TOXICITY OF 2,3,3',4,4',5-HEXACHLOROBIPHENYL(PCB 156) IN RATS

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Introduction
Research on the toxicology of PCBs has been focused on congener-specific studies because of the recognition that the isomeric content of PCBs present in environmental samples is different from that of commercial formulations, and that different PCB congeners have different toxic potencies. As part of the program on the toxicity PCB congeners[1,2], the present study was carried out to investigate the toxicity of 2,3,3',4,4',5-hexachlorobiphenyl (PCB 156). This congener is a *mono-ortho* substituted chlorinated biphenyl that has been identified in human milk[3].

Materials and Methods
PCB 156 was synthesized following the method of Bergman et al [4], and had a purity of > 99.9%. Groups of 10 male and 10 female rats were given PCB 156 in their diet at concentrations of 0, 0.01, 0.1, 1, or 10 ppm for 13 weeks. Clinical observation was made during the study. At the termination of the exposure period, the animals were killed and subjected to clinical chemistry, hematological and histological examination. Liver was homogenized and centrifuged at 9,000x g to obtain the supernatant for the analysis of ethoxyresorufin deethylase (EROD)[5] pentoxyresorufin dealkylase (PROD) [6] and UDP glucuronosyl transferase(UDPGT) [7] activities. The vitamin A content in liver and lung was determined according to the method of Håkansson et al[8]. Results were analyzed by one-way analysis of variance ($p < 0.05$) and Duncan's multiple range test.

Results and Discussion
Exposure of rats to PCB 156 in diet for 13 weeks elicited a broad range of effects including biochemical, hematological and morphological alterations in target organs. The body weight gain of male rats in the highest dose group appeared to be lower than control, however, the difference was not statistically significant. Cage-side observation revealed no signs of toxicity. Both the absolute and relative liver weights were increased in the 10 ppm group of both sexes, as were liver microsomal EROD and PROD activities (Table 1). The activity of UDPGT, a phase II enzyme, was also elevated in the highest dose group. The fact that both EROD and PROD activities were increased indicates that PCB 156 is a mixed-type inducer. Other PCB congeners that have demonstrated this type of enzyme induction activity include 2,3,3',4,4'-pentachlorobiphenyl (PCB 105) [2] and 2,2',3,3',4,4'-hexachlorobiphenyl(PCB128) [9], both of which increased the liver microsomal EROD and PROD activities at the 50 ppm level. Under a similar dietary exposure condition PCB 126[1] and 77[10] caused an elevation in liver EROD activity at 0.1 ppb and 1 ppm, respectively. A comparison of the EROD induction activity suggests that the potency of PCB 156 is approximately the same as PCB 105 and 128, but is much less than that of PCB 126 and 77. Of the biochemical endpoints determined for congener 156, the vitamin A content in liver seems to be the most sensitive indicator of PCB effect, which showed a significant decrease at levels as low as 0.1 ppm in female rats and 1 ppm in males (Table 1). Increased serum cholesterol was observed at the highest dose group; this observation is consistent with the results on other PCB congeners[1,2,9](Table 2). Anemia characterized by decreased red cells and indices was also noted in the highest dose group (Table 2). Treatment with the PCB congener resulted in pathological

changes in liver thyroid and thymus, however, these changes were mild in nature even at the highest dose (data not shown). The histotoxicity of this congener is also less potent than PCB 126 and 77. Based on the results presented above we conclude that the toxicity of PCB 156 was much less potent than that of PCB 126 and 77, and is in the same order of PCB 105 and 128.

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Table 1: Effects of PCB 156 on hepatic microsomal enzyme activities and vitamin A levels.

