TOXICITY STUDY OF 3,3',4,4'-TETRACHLOROBIPHENYL AND 2,3',4,4',5 PENTACHLOROBIPHENYL IN THE RAT

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ABSTRACT

Groups of 10 male and 10 female weanling Sprague Dawley rats were administered PCB congeners, 3,3',4,4',-tetrachlorobiphenyl (PCB #77) or 2,3',4,4',5-pentachlorobiphenyl (PCB #118) in diet at concentrations ranging from 10 to 10,000 ppb for a period of 13 weeks. Growth rate and food consumption were not affected. No clinical signs of toxicity were noted. The male rats given 10,000 ppb PCB #118 and females on 2,000 ppb PCB #118 showed a significant increase in hepatic microsomal ethoxyresorufin deethylase activity (EROD). The increased EROD activity was also observed in female rats given 10,000 ppb congener #77. Urinary ascorbic acid was increased in the groups of males treated with the congener #77 at 1,000 and 10,000 ppb. No other biochemical changes were observed. The hematological parameters were not affected. Both congener 77 and 118 were accumulated in fat and liver in a dose-dependent fashion. These data suggest that both congeners have a similar mode of action. Based on the biochemical and hematological data, the no observable effect level for PCB #77 was 100 ppb (approximately 10 μg/kg bw/day), and that for the congener #118 was 200 ppb (approximately 20 μg/kg bw/day). The histological and ultrastructural data will be reported elsewhere.

INTRODUCTION

Polychlorinated biphenyls (PCBs) are environmental contaminants that continue to be found in all environmental media, including Great Lakes fish in North America. Despite the widespread occurrence of PCB's, the full extent of human and wildlife health effects resulting from low-level, long-term exposure to these compounds is still not clear.

Numerous animal toxicity studies on PCBs have been documented addressing carcinogenesis, immunotoxicity, reproductive toxicity and neurotoxicity[1,2]. However, these studies were based on commercial PCB mixtures (Aroclors and Kaneclors™). Little information is available on individual PCB congeners.

Recent advances in analytical chemistry permit quantification of the specific PCB congeners in tissues and biological fluids and there is evidence to indicate that these congeners which are retained in animal tissues at different rates, may have different toxic potentials. In order to better assess the systemic effects resulting from long-term, low level

exposure to these pollutants, a research project was initiated to investigate the subchronic effects of eight congeners that are most frequently found in environmental samples and in human tissues. The present study reports the clinical, hematological and biochemical effects of PCB congeners #77 and #118.

MATERIALS AND METHODS

PCB congeners #77 and #118 were synthesized in Dr. A. Bergman's laboratory, Department of Environmental Chemistry, the University of Stockholm. The test substances had purity of greater than 99% and were free of dioxin contamination. Groups of 10 male and 10 female weanling Sprague Dawley rats were administered PCB #77 or #118 in diet for a period of 13 weeks. The dietary concentrations of PCB #77 were the same for the male and female groups: 10, 100, 1,000 and 10,000 ppb. The concentrations for PCB #118 were: 10, 100, 1,000 and 10,000 ppb for male rats, and 2, 20, 200, and 2,000 ppb for females.

Food consumption and body weights were determined weekly. Clinical observations were made daily. At the termination of the study the animals were anesthetized with Equesthesia™ and the following experiments performed:

Organ Weight Determination: Liver, spleen, brain, heart, thymus, kidney, gross and histopathology.

Serum Biochemistry: Inorganic phosphate, total protein, bilirubin, calcium, cholesterol, alkaline phosphatase, aspartate aminotransferase, total protein, calcium, glucose, uric acid and lactate dehydrogenase.

Other Biochemical Measurements: Liver aminopyrine demethylase[3], aniline hydroxylase[4] and ethoxyresorufin deethylase[5] activities, liver porphyrins[6] and urinary vitamin C[7]

Hematology: Erythrocyte count, hematocrit, red cell indices, total and differential of leucocytes, platelet count, and bone marrow M/E ratios,

Tissue PCB Residues Analyses: PCB (Congener Specific).

