**FAO Nutrition Meetings**

 **Report Series No. 48A**

 **WHO/FOOD ADD/70.39**

 **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

 which met in Geneva, 24 June -2 July 19701

 Food and Agriculture Organization of the United Nations

 World Health Organization

 1 Fourteenth report of the Joint FAO/WHO Expert Committee on Food

 Additives, FAO Nutrition Meetings Report Series in press; Wld Hlth

 Org. techn. Rep. Ser., in press.

 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)