Monsanto INDUSTRIAL CHEMICALS COMPANY

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SUBJECT TOXICITY OF POLYCHLORINATED DIBENZOFURANS

REFERENCE

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A literature search was made on the toxicity of polychlorinated dibenzofurans (PCDF). The literature, although sparse, does indicate that polychlorodibenzofurans are toxic. They are more toxic than are polychlorinated biphenyls but are approximately ten times less toxic than tetrachlorodibenzo-p-dioxin (TCDD). Data on the lethality of TCDD[14] reveal that a single oral LD_{50} ranges from 0.0006 mg/kg in male guinea pigs to 0.115 mg/kg in rabbits of mixed sex. Based on the available literature, the order of PCDF toxicity has been estimated to be:

Dichloro=Tetrachloro>Trichloro>Octachlorodibenzofuran.

The toxic effects reported include: (1) skin irritation (chloroacne) to humans[11] and rabbits[8,9]; (2) lesions resembling those produced by chick edema[9]; (3) edema formation in rabbits[8]; (4) liver damage in rabbits[5,8]; (5) death in chick embryos[2,3]; and (6) death to salmon[1].

A number of references indicate that PCDF are more toxic than polychlorobiphenyls (PCB) and are responsible for some of the toxic effects attributed to PCB[3,4,6,7]. Vos[2] conducted a chick embryo assay and found that a chromatographic fraction from two polychlorinated biphenyl preparations (Phenoclor DP6 and Clophen A6) containing tetrachloro, pentachloro, hexachloro and heptachlorodibenzofuran were highly toxic. A corresponding fraction from Aroclor 1260 which did not contain those compounds did not have a significant toxic effect on the chick embryo. Bowes[3] also attributed laboratory embryonic deaths to the chlorinated dibenzofurans in PCB.

Zitko[1] reported a median mortality rate of 120 days for juvenile Atlantic salmon which were fed dry fish food containing:

Dichlorodibenzofuran - 2.7 µgm/gm
Trichlorodibenzofuran - 5.7 µgm/gm
Tetrachlorodibenzofuran-2.8 µgm/gm
Octachlorodibenzofuran-9.1 µgm/gm

These data indicate the order of toxicity to be:

Dichloro=Tetrachloro>Trichloro>Octachlorodibenzofuran.

In contrast, a single dose of 2,8-dichlorodibenzofuran (122 mg/kg) administered to brook trout caused no fatalities[12].

Liver necrosis resulted following a single oral dose (0.5-1.0 mg/kg) of tri and tetrachlorodibenzofuran in rabbits. In comparison, a dose of

0.05-0.1 mg/kg of 2,3,7,8-tetrachlorodibenzo-p-dioxin produced liver necrosis and chloracne[5]. These data indicate that PCDD is perhaps 10 times more toxic than PCDF. The PCDF's were also found to be acne-inducing agents[8,10].

It is believed that toxicological studies on PCDF's are now in progress or will be in the near future by the Federal Drug Administration. There is also an indication that some toxicity studies on PCDF's have already been made. The source of the study, however, has not been clearly defined.

The sources used for this literature search were chemical abstracts and a bibliography in Environmental Health Perspectives, 1973, (5), pp 283-312.

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Attach.

POLYCHLORINATED DIBENZOFURANS

REFERENCES

Toxicity

1. Chlorinated dibenzylfurans are more toxic than polychlorinated biphenyls. A median mortality rate of 120 days was observed in juvenile Atlantic salmon fed on dry fish food containing

Dichlorodibenzofuran	- 2.7 µgm/gm
Trichlorodibenzofuran	- 5.7 µgm/gm
Tetrachlorodibenzofuran	- 2.8 µgm/gm
Octachlorodibenzofuran	- 9.1 µgm/gm

[Order of toxicity: Di>Tetra>Tri>Octa]

Zitko, V., Choi, O.M.K., Bull. Environ. Contam. Toxicol., 73, 10(2), 120-2.

2. A chick embryo assay indicated a high toxicity chromatographic fraction of 2 polychlorinated biphenyl preparations - Phenoclor DP6 and Clophen A6, containing tetrachlorodibenzofuran, pentachlorodibenzofuran, hexachlorodibenzofuran, and heptachlorodibenzofuran. A corresponding fraction from Aroclor 1260 did not contain these compounds and did not have a significant toxic effect on the chick embryo.

