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IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS

Some Monomers, Plastics and Synthetic Elastomers, and Acrolein

VOLUME 19

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of an IARC Working Group on the
Evaluation of the Carcinogenic Risk of Chemicals to Humans
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Simultaneous exposure to 1.75 g/m^3 (671 ppm) vinyl chloride with 200 ppm vinylidene chloride prevented vinylidene chloride-induced hepatic injury in fasted male rats. However, pre-exposure to concentrations of vinyl chloride which depleted hepatic glutathione concentrations significantly enhanced early acute hepatotoxic response to vinylidene chloride in fed rats (Jaeger *et al.*, 1975a,b).

Exposure of guinea-pigs to 260 g/m^3 (100 000 ppm) vinyl chloride for 2 hours/day for 3 months resulted in marked growth disturbances and intense histopathological and histochemical lesions in the liver, kidneys, spleen and lungs. Interruption of the exposure resulted in a regenerative effect, denoting a certain degree of reversibility of the hepatorenal lesions. Large quantities of vitamin C reduced the gravity of the lesions caused by vinyl chloride (Prodan *et al.*, 1975b).

Mice were exposed to 130, 650 or 2600 mg/m^3 (50, 250 or 1000 ppm) vinyl chloride for 6 hours/day on 5 days/week. The highest dose caused some acute deaths with toxic hepatitis and marked tubular necrosis in the renal cortex. From the 6th month of treatment, all mice became lethargic, lost weight quickly and died. Only a few mice exposed to 50 ppm survived for 12 months (Lee *et al.*, 1977).

The non-protein, free SH-groups of the liver are depleted in rats exposed to $390\text{--}5200 \text{ mg/m}^3$ (150–2000 ppm) vinyl chloride for 1–7 hours, as a function both of concentration and duration of exposure (Watanabe *et al.*, 1976a).

Vinyl chloride and two of its presumed metabolites, chloroethylene oxide and chloroacetaldehyde, depressed DNA synthesis in rat liver *in vivo* (Border & Webster, 1977).

Embryotoxicity and teratogenicity

Pregnant CF-1 mice were exposed by inhalation to 130 and 1300 mg/m^3 (50 and 500 ppm) vinyl chloride on days 6–15 of gestation, Sprague-Dawley rats to 1300 and 6500 mg/m^3 (500 and 2500 ppm) on days 6–15 of gestation, and New Zealand rabbits to 1300 and 6500 mg/m^3 (500 and 2500 ppm) on days 6–18 of gestation, for 7 hours/day, with or without simultaneous exposure to 15% ethanol in the drinking-water. A significantly increased incidence of several skeletal anomalies was observed in offspring of mice that received vinyl chloride plus ethanol (John *et al.*, 1977; Schwetz *et al.*, 1975).

Absorption, distribution, excretion and metabolism

The *in vivo* and *in vitro* metabolism of vinyl chloride has been studied and reviewed (Antweiler, 1976; Bartsch & Montesano, 1975; Bonse & Henschler, 1976; Green & Hathway, 1975, 1977; Haley, 1975; Hefner *et al.*, 1975; Malaveille *et al.*, 1975; Müller & Norpoth, 1975; Müller *et al.*, 1976; Plugge & Safe, 1977; Watanabe & Gehring, 1976; Watanabe *et al.*, 1976b,c).

