1,4-BENZOQUINONE (*para*-QUINONE)

Data were last reviewed in IARC (1977) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

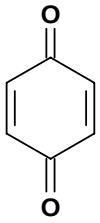
1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 106-51-4

Systematic name: 2,5-Cyclohexadiene-1,4-dione

Synonym: *para*-Benzoquinone

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_6H_4O_2$ Relative molecular mass: 108.09

1.1.3 *Physical properties* (for details, see IARC, 1977)

(*a*) *Melting-point*: 115.7°C

(*b*) *Conversion factor*: $mg/m^3 = 4.73 \times ppm$

1.2 Production and use

1,4-Benzoquinone was first produced commercially in 1919, and has since been manufactured in several European countries, Japan and the United States. Its major use is in hydroquinone production, but it is also used as a polymerization inhibitor and as an intermediate in the production of a variety of substances, including rubber accelerators and oxidizing agents (IARC, 1977).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

1,4-Benzoquinone was tested for carcinogenicity in mice by skin application and inhalation and in rats by subcutaneous injection. The available data are insufficient to evaluate the carcinogenicity of this compound (IARC, 1977).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

1,4-Benzoquinone is readily absorbed from the gastrointestinal tract and subcutaneous tissue [species not specified]. It is excreted partly unchanged and partly as hydroquinone, the major proportion of which is eliminated as acid conjugates (IARC, 1977).

4.2 Toxic effects

4.2.1 *Humans*

Application of 1,4-benzoquinone causes local skin changes including discoloration, erythema and the appearance of papules; necrosis can occur. Exposure to vapours induces serious vision disturbances; injury extends through the entire conjunctiva and cornea (IARC, 1977).

4.2.2 *Experimental systems*

1,4-Benzoquinone depresses respiration in tissue preparations. Large doses induce local irritation, clonic convulsions, decreased blood pressure and death due to paralysis of the medullary centres. Signs of kidney damage were observed in severely poisoned animals (IARC, 1977).

1,4-Benzoquinone is a metabolite of benzene. Exposure to 1,4-benzoquinone of cultured murine peritoneal macrophages for 10 min at 12.5 μM inhibited Fc and complement receptor-mediated phagocytosis by ≥ 90%, although macrophage viability was unaffected. In this comparative study, 1,4-benzoquinone was the most potent of the benzene metabolites tested, and Fc receptor-mediated phagocytosis was not regained after overnight incubation in the presence of 1,4-benzoquinone. There was little effect upon Fc receptor-binding of target cells, whereas there was a marked decrease in the filamentous actin content of the macrophages. 1,4-Benzoquinone bound in only low amounts to purified actin and did not affect its assembly; thus disruption of filamentous actin occurs by some mechanism other than direct alkylation (Manning *et al*., 1994).

The development of colony-forming unit-erythroid of bone marrow from male Swiss-Webster and C57BL/6J mice was reduced upon exposure to 1,4-benzoquinone in a dose-dependent manner from 10 μM, the lowest concentration tested (Neun *et al*., 1992).

At a concentration of 3 μM, 1,4-benzoquinone caused 50% inhibition of CPP32, an interleukin-1β-enzyme/Ced-3 cysteine protease involved in the implementation of apoptosis and which is present in myeloid cells (Hazel *et al*., 1996).

1,4-Benzoquinone was reported to be dysmorphogenic to rat embryos in an in-vitro system at a concentration of 10 μM but not at 50 μM for 30 h. It was lethal at 100 μM (Chapman *et al*., 1994).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

Results of mutation tests with *Salmonella typhimurium* are inconclusive, but 1,4-benzoquinone does not cause mutations in *Neurospora crassa*. In cultured mammalian cells, it induced DNA strand breakage, mutation at the *hprt* locus and micronuclei. It also induced micronuclei in the bone-marrow cells of mice treated *in vivo*. Dominant lethal effects were not induced in male mice by a single low dose.

5. Evaluation

No epidemiological data relevant to the carcinogenicity of 1,4-benzoquinone were available.

There is *inadequate evidence* in experimental animals for the carcinogenicity of 1,4-benzoquinone.

Overall evaluation

1,4-Benzoquinone is *not classifiable as to its carcinogenicity to humans (Group 3)*.

6. References

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Table 1. Genetic and related effects of 1,4-benzoquinone

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	5.0	Nazar *et al*. (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	16.5	Mortelmans *et al*. (1986)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	16.5	Mortelmans *et al*. (1986)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	16.5	Mortelmans *et al*. (1986)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	16.5	Mortelmans *et al*. (1986)
NCF, *Neurospora crassa*, forward mutation to pyrimidine dependence	–	NT	NG	Reissig (1963)
NCR, *Neurospora crassa*, reverse mutation to *arg*$^+$	–	NT	NG	Reissig (1963)
DIA, DNA strand breaks, mouse lymphoma L5178YS cells *in vitro*	+	NT	0.11	Pellack-Walker & Blumer (1986)
G9H, Gene mutation, Chinese hamster lung V79 cells, *hprt* locus *in vitro*	+	NT	0.54	Ludewig *et al*. (1989)
SIC, Sister chromatid exchange, Chinese hamster lung V79 cells *in vitro*	–	NT	11	Ludewig *et al*. (1989)
MIA, Micronucleus test, Chinese hamster lung V79 cells *in vitro*	+	NT	5.4	Ludewig *et al*. (1989)
MIA, Micronucleus test, animal cell lines (V79, IEC-17 and 18) *in vitro*	+	NT	0.01	Glatt *et al*. (1990)
DIH, DNA strand breaks, cross-links or related damage, human lymphocytes *in vitro* (comet assay)	–	+	11	Anderson *et al*. (1995)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	NT	0.55	Erexson *et al*. (1985)
MIH, Micronucleus test, HuFoe-15 embryonal human liver cells *in vitro*	+	NT	0.01	Glatt *et al*. (1990)
MIH, Micronucleus test, human lymphocytes *in vitro*	+	NT	0.275	Yager *et al*. (1990)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
MVM, Micronucleus test, pregnant CD-1 mouse bone-marrow cells *in vivo*	(+)		20 po × 1	Ciranni *et al*. (1988a)
MVM, Micronucleus test, fetal CD-1 mouse liver cells *in utero*	(+)		20 (to dam) × 1	Ciranni *et al*. (1988a)
MVM, Micronucleus test, CD-1 mice *in vivo*	(+)[c]		20 po × 1	Ciranni *et al*. (1988b)
DLM, Dominant lethal test, male C3H and (C3H × 101)F_1 mice *in vivo*	–		6.25 ip × 1	Röhrborn & Vogel (1967)

[a] +, positive; (+), weak positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; NG, not given; po, oral; ip, intraperitoneal

[c] Negative if 5 mg/kg bw is given by the intraperitoneal route, which causes greater toxicity.

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