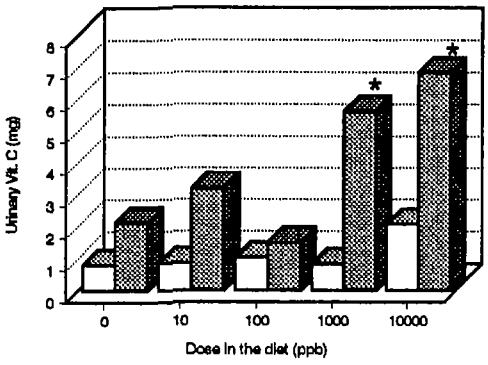
RESULTS AND CONCLUSIONS

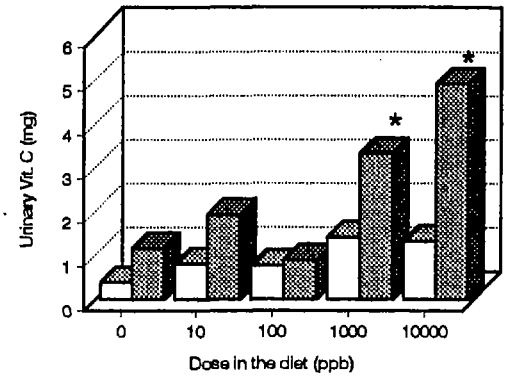
Growth rate and food consumptions were not affected by treatment with either congener. There was a trend towards decreased weight gain in the high-dose males given PCB #77, but the decrease was not statistically significant. Gross observations revealed no signs of toxicity and all animals survived till the termination of the study. The organ weights of the treated animals were not different from the control.

Of the biochemical parameters determined in the present study, only hepatic microsomal EROD activity and urinary ascorbic acid levels were affected (Figure 1). Hepatic EROD activity was increased in male and female rats given the 10,000 ppb and 2,000 ppb PCB 118 diet respectively. The increase in this enzyme activity was also observed in animals of both sexes given the 10,000 ppb PCB #77 diet.

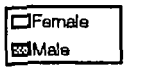
Urinary ascorbic acid was determined at Week 6 and 12 of the study for PCB 77. Increased ascorbic acid was observed in males fed either the 1,000 or 10,000 ppb diet at Week 6 and 12 of the study (Figure 1). Liver porphyrins were not affected in any of the treated groups. No hematological or other biochemical changes were observed. Both congeners #77 and 118 were accumulated in fat and liver in a dose-dependent fashion. It would appear that both congeners have a similar mode of action, and that ascorbic acid seemed to be a more sensitive biological indicator of PCB #77 exposure. Based on the

Urinary Vit. C at Week 6 and 12, PCB # 77

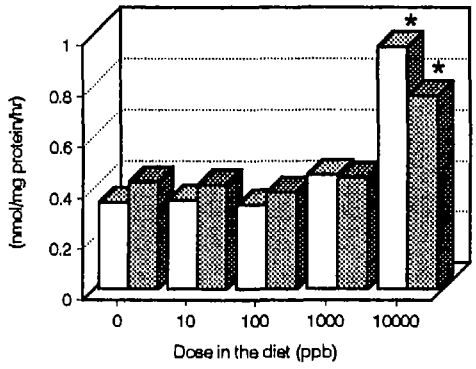




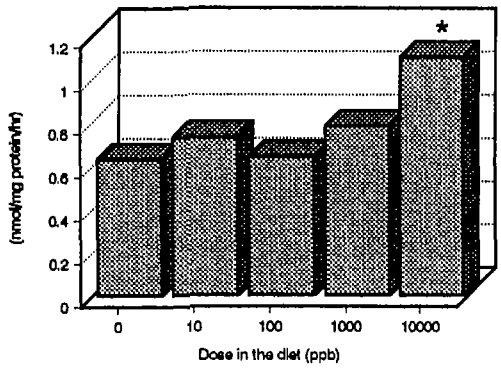
EROD - Activity, PCB # 77

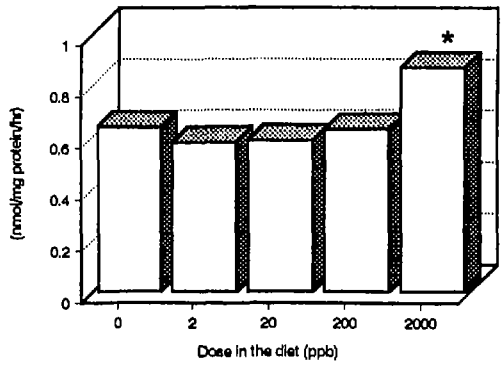


* significantly different (p 0.05)



EROD - Activity, PCB # 118





biochemical and hematological effects the no observable effect level for PCB #118 was judged to be 200 ppb in diet (approximately 20 μg/kg bw/day) and that for PCB 77 was 100 ppb (10 μg/kg bw/day). In a subchronic study with PCB #126, the toxic effects, including hepatomegaly, growth suppression, elevation in liver unporphyrin, Vitamin A decrease and anemia were observed at 10 ppb in diet, and the no observable effect level was established at 1 ppb in diet or 0.08-0.09 μg/kg bw/day[8]. Comparing the potencies of the three PCB congeners, it appears that PCB 118 and 77 are at least 100-200 fold less toxic than 126. Histopathological and ultrastructural data will be reported elsewhere.

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