Hydroquinone

Hydroquinone is a high-volume commodity chemical. It is used as a developer for black-and-white photography, medical and industrial x-ray films, and graphic arts films. It is used as a reducing agent, an antioxidant and antiozonate for rubber, a polymerization inhibitor for acrylic and vinyl acetate monomers, a stabilizer in paints, varnishes, motor fuels and oils, and a chemical intermediate for agrochemicals, performance plastics, and dyes. It is used as an ingredient in skin lighteners, it is present in tobacco smoke, and it occurs naturally in trace amounts in some fruits, vegetables, grains, dairy products, coffee, tea, beer, and wine (McDonald *et al*., 2001). Occupational exposure is expected during manufacture and use. The general population may be exposed through its use as a photographic developer and a skin lightener, through exposure to tobacco smoke, and through consumption of foods containing hydroquinone in trace amounts.

Hydroquinone 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

- Occupational cohort studies
  - Photographic processors: Friedlander *et al*. (1982)
  - Chemical plant workers: Pifer *et al.* (1986)
  - Chemical plant workers with at least six months employment in hydroquinone manufacturing or other areas where hydroquinone was used: Pifer *et al.* (1995)
  - Danish lithographers: Nielsen *et al*. (1996), as described in IARC (1999)
  - Motion picture film processors: Fryzek *et al*. (2005)

Animal carcinogenicity data

- Oral studies in rats
  - Two-year gavage studies in male and female Fischer 344/N rats: NTP (1989), Kari *et al*. (1992)
  - Two-year diet studies in male and female Fischer 344 rats: Shibata *et al*. (1991)
  - Two-year diet studies in Sprague Dawley rats: Carlson and Brewer (1953), as described in NTP (1989, p. 20)
  - 51-week diet study in male Fischer 344 rats: Hirose *et al*. (1989), as described in IARC (1999)
  - 49-week diet study in male Fischer 344 rats: Yamaguchi *et al*. (1989), as described in IARC (1999)

- Oral studies in mice
  - Two-year gavage studies in male and female B6C3F$_1$ mice: NTP (1989), Kari *et al*. (1992)
  - 96-week diet studies in male and female B6C3F$_1$ mice: Shibata *et al*. (1991)

- Cholesterol pellet urinary bladder implantation study in mice
  - Observed for 25 weeks after pellet implantation: Boyland *et al*. (1964)

- Co-carcinogenicity study in mice
  - Female ICR/Ha Swiss mice administered hydroquinone and benzo[a]pyrene dermally for one year: Van Duuren and Goldschmidt (1976), as described in NTP (1989, p. 20)

- Initiation study in mice
  - Male "S" strain mice (skin tumor assay: single dermal application of hydroquinone as initiator—promotion with croton oil, assessed 22 weeks after initiation): Roe and Salaman (1955), as described in NTP (1989, p. 20)

- Promotion studies in rats
  - Male Fischer 344 rats (bladder tumor assay: initiation—ureteric ligation—promotion with hydroquinone in diet for 22 weeks, observed for an additional two weeks): Miyata *et al*. (1985), as described in IARC (1999)
  - Male Fischer 344 rats (stomach tumor assay: initiation—promotion with hydroquinone in diet for 51 weeks): Hirose *et al*. (1989), as described in IARC (1999)
  - Male Sprague-Dawley rats (liver tumor assay: initiation and /or partial hepatectomy—promotion with hydroquinone in diet for six weeks or gavage for seven weeks): Stenius *et al*. (1989), as described in IARC (1999)
  - Male Fischer 344 rats (upper digestive tract tumor assay: initiation—promotion with hydroquinone in diet for 49 weeks): Yamaguchi *et al*. (1989), as described in IARC (1999)
  - Male Fischer 344/Du Crj rats (initiation—promotion with hydroquinone in diet for 30 weeks: Hasegawa *et al*. (1990), as described in IARC (1999)
  - Male Fischer 344 rats (bladder tumor assay: initiation—promotion with hydroquinone in diet for 36 weeks): Kurata *et al*. (1990), as described in IARC (1999)
  - Male Wistar/Crj rats (liver and kidney tumor assay: initiation—promotion with hydroquinone in diet for 36 weeks): Okazaki *et al*. (1993), as described in IARC (1999)

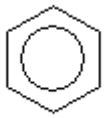
- Promotion studies in hamsters
    - Female Syrian golden hamsters (pancreatic tumor assay: initiation—promotion with hydroquinone in diet for 16 weeks): Maruyama *et al.* (1991), as described in IARC (1999)

Other relevant data

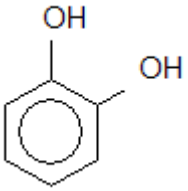
- Genotoxicity
    - *In vitro* tests
        - *Salmonella typhimurium* reverse mutation assay: NTP (1989), Hakura *et al*. (1996)
        - Syrian hamster embryo (SHE) cell mutation assay: Tsutsui *et al*. (1997)
        - Induction of trifluorothymidine-resistence in mouse lymphoma cells: NTP (1989)
        - Sister chromatid exchange in Chinese hamster ovary (CHO) cells: NTP (1989)
        - Sister chromatid exchange in SHE cells: Tsutsui *et al*. (1997)
        - Sister chromatid exchange in human lymphocytes: Silva M *et al.* (2004)
        - Chromosomal aberrations in CHO cells: NTP (1989)
          Chromosomal aberrations in SHE cells: Tsutsui *et al*. (1997)
        - Chromosome aneuploidy assay in human lymphocytes: Eastmond *et al*. (1994)
        - Micronucleus assay in Chinese hamster V79 cells: Dobo and Eastmond (1994)
        - Micronucleus assay in human lymphocytes: Yager *et al*. (1990), Robertson *et al*. (1991), Silva M *et al.* (2004)
        - Unscheduled DNA synthesis in SHE cells: Tsutsui *et al*. (1997)
        - DNA damage in human white blood cells: Andreoli *et al*. (1999),
        - DNA damage in human hepatoma HepG2 cells: Luo *et al*. (2008)
        - Morphological cell transformation assay in SHE cells: Tsutsui *et al*. (1999)
    - *In vivo* tests
        - *Drosophila* sex-linked recessive lethal mutation assay: NTP (1989)
        - Micronucleus assay in mouse bone marrow: Adler & Kliesch (1990), Marrazzini *et al*. (1994), Chen and Eastmond (1995)
        - Chromosomal aberrations in mice: Marrazinni *et al*. (1994)
        - Aneuploidy in mice: Marrazinni *et al*. (1994), Chen and Eastmond (1995)
    - Reviews: NTP (1989, pp. 16, 18-20), IARC (1999, pp. 703-710)

- Metabolite of a carcinogen
    - Hydroquinone is a metabolite of the Proposition 65 carcinogen benzene.

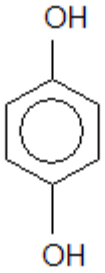
- Structure activity comparisons



Benezene
(Proposition 65 carcinogen)



Catechol
(Proposition 65 carcinogen)



Hydroquinone

Reviews

- McGregor D (2007)
- McDonald *et al*. (2001)
- IARC (1999)

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[1] Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.

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