DICHLOROACETYLENE

Data were last reviewed in IARC (1986) 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.: 7572-29-4
Chem. Abstr. Name: Dichloroethyne
IUPAC Systematic Name: Dichloroacetylene

1.1.2 *Structural and molecular formulae and relative molecular mass*

ClC≡CCl

C_2Cl_2 Relative molecular mass: 94.93

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Volatile liquid with a disagreeable, sweetish odour (American Conference of Governmental Industrial Hygienists, 1991)
(*b*) *Boiling-point*: 33°C (explodes) (American Conference of Governmental Industrial Hygienists, 1991; Lide, 1997)
(*c*) *Melting-point*: –66°C (Lide, 1997)
(*d*) *Solubility*: Soluble in ethanol, diethyl ether and acetone (Lide, 1997)
(*e*) *Stability*: Explodes on heating strongly, ignites on contact with air; severe explosion hazard when shocked or exposed to heat or air; can react vigorously with oxidizing materials (American Conference of Governmental Industrial Hygienists, 1991)
(*f*) *Conversion factor*: $mg/m^3 = 3.9 \times ppm$

1.2 Production and use

Dichloroacetylene is not available in commercial quantities. It is reported to be a by-product in the synthesis of vinylidene chloride (Reichert *et al*., 1980). The compound may also be produced from the pyrolysis of various chlorohydrocarbons.

Dichloroacetylene is not known to be used commercially.

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997), fewer than 100 workers in the United States were potentially exposed to dichloroacetylene (see General Remarks).

1.3.2 *Environmental occurrence*

No data were available to the Working Group.

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has not recommended an 8-h time-weighted average threshold limit value but has recommended 0.39 mg/m^3 as the ceiling value for occupational exposures to dichloroacetylene in workplace air. Similar values have been used as standards or guidelines in other countries (International Labour Office, 1991).

No international guideline for dichloroacetylene in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Dichloroacetylene was tested for carcinogenicity in mice and rats by inhalation. A treatment-related increase was observed in the incidence of adenocarcinomas of the kidney in male mice. In rats, the occurrence of benign tumours of the liver and kidney and an increased incidence of lymphomas were reported (IARC, 1986).

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*

The metabolism of inhaled [^{14}C]dichloroacetylene has been studied in male Wistar rats exposed to 20 or 40 ppm [78 or 156 mg/m^3] atmospheres for 1 h. During the next

96 h, elimination of retained (approximately 17%) 20 and 40 ppm doses, respectively, was: urine, 68% and 60%; faeces, 28% and 27%. About 3.5% remained in the carcasses. Metabolites of dichloroacetylene that were identified were: *N*-acetyl-*S*-(1,2-dichlorovinyl)-L-cysteine (62%), dichloroethanol (12%), dichloroacetic acid (9%), oxalic acid (8%) and chloroacetic acid (5%) in urine; and *N*-acetyl-*S*-(1,2-dichlorovinyl)-L-cysteine in faeces. In bile, only *S*-(1,2-dichlorovinyl)glutathione was identified. Biliary cannulation did not influence the renal excretion of *N*-acetyl-*S*-(1,2-dichlorovinyl)-L-cysteine, a result that was interpreted to indicate that glutathione conjugation also occurs in the kidney. The identified metabolites are consistent with the existence of two metabolic pathways (Figure 1): the major pathway involves glutathione conjugation, while a minor pathway is cytochrome P450-dependent oxidation that accounts for the formation of 1,1-dichloro-compounds after chlorine migration (Kanhai *et al*., 1991).

In-vitro studies have demonstrated that glutathione conjugation of dichloroacetylene is predominantly enzymatic and the rate of reaction resulting in the formation of *S*-(1,2-dichlorovinyl)glutathione is similar for microsomes from rat kidney and liver (Kanhai *et al*., 1989). However, under different reaction conditions (20–500-fold higher protein concentrations), the rate was highest for microsomes from liver, followed by lung, brain and kidney (Patel *et al*., 1994). The further handling of this metabolite in kidney is not clearly defined, but it is known that γ-glutamyltranspeptidase and dipeptidases (e.g., in biliary epithelium) can transform *S*-(1,2-dichlorovinyl)glutathione to *S*-(1,2-dichlorovinyl)-L-cysteine, which can then be acetylated in tissues or by intestinal bacteria (Meister, 1988). An alternative to acetylation is β-lyase-mediated metabolism to form chlorothioketene as an intermediate (Dekant *et al*., 1988), which can react with tissue nucleophiles or with water, when it forms chloroacetic acid. Cysteine conjugate β-lyase activity has also been shown in rat cerebellar tissue (Patel *et al*., 1994).

