Inhibition of Tumor Growth in Rats by Feeding a Polychlorinated Biphenyl, Aroclor 1254

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Polychlorinated biphenyls (PCBs) are globally distributed, highly persistent environmental contaminants (RISEBROUGH et. al. 1968, PEAKALL and LINCER 1970). Several adverse toxicological effects have been attributed to PCB exposure, including a potential hepatocarcinogenicity (ITO et. al. 1973, ITO et. al. 1974, KIMBROUGH and LINDER 1974). PCBs have also been reported to act as immunosuppressive agents (VOS and BEEMS 1971, VOS and DE ROIJ 1972, KOLLER and THIGPEN 1973). Since a suppressed immunologic state in the host can enhance the generation and growth of tumors (BURNET 1970, GATTI and GOOD 1971, PENN and STARZL 1972, HERBERMAN 1974), we conducted the following study to determine the effects of host exposure to PCBs on tumor growth per se, utilizing a transplantable tumor in rats.

MATERIALS AND METHODS

Aroclor 1254[1], dissolved in corn oil, was incorporated into specially prepared powdered diets at levels of 0, 100, 400 or 800 ppm and fed to groups of male and female Sprague Dawley rats, eight of each sex per group. Subsequently, three additional groups of 20 male rats were placed on diets containing 0, 5 or 25 ppm PCB. All animals were approximately one month of age at the start of the experiment. Food consumption was measured three times per week for each animal and body weights were recorded weekly.

Following 30 days of exposure to the contaminanted diets, the animals were inoculated with the Walker 256 carcinosarcoma in the flexor muscle mass of each hind limb. Each injection consisted of 1×10^5 Walker tumor cells (obtained from the ascites form of the tumor) in a volume of 0.1 ml. The tumors were allowed to grow for nine days, during which time the animals remained on their respective diets. At sacrifice, the animals were killed by ether asphyxiation and the tumors were removed, dissected free of surrounding connective tissue

[1] Monsanto Chemical Co., St. Louis, Missouri

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and weighed on an analytical balance.

RESULTS

The mean tumor weights of all PCB-fed groups were significantly smaller than the mean tumor weight of their sex-matched control after the nine-day tumor growth period (Table 1). In both male and female rats, the magnitude of tumor weight inhibition directly correlated with the concentration of PCB in the diet. Although female rats consistently showed smaller tumors than their male counterparts, the degree of tumor weight inhibition observed at each dose level was comparable in both sexes.

As shown in Table 1, the body weight gain of the animals was also affected by PCB exposure. Male rats fed diets containing 100 ppm or less PCB showed no significant alteration in body weight gain. At dietary levels of 400 and 800 ppm, however, a significant inhibition of body weight gain occurred which was dose-dependent. Female rats appeared to be more sensitive to this parameter of PCB intoxication showing reduced body weight gain at the 100 ppm level. The observed alteration in body weight gain could be accounted for, in part, by an observed decrease in food consumption by the PCB-fed rats (Table 1). It is possible that an adverse taste was associated with the higher dietary levels of PCB as the animals showed reduced food consumption immediately after being placed on the contaminated diets.

DISCUSSION

The results of this study suggest that PCB (Aroclor 1254) exposure can inhibit the growth of at least one experimental tumor, the Walker 256 carcinosarcoma in rats. The tumor inhibitory response is dose-related and is observable at levels of PCB routinely found in the environment (MAUGH 1975). Obviously, the implications for tumor growth in humans are difficult to extrapolate. Related studies are in progress to further define the antitumor potential of PCBs. Preliminary studies utilizing the intraperitoneal route of exposure indicate that the anti-tumor action of PCB is specific and is not due solely to a non-specific inhibition resulting from reduced food consumption or decreased body weight gain. The mechanism of action of PCBs on tumor growth remains to be determined.

TABLE 1
Effect of Dietary Exposure to PCB, Aroclor 1254, on the Weight of the Walker Tumor Nine Days after Inoculation (10^5 cells, IM) in Male and Female Rats.

PCB in Feed (ppm)	PCB Intake† (mg/kg)	Number of Animals	Number of Tumors	Body Weight Net Gain (g ± s.e.)††	Tumor Weight mean (g ± s.e.)	Tumor Weight exp/control (x 100)
Males:						
0	--	28Ψ	52	181 ± 4	4.92 ± 0.33*	--
5	23	20	38	184 ± 4	4.12 ± 0.33*	84.1
25	113	20	40	194 ± 6	3.90 ± 0.33*	79.4
100	300	8	16	188 ± 9	3.67 ± 0.35	74.7
400	1112	8	14	117 ± 14**	2.90 ± 0.74**	59.1
800	2063	8	16	70 ± 8**	2.01 ± 0.30**	40.9
Females:						
0	--	8	16	89 ± 5*	3.99 ± 0.23*	--
100	320	8	16	71 ± 5**	3.02 ± 0.21**	75.7
400	1102	8	16	35 ± 5**	2.27 ± 0.32**	56.9
800	2126	8	16	22 ± 2**	1.81 ± 0.14**	45.4

† Total PCB intake, day 0 to day 39, calculated from food consumption measurements.
†† Net gain in body weight, day 0 to day 39.
Ψ Since the mean tumor weight of the two male control groups (4.86 vs 4.98) did not differ statistically, data were analyzed with combined control values.
* $p < 0.05$, ** $p < 0.01$, Student's t test, one-tailed.

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