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**TOXICOLOGICAL EVALUATION OF SOME**

**EXTRACTION SOLVENTS AND CERTAIN**

**OTHER SUBSTANCES**

The content of this document is the

result of the deliberations of the Joint

FAO/WHO Expert Committee on Food Additives

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Food and Agriculture Organization of the United Nations

World Health Organization

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1,2-DICHLORETHANE (Ethylene dichloride)

Biological Data

Biochemical aspects

1,2-dichloroethane is absorbed through the shaved rabbit skin and

partially excreted through the lungs. Absorption also occurs via the

lungs or gastro-intestinal tract (Patty, 1958). It probably

metabolises to oxalic acid but rabbits exhale it mainly unchanged

(Williams, 1959). Oral administration to female rats depressed hepatic

glutathione level by approximately 50% (Johnson, 1965).

Acute toxicity

Animal Route LD50 LD100 Reference

mg/kg

body weight

mouse inhalation - 9 000 ppm Lazarew, 1929

oral 910 - Spector, 1955

i.p. 470 - Baganz et al., 1961

rat oral 680-770 - McCollister et al., 1956

s.c. 1 000 - Highman et al., 1951

inhalation 1 000 - Carpenter, 1949

guinea-pig inhalation - 3 000 ppm Heppel et al., 1944

rabbit percutaneous 2 800 - Patty, 1958

s.c. - 1.6 g/kg Barsoum & Saad, 1934

oral 910 - Spector, 1955

dog oral 5 700 2.5 g/kg Spector, 1955

i.v. - 175 mg/kg Barsoum & Saad, 1934

man oral - 56 ml Hueper & Smith, 1955

The compound has the anaesthetic and CNS depressant properties common

to chlorinated hydrocarbons and causes lacrimation, conjunctivitis and

nasal irritation followed by vertigo, ataxia and shallow respiration

(Browning, 1965). Inhalation and s.c. injection produce corneal

opacities but only in dogs and foxes, not in man. These lesions were

usually reversible and not due to direct vapour contact. Tolerance may

develop. Histology revealed corneal oedema, endothelial degeneration

and polymorph infiltration (Browning, 1965). Rats exposed to 3 000 ppm

showed liver, kidney and adrenal changes (Spencer et al., 1951). Oral

administration in dogs caused kidney, liver and G.I. tract irritation

van Oettingen, 1955). Ethylene dichloride has slight haemolytic

activity (Heppel et al., 1946; Spencer et al., 1951). Single i.p.

administration to male mice produced a non-related proteinurea but no

glycosurea (Plaa & Larson, 1965).

Short-term tests

Inhalation exposure of guinea-pigs, rats, rabbits, cats, monkeys

and dogs, on a 5x weekly basis, for 7 hours/day for over 6 months,

indicates 100 ppm in air to be a "no effect" level. Species

sensitivity is variable, but effects on guinea-pig liver parenchyma

and on body weight were observed at 200 ppm levels. The only

consistent abnormal findings in all species were fatty changes in the

liver. Monkeys and guinea-pigs also showed changes in renal tubular

epithelium histology.

Observations in man

In man, acute poisoning by ingestion produces depressed

consciousness, haemorrhagic colitis, nephrosis, renal tubular

calcification, and circulatory failure, death occurring with doses of

0.3-0.9 g/kg (Hueper 9, Smith, 1955; Hinkel, I965). Repeated skin

application causes dermatitis (Patty, 1958). Excessive single or

repeated inhalation by man causes pulmonary oedema, fatty degeneration

of the liver and kidney injury (Hadengue & Martin, 1953; Torkelson et

al., 1966). Chronic individual exposure for 9 weeks to 5 months

produced nausea, vomiting, loss of weight and epigastric pain, some

tongs tremor and nystagmus but no haematological, urinary or ECG

changes (McNally & Fostvedt, 1941), Chronic exposure also produces

liver, kidney and adrenal lesions (Patty, 1958). The TLV is 50 ppm

(Amer. Conf. Gov. Ind. Hyg., 1969).

Special studies

Ethylene dichloride - extracted whole fish flour was fed at 11.5%

and 23% of the protein of the diet to groups of 6 male rats for 3

weeks. No toxic effect on growth rate or liver weight were noted.

However lysine and methionine levels were slightly reduced (Morrison

et al., 1962). Further examination pointed to reactions between alkyl

halides and -SH groups to form thioethers (R-S-CH2-CH2-S-R).

Extracted fish protein contained less histidine and cystine and

inhibited the release of cystine by in vitro pancreatic digestion.

S,S1-ethylene bis cysteine was isolated from extracted protein but

was found to be unstable to autoclaving (Morrison & Munro, 1965).

Chlorocholine chloride (2-chloroethyl-trimethyl ammonium chloride) is

also formed only under extreme conditions of treatment which is toxic

to rats at intake levels above 2 400 ppm (Munro & Morrison, 1967).

Comments

This solvent has anaesthetic properties and as with many

chlorinated hydrocarbons, large doses appear to exert a toxic action

on the liver, kidney and adrenal. The formation of toxic interaction

compounds with certain food constituents occurs under grossly abnormal

and excessively severe conditions.

Tentative Evaluation

In foods suitable for dichloroethane extraction the use should be

restricted to that determined by good manufacturing practice, which is

expected to result in minimal residues unlikely to have any

toxicological effect. Manufacturing practice must also ensure that

toxic interaction products with treated foods do not occur.

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See Also:

[Toxicological Abbreviations](http://www.inchem.org/documents/eintro/eintro/abreviat.htm)

[Dichloroethane, 1,2- (EHC 176, 1995, 2nd edition)](http://www.inchem.org/documents/ehc/ehc/ehc176.htm)

[Dichloroethane, 1,2- (EHC 62, 1987, 1st edition)](http://www.inchem.org/documents/ehc/ehc/ehc62.htm)

[Dichloroethane, 1,2- (ICSC)](http://www.inchem.org/documents/icsc/icsc/eics0250.htm)

[Dichloroethane, 1,2- (WHO Food Additives Series 30)](http://www.inchem.org/documents/jecfa/jecmono/v30je07.htm)

[Dichloroethane, 1,2- (WHO Pesticide Residues Series 1)](http://www.inchem.org/documents/jmpr/jmpmono/v071pr14.htm)

[Dichloroethane, 1,2- (Pesticide residues in food: 1979 evaluations)](http://www.inchem.org/documents/jmpr/jmpmono/v079pr21.htm)

[Dichloroethane, 1,2- (CICADS 1, 1998)](http://www.inchem.org/documents/cicads/cicads/cicad01.htm)

[Dichloroethane, 1,2- (IARC Summary & Evaluation, Volume 71, 1999)](http://www.inchem.org/documents/iarc/vol71/015-dichloretha.html)