4.2 Toxic effects

4.2.1 *Humans*

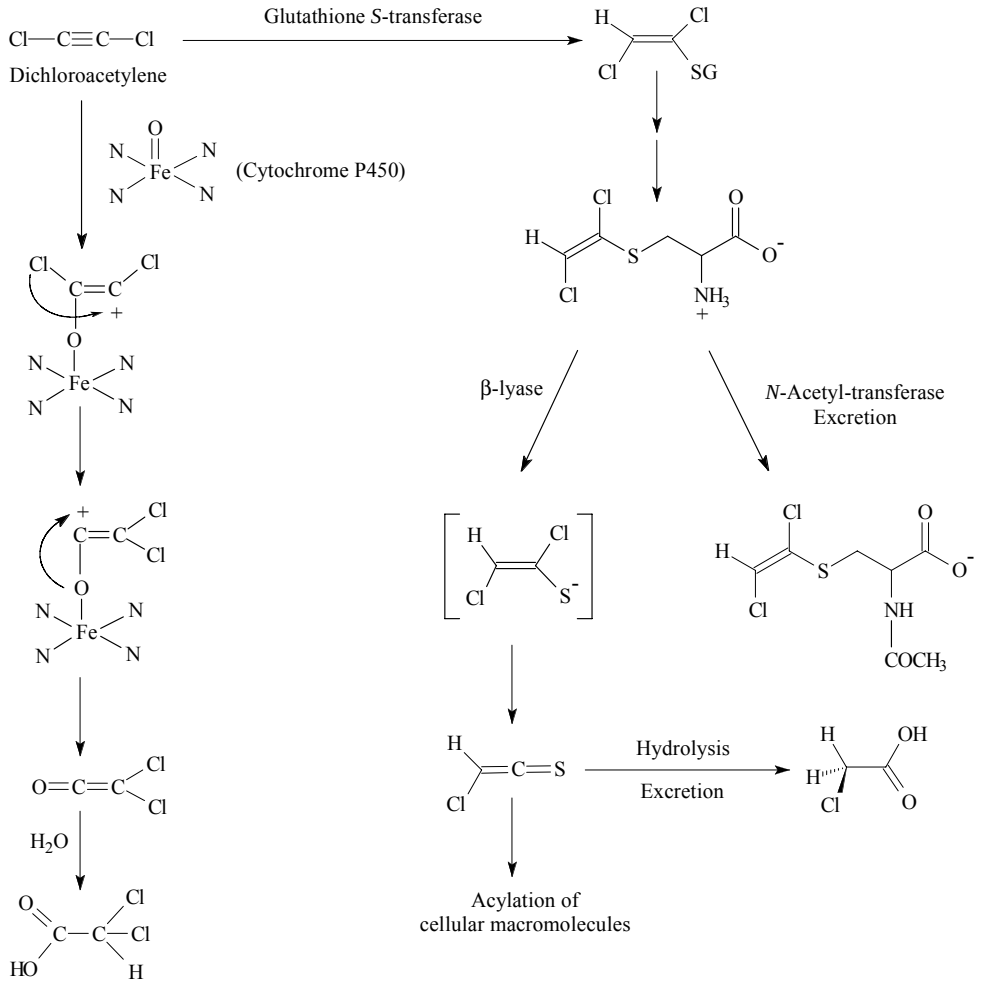
Toxic effects observed after accidental exposure to dichloroacetylene were mainly neurological disorders that persisted for periods ranging from several days to years (IARC, 1986).

4.2.2 *Experimental systems*

Dichloroacetylene inhalation induced nephrotoxic effects in rats and male rabbits including tubular and focal necrosis in the collecting tubules and increased mitotic activity in the renal epithelium. Hepatotoxic effects and neuropathological changes were also reported in male rabbits (IARC, 1986).

In-vitro studies on LLC-PK_1 cells with *S*-(1,2-dichlorovinyl)-L-cysteine have shown that Ca^{++} release from mitochondria is followed by DNA double-strand breaks and increased poly(ADP-ribosyl)ation of nuclear proteins. The DNA fragmentation is secondary to the activation of Ca^{++} and Mg^{++}-dependent endonucleases (Vamvakas *et al*., 1992). However, at low, nontoxic concentrations (1 or 5 μM), *S*-(1,2-dichlorovinyl)-L-cysteine exposure for

Figure 1. Proposed metabolic pathways of dichloroacetylene by glutathione conjugate formation and cytochrome P450 oxidation



Redrawn from Kanhai *et al.* (1991)
SG, glutathionyl

seven weeks resulted in the appearance of stable, dedifferentiated clones that had lost a number of the characteristics of the renal tubule cells from which they were derived. There was also increased poly(ADP-ribosyl)ation and enhanced *c-fos* expression (Vamvakas *et al.*, 1996). Increased poly(ADP-ribosyl)ation was also induced *in vivo*, following administration to male Wistar rats of *S*-(1,2-dichlorovinyl)-L-cysteine. A similar response was observed with certain renal carcinogens (potassium bromate and ferric nitriloacetate) but not others (trimethylpentane and *N*-nitrosodimethylamine) (McLaren *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 also Table 1 for references)

Dichloroacetylene was mutagenic to *Salmonella typhimurium* in the presence or absence of an exogenous metabolic system (IARC, 1986).

5. Evaluation

No epidemiological data relevant to the carcinogenicity of dichloroacetylene were available.

There is *limited evidence* in experimental animals for the carcinogenicity of dichloroacetylene.

Overall evaluation

Dichloroacetylene is *not classifiable as to its carcinogenicity to humans (Group 3).*

6. References

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Table 1. Genetic and related effects of dichloroacetylene

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	5000 ppm	Reichert *et al.* (1983)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	5000 ppm	Reichert *et al.* (1983)

[a] +, positive; –, negative
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL

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