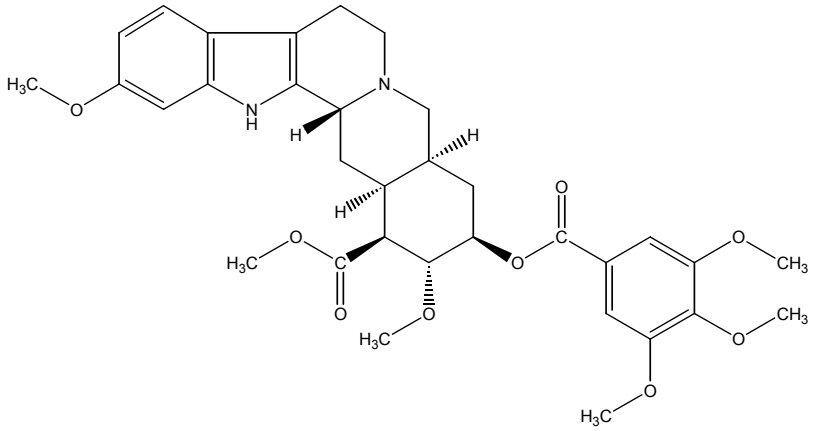
RESERPINE
CAS No. 50-55-5
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

Reserpine is *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity in experimental animals (NCI 1980). When administered in the diet, reserpine increased the incidence of adrenal medullary pheochromocytomas in male rats and mammary adenocarcinomas in female mice, and induced undifferentiated carcinomas of the seminal vesicles in male mice. When administered by subcutaneous injection, reserpine slightly increased adrenal pheochromocytomas in rats and mammary neoplasms in mice. An IARC Working Group considered the evidence for the carcinogenicity of reserpine in experimental animals to be limited (IARC 1980, 1982, 1987).

No adequate human studies of the relationship between exposure to reserpine and human cancer have been reported (IARC 1976, 1980, 1982, 1987). The available evidence relating exposure to reserpine with breast cancer is not consistent, both between and within studies. However, because of sampling variation, a small increase in the risk of breast cancer development can not be eliminated (IARC 1980).

PROPERTIES

Reserpine occurs as white or slightly yellow crystals or crystalline powder. It is very sparingly soluble in water, slightly soluble in acetone, methanol, ethanol, diethyl ether, and aqueous solutions of acetic and citric acids, and soluble in chloroform, dichloromethane, glacial acetic acid, benzene, and ethyl acetate. Reserpine is sensitive to oxidation and hydrolysis. The compound acquires a yellow color with pronounced fluorescence, especially after the addition of acid or exposure to light. When heated to decomposition, it emits toxic fumes of nitrogen oxides (IARC 1976, HSDB 2001, NTP 2001).

USE

Reserpine is a naturally occurring alkaloid produced by several members of the genus *Rauwolfia*, a climbing shrub indigenous to southern and southeast Asia. The compound is used primarily as a peripheral antihypertensive and as a central depressant and sedative. It is used for the management of hypertension and as a sedative for mild anxiety and chronic psychoses. Reserpine has also been used in poultry feeds as a sedative and to prevent aortic rupture in turkeys (IARC 1976, NTP 2001). It has also found use as a radioprotective agent and experimentally as a contraceptive (Kirk-Othmer 1979, 1983). Extracts of *Rauwolfia serpentina* have been used medicinally in India for centuries. They were used in primitive Hindu medicine for a variety of conditions, including snakebite, hypertension, insomnia, and insanity (IARC 1976).

PRODUCTION

There is no known commercial production of synthetic reserpine; the chemical is extracted from the roots of *Rauwolfia serpentina* with alcohols or aqueous acid and then purified (IARC 1976). Chem Sources (2001) identified 12 current U.S. suppliers for reserpine. Six producers of reserpine in the U.S. were identified in 1974 (IARC 1976) and one producer was identified in 1977 (TSCA 1979). Annual U.S. sales of reserpine for use in human medicine were approximately 440,000 lb in 1976 (IARC 1976). The U.S. imported 22 lb in 1970 and 103 lb in 1983 and 1984. U.S. exports are negligible (HSDB 2001).

EXPOSURE

The use of reserpine as a drug may result in its release to the environment in various waste streams. Occupational exposure may occur through dermal contact at workplaces where reserpine is produced or used (HSDB 2001). The National Occupational Exposure Survey (1981-1983) indicated that 5,516 workers, including 2,344 women, potentially were exposed to reserpine. This estimate was derived from observations of the actual use of the compound (97% of total observations) and the use of trade name products known to contain the compound (3%) (NIOSH 1984). Health professionals such as doctors, nurses, and pharmacists, may be potentially exposed while dispensing, preparing, or administering the pharmaceutical to patients with hypertension.

REGULATIONS

Under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), EPA has established a reportable quantity (RQ) for reserpine of 5,000 lb. Reserpine is regulated as a hazardous constituent of waste under the Resource Conservation and Recovery Act (RCRA).

FDA regulates reserpine as a prescription drug approved for human use and formerly regulated its use in animal diets. FDA has revoked the use of reserpine as a component of premixed turkey feed.

OSHA regulates reserpine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 158.

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