

Hydralazine and Its Salts

Hydralazine and its salts are antihypertensive agents that act to dilate arterial smooth muscle. Hydralazine chloride is a prescription drug.

Hydralazine and its salts passed the human and animal data screens, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

- Case-control study as reviewed in IARC (1980, pp. 94-95)
 - Elevated relative risk estimate (*not significant*) for breast cancer in National Breast-Cancer Screening project: Williams (1978)
- Cohort studies (*no increased risk*) as reviewed in IARC (1987, pp. 222-223)
 - all cancers: Rogers (1984)
 - breast cancers: Kaufman (1987)
- Case report as reviewed in IARC (1980, pp. 94-95)
 - Four of 24 patients with hydralazine toxicity developed cancer (2 breast carcinomas and 2 lung carcinomas). One of 92 patients without hydralazine toxicity developed cancer: Perry (1963)

Animal carcinogenicity data

- Lifetime drinking water studies
 - Male and female Swiss mice: Toth (1978)
 - *Increase in lung tumors (by pairwise comparison) in male and female mice*
 - Male and female Swiss mice: Drozd et al. (1987)
 - *Increase in lung tumors (by pairwise comparison) in male and female mice*
- Long-term diet studies
 - 2-year gavage studies in male and female Sprague-Dawley rats: FDA (1985)
 - *Increase in benign interstitial cell tumors (by pairwise comparison) in testes of males*
 - *Increase in benign hepatic neoplastic nodules (by pairwise comparison) in males and females*

- 87-week diet study in male Sprague-Dawley rats: Gershbein (1992) as reviewed in CCRIS (1996)
 - *No treatment-related findings*
- Subcutaneous study
 - Weekly dosages in intact and partially hepatectomized male Sprague-Dawley rats: Gershbein (1992) as reviewed in CCRIS (1996)
 - *No treatment-related findings*

Other relevant data

- Genotoxicity : as reviewed by IARC or FDA (1986) or cited in CCRIS (1996)
 - Mutagenicity in *Salmonella typhimurium* strain TA100, TA102, TA1530, and TA 1535 (*positive*)
 - Mutagenicity in *Salmonella typhimurium* strain TA1537, TA 1538, TA 98 (*negative*): Tosk et al (1979)
 - *In vitro* poly A test (*positive*)
 - *Salmonella* intrasanguine host mediated assay/NMRI mouse in tester strains TA100, TA1535, TA1537 (*positive*)
 - Sister chromatid exchange in Chinese hamster (*negative*)
 - BALB/3T3 cell formation assay (*negative*)
 - DNA repair test in rat hepatocytes (*positive and negative*)
 - DNA repair test in human fibroblasts (*negative*)
 - DNA repair test in rabbit hepatocytes (*positive in slow acetylator hepatocytes; negative in fast acetylator hepatocytes*)
 - Unscheduled DNA synthesis in rat hepatocytes (*negative*)
 - Unscheduled DNA synthesis in rat liver (*positive*)
- Mechanistic considerations
 - Decrease of superoxide dismutase and increase of free radicals in lung tissue: Drozd et al. (1987)

Reviews

- IARC (1980)
- IARC (1987)

References¹

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CCRIS (1996). Hydralazine Hydrochloride. Record number 334. National Library of Medicine (last updated on 01/02/1996)

Toth B (1978). Tumorigenic effect of 1-Hydrazinophthaline hydrochloride in mice. *J Natl Cancer Institute* **61**(5):1363-1365.

¹ Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.