   Vos, J.G., Koeman, J.H., VanderMaas, TenNoever deBraun, M.D., DeVos, R.H., Food Cosmet. Toxicol., 1970, 8 (6), 625-33 (Eng.).

3. Embryonic deaths have been recorded in the laboratory among birds treated with PCB. These deaths have been attributed to chlorinated dibenzofuran contaminants. Also, birth defects in wild populations of birds and sea lions are believed caused by chlorinated dibenzodioxins.

   Bowes, G.W., Simoneit, B.R., Burlingame, A.L., DeLappe, B.W., Peakall, P.B., Risebrough, R.W., Environ. Health Perspect. (#5), 191 (1973).

4. Dibenzofurans were implicated as being responsible for some of the toxic effects attributed to PCBs. Waldbott, G.L., "Effects of Environmental Pollutants", C. V. Mosby Co., St. Louis, Mo., 1973.

5. The tri and tetrachlorodibenzofuran single oral liver necrotic dose (0.5 to 1.0 mg/kg) in rabbits.

   The 2,3,7,8-tetrachlorodibenzo-p-dioxin caused lethal liver necrosis and chloracne in rabbits at a dose range of 0.05 to 0.1 mg/kg.

   Fishbein, L., "Polychlorinated Biphenyls and the Environment.", Report No. ITF-PCB-72-1 (com-72-10419), Interdepartmental Task Force on PCBs, Washington, D.C., May 1972, pp 122-151.

6. Some commercial PCB mixtures may contain trace amounts of dibenzofurans or other toxic impurities. These may be the cause of some toxic effects of the PCBs.

Hammond, A.L., Science, 175, 155-156 (January 14, 1972).

7. The most toxic impurities in polychlorinated biphenyls were found to be chlorinated benzofurans.

Vos, J.G., Tijdschr. Diergeneesh, 97, (22), 1378-85 (1972)(Neth.).

8. The major acnegenic action of crude PCB mixtures originates from chlorinated dibenzofurans. The probable contribution of chlorinated dibenzofurans and pure PCB to the toxicity of technical PCB preparations in rabbits.

	Furan	PCB
Chloracne	++	+
Edema Formation	++	-
Liver Damage	++	+
Hepatic Porphyria	-	++

Vos, J.G., Notenboom-Ram, E., Toxicol. Appl. Pharmacol 23, 563-578 (1972).

9. Lesions resembling those produced by chick edema factor were traced to a PCB contaminant, chlorinated dibenzofurans.

Anonymous, Food Cosmet. Toxicol. 9 (4), 568-571 (1971).

10. Trichlorodibenzofuran, tetrachlorodibenzofuran and 2,3,6,7-tetrachlorodibenzodioxin were especially effective acne-inducing agents on rabbit ears. The tetrachlorodibenzodioxin was the most toxic - concentrations of 0.01 to 0.002%. Higher concentrations caused liver necrosis and death. Single oral administration of 0.05 to 0.1 mg/kg body weight caused death in 1-2 weeks.

Kimmig, J., Schulz, K.H., Naturwiss, 44, 337-8 (1957)(Ger.).

11. Trichloro and tetrachlorodibenzofurans, and tetrachlorodibenzo-p-dioxin were found to be active skin irritants to humans.

Kimmig, J., Schulz, K.H., Dermotologia, 115 (4), 540-6 (1957) (Ger.).

12. A single dose of 2,8-dichlorodibenzofuran 122 mg/kg administered to brook trout caused no mortality. Low acute toxicity and residual levels are due to poor adsorption in the gut.

Zitko, V., Wildish, D.J., Hutzinger, O., Choi Puk, Environ. Health Perspect., 1973, (5), 187-9 (Eng.).

13. Pentadichlorodibenzofuran and 2,3,7,8-tetrachlorodibenzodioxin were given orally to female mice and their hepatic enzyme-inducing activities were evaluated. Both were highly active in reducing the hexobarbitol sleeping time in mice.

The furan was 170 times and dioxin was 1250 times as effective as PCB based on their RD_{60} values (values which reduce sleeping time to 60% levels of the control)

Araki, Yasunoi, Fukuoka-Igaku-Zasshi, 1974, 65 (1), 61-4.

14. Toxicology of chlorinated dibenzo-p-dioxins.

Schwetz, B.A., Norris, J.M., Sparschu, G.L., Rowe, V.K., Gehring, P.J.,'Chlorodioxins - Origin and Fate', Advances in Chemistry, Series No. 120, American Chemical Society, pp 55-69 (1973).