PCB 156 in diet (ppm)	Final Body Weight (g)	Liver Weight (% b.w.)	EROD (nmol/mg protein/min)	PROD (nmol/mg protein/min)	UDPGT (nmol/mg protein/min)	Liver Vitamin A (μg/g)	Lung Vitamin A (μg/g)
Male							
0	516 ± 64	3.6 ± 0.4	0.07 ± 0.02	0.24 ± 0.09	254 ± 70	431 ± 97	9.3 ± 5.4
0.01.1	558 ± 50	3.5 ± 0.4	0.07 ± 0.02	0.29 ± 0.18	193 ± 47	404 ± 68	8.9 ± 6.0
1	533 ± 52	3.6 ± 0.7	0.08 ± 0.03	0.27 ± 0.13	212 ± 44	362 ± 71*	8.2 ± 4.4
10	538 ± 55	3.5 ± 0.2	0.44 ± 0.27	0.26 ± 0.09	509 ± 352*	321 ± 40*	5.6 ± 3.1
	488 ± 39	5.1 ± 0.6*	9.61 ± 4.92*	1.05 ± 0.74*	1137 ± 257*	123 ± 45*	3.0 ± 1.2*
Female							
0	285 ± 28	3.4 ± 0.2	0.11 ± 0.04	0.08 ± 0.02	160 ± 71	682 ± 72	7.7 ± 2.1
0.01	296 ± 35	3.2 ± 0.2	0.11 ± 0.04	0.07 ± 0.03	201 ± 93	517 ± 98*	6.2 ± 2.9
0.1	285 ± 12	3.2 ± 0.3	0.17 ± 0.07	0.10 ± 0.03	176 ± 26	532 ± 64*	5.6 ± 2.3
1	281 ± 24	3.3 ± 0.2	0.96 ± 0.55	0.25 ± 0.11*	664 ± 297*	452 ± 181*	5.5 ± 2.9
10	266 ± 19*	4.3 ± 0.5*	10.9 ± 2.9*	0.92 ± 0.30*	1297 ± 150*	176 ± 83*	6.1 ± 3.5

* Significantly different from control ($P < 0.05$).

Table 2: Biochemical and hematological effects of PCB 156.

PCB 156 In diet (ppm)	Cholesterol (mg/dL)	Hemoglobin (g/L)	Hematocrit (%)	Erythrocyte ($\times 10^6/\mu L$)	MCH (pg)	MCV (fl)	MCHC (%)	Einosinophils (%)
Male								
0	102 ± 15	17 ± 0.5	0.46 ± 0.01	8.9 ± 0.3	18.6 ± 0.9	51.4 ± 2.4	363 ± 4	1.3 ± 0.3
0.01	104 ± 33	17 ± 0.7	0.45 ± 0.02	8.9 ± 0.3	18.6 ± 0.6	51.0 ± 1.3	366 ± 6	1.3 ± 0.3
0.1	109 ± 28	17 ± 0.7	0.45 ± 0.02	8.9 ± 0.5	18.6 ± .08	50.7 ± 1.6	366 ± 7	1.4 ± 0.4
1	93 ± 14	17 ± 0.7	0.46 ± 0.02	9.1 ± 0.3	18.2 ± 0.8	50.5 ± 1.9	361 ± 6	1.5 ± 0.7
10	148 ± 38*	15 ± 0.6*	0.42 ± 0.02*	8.5 ± 0.4*	17.2 ± 0.6*	49.4 ± 1.6*	349 ± 5*	0.7 ± 0.2*
Female								
0	90 ± 19	17 ± 0.5	0.45 ± 0.01	8.5 ± 0.3	19.5 ± 0.3	53.7 ± 1.0	363 ± 5	1.1 ± 0.5
0.01	96 ± 15	16 ± 0.6	0.45 ± 0.02	8.3 ± 0.3	19.7 ± 0.5	53.9 ± 0.7	366 ± 6	1.1 ± 0.3
0.1	102 ± 25	16 ± 0.6	0.44 ± 0.02	8.3 ± 0.3	19.5 ± 0.7	53.0 ± 1.8	367 ± 4	1.3 ± 0.6
1	111 ± 17	16 ± 0.8	0.44 ± 0.02	8.4 ± 0.4	19.5 ± 0.3	53.3 ± 0.9	365 ± 6	0.9 ± 0.3
10	125 ± 31*	15 ± 1.3*	0.41 ± 0.04*	8.1 ± 0.6*	18.4 ± 0.6*	51.4 ± 1.7*	358 ± 5*	0.7 ± 0.4*

* Significantly different from control ($P < 0.05$).