

Gentian Violet

Gentian violet is a triphenylmethane dye mixture containing crystal violet (hexamethylpararosaniline chloride, 96%), methyl violet (pentamethylpararosaniline chloride) and brilliant green (tetramethylpararosaniline chloride). It is used as an anti-infective agent and in the Gram stain test for bacterial identification. Other applications include uses for hair dye or dyes for paper or textiles. It is no longer used as an additive in livestock feed. Occupational exposure may occur during the manufacture or use of gentian violet. Consumers may be exposed as a result of its use in anti-infective agents or hair dye.

Gentian violet passed the animal data screen, 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

No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Two-year feeding studies in mice
 - Male and female B6C3F₁ mice: Littlefield *et al.* (1985)
 - *Increases in hepatocellular carcinoma, type-A reticulum cell sarcoma in multiple organs (uterus, bladder, ovaries and vagina), and Harderian gland adenoma in females (by pairwise comparison and trend for all endpoints)*
 - *Increases in hepatocellular carcinoma (by pairwise comparison and trend) and Harderian gland adenoma (by pairwise comparison) in males*
- Lifetime feeding studies in rats
 - Male and female F344 rats exposed from conception through 104 weeks after birth: Littlefield *et al.* (1989)
 - *Increases in thyroid follicular cell adenocarcinoma (by pairwise comparison and trend) and hepatocellular adenoma (by pairwise comparison) in females*
 - *Increases in thyroid follicular cell adenocarcinoma and hepatocellular adenoma in males (by pairwise comparison and trend)*

Other relevant data

- Genotoxicity
 - Mutagenicity in *E. coli* (positive): Docampo and Moreno (1990, pp. 167-169)
 - Mutagenicity in *Salmonella typhimurium* (positive and negative): Aidoo *et al.* (1990)
 - Mutagenicity in Chinese hamster ovary (CHO) cells (negative): Aidoo *et al.* (1990)
 - *In vitro* (positive) and *in vivo* (negative) mouse DNA damage assays: Aidoo *et al.* (1990)
 - Gene amplification assays in a Chinese hamster cell line (positive): Aidoo *et al.* (1990)
 - Binding to DNA (positive): Docampo and Moreno (1990, pp. 167-169)
 - Chromosome breaks (positive): Docampo and Moreno (1990, pp. 167-169)
 - Reviews and compilations: Littlefield *et al.* (1989, pp. 239-240); CCRIS (1994); GENE-TOX (1995)

- Metabolism: Docampo and Moreno (1990, p. 171-174)

- Structure activity considerations
 - Benzyl violet 4B, an alkyl sulfonate derivative of gentian violet, is a Proposition 65 carcinogen: Littlefield *et al.* (1989, p. 240)
 - Magenta, a ring-methylated primary amine analog of gentian violet, is classified as an IARC Group 2B carcinogen: Baan *et al.* (2008)

References¹

Aidoo A, Gao N, Neft RE, Schol HM, Hass BS, Minor TY, Heflich RH (1990). Evaluation of the genotoxicity of gentian violet in bacterial and mammalian cell systems. *Teratog Carcinog Mutagen* **10**:449-62.

Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Coglianò V (2008). Carcinogenicity of some aromatic amines, organic dyes, and related exposures. *Lancet Oncol* **9**(4): 322-323.

Chemical Carcinogenesis Research Information System (CCRIS, 1994)
<http://toxnet.nlm.nih.gov> (accessed on July 9, 2009).

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.

Docampo R, Moreno SN (1990). The metabolism and mode of action of gentian violet. *Drug Metab Rev* **22**:161-78.

Genetic Toxicology Data (GENE-TOX, 1995) <http://toxnet.nlm.nih.gov/> (accessed on July 9, 2009)

Littlefield NA, Blackwell BN, Hewitt CC, Gaylor DW (1985). Chronic toxicity and carcinogenicity studies of gentian violet in mice. *Fundam Appl Toxicol* **5**:902-12.

Littlefield NA, Gaylor DW, Blackwell BN, Allen RR (1989). Chronic toxicity/carcinogenicity studies of gentian violet in Fischer 344 rats: two-generation exposure. *Food Chem Toxicol* **27**:239-47.