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TOXICOLOGICAL EVALUATION OF SOME EXTRACTION SOLVENTS AND CERTAIN OTHER SUBSTANCES

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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	LD_{50} mg/kg body weight	LD_{100}	Reference

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 ($R\text{-}S\text{-}CH_2\text{-}CH_2\text{-}S\text{-}R$). Extracted fish protein contained less histidine and cystine and inhibited the release of cystine by in vitro pancreatic digestion. S,S[1]-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
- Dichloroethane, 1,2- (EHC 176, 1995, 2nd edition)
- Dichloroethane, 1,2- (EHC 62, 1987, 1st edition)
- Dichloroethane, 1,2- (ICSC)

Dichloroethane, 1,2- (WHO Food Additives Series 30)
Dichloroethane, 1,2- (WHO Pesticide Residues Series 1)
Dichloroethane, 1,2- (Pesticide residues in food: 1979 evaluations)
Dichloroethane, 1,2- (CICADS 1, 1998)
Dichloroethane, 1,2- (IARC Summary & Evaluation, Volume 71, 1999)