TOXICOLOGY AND APPLIED PHARMACOLOGY 19, 617–633 (1971)

Dermal Toxicity Studies of Technical Polychlorinated Biphenyls and Fractions Thereof in Rabbits

J. G. VOS AND R. B. BEEMS

Institute of Veterinary Pathology and Institute of Veterinary Pharmacology and Toxicology, University of Utrecht, Biltstraat 172, Utrecht, The Netherlands

Received October 5, 1970

Dermal Toxicity Studies of Technical Polychlorinated Biphenyls and Fractions Thereof in Rabbits. VOS, J. G., and BEEMS, R. B. (1971). *Toxicol. Appl. Pharmacol.* 19, 617–633. A significant difference in toxicity between 3 polychlorinated biphenyl (PCB) preparations was found in a prior study: Clophen A 60 and Phenoclor DP6 showing the highest, Aroclor 1260 the lowest, toxicity (Vos and Koeman, 1970). A subsequent study revealed the presence of tetra- and pentachlorodibenzofuran in Phenoclor and Clophen (Vos *et al.*, 1970). In the present study, application of 118 mg of the 3 PCB's (5 times per wk, for 38 days) on the back skin of rabbits also resulted in differences in toxicity.

PCB-induced skin lesions were hyperplasia and hyperkeratosis of the epidermal and follicular epithelium. Histopathology of the liver included centrolobular degeneration, centrolobular liver cell atrophy, focal necrosis, and cytoplasmic hyalin degeneration. Definite hyperplasia and hyperkeratosis of the follicular epithelium of the ear skin were seen after the topical application of fractions of Phenoclor and Clophen eluted from chromatographic columns with 25% diethylether in hexane. The fraction from Aroclor caused a minimal hyperplasia and hyperkeratosis of the follicular epithelium. PCB-induced kidney lesions were hydropic degeneration of the convoluted tubules and tubular dilatation with the presence of casts. This dilatation was demonstrated also by a significantly increased relative percentage of the diameter which corresponds to the space of Bowman. Moreover, thymus atrophy and lymphopenia were found. Fecal coproporphyrin and protoporphyrin excretion was increased.

Polychlorinated biphenyls (PCB) have been identified in tissues of fish and wildlife in many countries (Jensen, 1966; Holmes *et al.*, 1967; Holden and Marsden, 1967; Koeman *et al.*, 1967; Risebrough *et al.*, 1968; Koeman *et al.*, 1969; Jensen *et al.*, 1969; Duke *et al.*, 1970; Prestt *et al.*, 1970).

PCB preparations are extremely stable, oily fluids with very low aqueous solubility. They are used as lubricants, as heat transfer media, in protective coatings for wood, metal, and concrete, and for many other applications. Which of these applications has contributed to the present environmental contamination has not yet been established.

Inhalation and feeding experiments in rats with 65% chlorinated PCB resulted in liver injury (Drinker *et al.*, 1937; Bennett *et al.*, 1938). Liver damage and skin lesions have been described after inhalation, ingestion, and application to the skin using rabbits, guinea pigs, and mice (von Wedel *et al.*, 1943). Hydropericardium occasionally accompanied by abdominal edema was found in chicks fed PCB (McCune *et al.*, 1962; Flick

MONS 212787

PLAINTIFF'S EXHIBIT 46
7-28-00

001645

WATER_PCB-SD0000047053