- John, J.A., Smith, F.A., Leong, B.K.J. & Schwetz, B.A. (1977) The effects of maternally inhaled vinyl chloride on embryonal and fetal development in mice, rats, and rabbits. Toxicol. ppl. Pharmacol., 39, 497-513
- Jühe, S. & Lange, C.-E. (1972) Sclerodermal skin changes, Raynaud's syndrome and acro-osteolyses in workers in the PVC-producing industry (Ger.). Dtsch. med. Wschr., 97, 1922-1923
- Kappus, H., Bolt, H.M., Buchter, A. & Bolt, W. (1975) Rat liver microsomes catalyse covalent binding of ^{14}C -vinyl chloride to macromolecules. Nature (Lond.), 257, 134-135
- Kappus, H., Bolt, H.M., Buchter, A. & Bolt, W. (1976) Liver microsomal uptake of [^{14}C]vinyl chloride and transformation to protein alkylating metabolites *in vitro*. Toxicol. appl. Pharmacol., 37, 461-471
- Keplinger, M.L., Goode, J.W., Gordon, D.E. & Calandra, J.C. (1975) Interim results of exposure of rats, hamsters, and mice to vinyl chloride. Ann. NY Acad. Sci., 246, 219-224
- Kogan, A.K. & Tugarinova, V.N. (1959) On the blastomogenic action of polyvinyl chloride (Russ.). Vop. Onkol., 5, 540-545
- Laib, R.J. & Bolt, H.M. (1977) Formation of imidazol derivatives of nucleic acid bases (DNA and RNA) by metabolites of vinyl chloride in vivo and in vitro (Abstract P 26). In: Proceedings of the 4th Meeting of the European Association for Cancer Research, Lyon, 1977, Lyon, University of Lyon, Faculty of Medicine, p. 84
- Lange, C.-E., Jühe, S., Stein, G. & Veltman, G. (1974a) Vinyl chloride disease - a systemic sclerosis due to occupational exposure? (Ger.) Int. Arch. Arbeitsmed., 32, 1-32
- Lange, C.-E., Jühe, S. & Veltman, G. (1974b) Appearance of angiosarcomas of the liver in two workers in the PVC production industry (Ger.). Dtsch. med. Wschr., 99, 1598-1599
- Lange, C.-E., Jühe, S., Stein, G. & Veltman, G. (1975) Further results in polyvinyl chloride production workers. Ann. NY Acad. Sci., 246, 18-21
- Laramy, R.E. (1977) Analytical chemistry of vinyl chloride - a survey. American Laboratory, December, pp. 17-27
- Lee, C.C., Bhandari, J.C., Winston, J.M., House, W.B., Peters, P.J., Dixon, R.L. & Woods, J.S. (1977) Inhalation toxicity of vinyl chloride and vinylidene chloride. Environ. Health Perspect., 21, 25-32

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- Rona, A. (1971) Instrumental investigation of adhesives used in the building industry. In: Symposium on Synthetic Resins in Building Construction, Paper RILEM (Reunion Int. Lab. Essais Rech. Mater. Constr.), 1967, Vol. 2, pp. 464-471 [Chem. Abstr., 76, 100475w]
- Rosenkranz, S., Carr, H.S. & Rosenkranz, H.S. (1974) 2-Haloethanols: mutagenicity and reactivity with DNA. Mutat. Res., 26, 367-370
- Russell, F.E., Simmers, M.H., Hirst, A.E. & Pudenz, R.H. (1959) Tumours associated with embedded polymers. J. natl Cancer Inst., 23, 305-315
- Safe Drinking Water Committee (1977) Drinking Water and Health, Washington DC, National Academy of Sciences, p. 794
- Saggese, M.F., Wakeman, I.B. & Owens, F.V. (1976) PVC with no VCM. Modern Packaging, September, pp. 19-21, 62
- Salmon, A.G. (1976) Cytochrome P-450 and the metabolism of vinyl chloride. Cancer Lett., 2, 109-114
- Šarič, M., Kulčar, Ž., Zorica, M. & Gelić, I. (1976) Malignant tumors of the liver and lungs in an area with a PVC industry. Environ. Health Perspect., 17, 189-192
- used* Schwetz, B.A., Leong, B.K.J., Smith, F.A., Balmer, M. & Gehring, P.J. (1975) Results of a vinyl chloride-teratology study in mice, rats, and rabbits (Abstract No. 29). Toxicol. appl. Pharmacol., 33, 134
- Shackelford, W.M. & Keith, L.H. (1976) Frequency of Organic Compounds Identified in Water, EPA-600/4-76-062, Athens, Ga, US Environmental Protection Agency, pp. 129-130
- Smith, P.M., Crossley, I.R. & Williams, D.M.J. (1976a) Portal hypertension in vinyl-chloride production workers. Lancet, ii, 602-604
- Smith, P.M., Williams, D.M.J. & Evans, D.M.D. (1976b) Hepatic angiosarcoma in a vinyl chloride worker. Bull. NY Acad. Med., 52, 447-452
- Smyth, H.F., Jr & Weil, C.S. (1966) Chronic oral toxicity to rats of a vinyl chloride-vinyl acetate copolymer. Toxicol. appl. Pharmacol., 9, 501-504
- Sokol, W.N., Aelony, Y. & Beall, G.N. (1973) Meat-wrapper's asthma. A new syndrome? J. Am. med. Assoc., 226, 639-641
- Spiertas, R. & Kaminski, R. (1978) Angiosarcoma of the liver in vinyl chloride/polyvinyl chloride workers. 1977 Update of the NIOSH Register. J. occup. Med., 20, 427-429

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