. It is stable under moderately acidic and alkaline conditions and in cold, dilute aqueous solutions when protected from light (IARC 1986). It is rapidly degraded by dilute hypochlorite (IARC 1993). It is insoluble in water (at 20°C) and soluble in dimethylsulfoxide, 95% ethanol (at 16°C), methanol, acids, and alcohol.

USE

IQ is one of a number of HCAs found in cooked food, primarily in meats and fish. It has no commercial uses, but it is used for research purposes.

PRODUCTION

IQ is produced commercially in small quantities for research. Chemical synthesis was first reported in 1980. 5,6-Diaminoquinoline was reacted with cyanogen bromide, which produced a cyclic intermediate that was converted to the tetramethyl ammonium salt and then heated under reduced pressure to form IQ. The IQ was purified by sublimation, silica-gel column chromatography, and crystallization from aqueous methanol (IARC 1993).

EXPOSURE

The most likely route of human exposure is through consumption of food containing IQ, such as broiled or fried beef, fish, or eggs (IARC 1993). IQ also is present in cigarette smoke (Yamashita *et al*. 1986). Estimated daily exposure of the U.S. population to IQ and other HCAs ranges from 100 ng to 10 μg, based on analysis of various foodstuffs. Overall U.S. exposure to IQ is difficult to estimate because it depends on the type of meat, cooking temperature, and manner of preparation (Turesky *et al*. 1993).

Occupational exposure to IQ may occur where employees prepare or serve broiled or fried foods, such as beef, fish, or eggs, but no studies that examined this question were found in the literature. It is not known whether exposure to IQ by ingestion, inhalation, or dermal contact would occur in this setting.

REGULATIONS

OSHA regulates 2-amino-3-methylimidazo[4,5-*f*]quinone under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 12.

REFERENCES

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Naturally Occurring and Synthetic Food Components, Furocoumarins and Ultraviolet Radiation. Vol. 40. Lyon, France: IARC, 1986. 444 pp.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Some Naturally Occurring Substances: Food Items and Constituents, Heterocyclic Aromatic Amines, and Mycotoxins. Vol. 56. Lyon, France: IARC, 1993. 571 pp.

Turesky, R.J., W.G. Stillwell, P.L. Skipper, and S.R. Tannenbaum. Metabolism of the food-borne carcinogens 2-amino-3-methylimidazo-[4,5-*f*]quinoline and 2-amino-3,8-dimethylimidazo[4,5-*f*]-quinoxaline in the rat as a model for human biomonitoring. Environ. Health Perspect., Vol. 99, 1993, pp. 123-128.

Yamashita, M., K. Wakabayashi, M. Nagao, S. Sato, Z. Yamaizumi, M. Takahashi, N. Kinae, I. Tomita, and T. Sugimura. Detection of 2-amino-3-methylimidazo[4,5-f]quinoline in cigarette smoke condensate. Jpn. J. Cancer Res., Vol. 77, 1986, pp. 419-422.