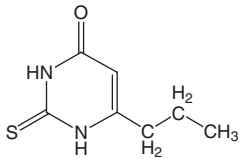
Propylthiouracil
CAS No. 51-52-5

Reasonably anticipated to be a human carcinogen
First Listed in the *Fourth Annual Report on Carcinogens* (1985)



Carcinogenicity

Propylthiouracil is *reasonably anticipated to be a human carcinogen* based on sufficient evidence for carcinogenicity in experimental animals (IARC 1974, 1982, 1987, 2001). When administered in the diet, propylthiouracil induced chromophobe adenomas of the anterior pituitary and carcinomas of the thyroid in mice and solid and cystic type adenomas of the thyroid in female rats. Propylthiouracil administered in the drinking water induced increased incidences of thyroid carcinomas and adenomas in rats of both sexes, malignant thyroid lesions, with some metastases, in hamsters of both sexes, and thyroid adenomas in male guinea pigs. Simultaneous administration of propylthiouracil and dried thyroid powder induced single or multiple chromophobe adenomas of the pituitary and carcinomas and adenomas of the thyroid in rats of both sexes. Administration of propylthiouracil and potassium iodide in the drinking water increased the incidence of thyroid adenomas and induced one carcinoma in rats. In a short-term study, oral administration of propylthiouracil induced hyperplasia of the thyroid in dogs (IARC 1974, 1982).

No adequate data were available from human studies to evaluate the carcinogenicity of propylthiouracil in humans (IARC 1974, 1982, 1987, 2001). In a survey of 331 hyperthyroid patients treated with antithyroid drugs and later with thyroidectomy, four malignant thyroid lesions were detected in patients diagnosed with Grave's disease; for these patients, drug therapy had continued for at least one year. There has also been a single case report of acute myeloblastic leukemia in a woman following propylthiouracil treatment (Aksoy *et al.* 1974, IARC 1982). Two case-control studies of thyroid cancer did not show a significant association with treatment with anti-thyroid medications (IARC 2001).

Properties

Propylthiouracil occurs as a white, crystalline powder with a starch-like appearance and a bitter taste. It is sensitive to light and prolonged exposure to air. It is slightly soluble in water at 20°C, soluble in boiling water, ethanol, acetone, and aqueous solutions of ammonia and alkali hydroxides, and practically insoluble in ether, chloroform, and benzene. It forms complexes with metals and reacts with sulfhydryl-oxidizing agents (IARC 1974, HSDB 2001).

Use

Propylthiouracil is commercially available in the United States as a USP grade containing 98 to 100.5% active ingredient on a dried basis, with small amounts of thiourea present as an impurity. Propylthiouracil has been used since the 1940s as an antithyroid agent for the treatment of hyperthyroidism. Veterinary applications of propylthiouracil reportedly included its use as a metabolic depressant to promote fattening in animals, but this use has been banned (IARC 1974, 2001).

Production

Current production data for propylthiouracil are not available. Chem Sources (2001) identified 10 U.S. suppliers of the compound. The 1979 TSCA Inventory identified one producer of propylthiouracil producing 500 lb in 1977 and one importer with no reported import volume (TSCA 1979). No current data on import or exports of propylthiouracil were available.

Exposure

The primary route of potential human exposure to propylthiouracil is ingestion of the compound as a drug. Potential occupational exposure to propylthiouracil may occur during the production, formulation, packaging, or administration of pharmaceuticals. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 297 workers were potentially exposed to propylthiouracil in the workplace (NIOSH 1976). The National Occupational Exposure Survey (1981-1983) indicated that 1,775 workers, including 817 women, potentially were exposed to propylthiouracil. This estimate was derived from observations of the use of the actual compound (89% of total observations) and trade name products (11%) (NIOSH 1984, HSDB 2001).

Regulations

CPSC

Any orally-administered, prescription drug for human use requires child-resistant packaging

EPA

Resource Conservation and Recovery Act
Listed as a Hazardous Constituent of Waste

FDA

Propylthiouracil is a prescription drug subject to specific labeling requirements

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