Effect of Dietary Xenobiotics on the Metabolism of Trace Elements in Rats

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SUMMARY

Exeriments were conducted with growing male rats to study effects of dietary addition of PCB and some other xenobiotics on tissue levels of essential trace elements; iron, zinc, copper, manganese, molybdenum, chromium, nickel, and cobalt. The animals were fed ad libitum the test diets containing xenobiotics for 14 to 15 days. Analysis of the elements was performed using a polarized Zeeman atomic absorption spectrophotometer. Dietary addition of 0.02% or 0.05% PCB significantly raised liver concentration of copper. Other elements in liver were not markedly influenced by PCB intake. Kidney and serum levels of copper were also found to be increased by PCB. Dietary addition of other xenobiotics such as 0.3% caffein, 0.05% DDT, 0.3% flavone, 0.3% chloretone, and 0.3% BHA also caused an incrase in tissue copper. In general, serum copper was correlated with serum cholesterol in these dietary manipulation.

INTRODUCTION

We previously reported that feeding of polychlorinated biphenyls (PCB) to rats caused an increase in liver and serum levels of cholesterol and ascorbic acid[1]. Similar effect has been reported with some other xenobiotics including 1, 1, 1-trichloro-2, 2-bis (ρ -chlorophenyl) ethane (DDT), 2, 6-di-tert-butyl- ρ -cresol (BHT), pentobarbital, and caffein[2]. Studies on the metabolism of other vitamins including vitamin A and vitamin E in animals fed PCB have been also reported[3]. However, only limited data are available concerning the influence of xenobiotics on the minerals. Yagi *et al.* reported some changes in tissue levels of sodium, potassium and magnesium in rats by feeding PCB[4]. In the present study, we examined the influence of PCB and some other xenobiotics on tissue levels of eight essential trace elements in rats.

METHODS

After feeding the commercial stock diet for 3 days, male rats of the Wistar strain, weighing 40–60g, were used. Room temperature was kept at 24°C and illuminated for 12 h from 8:00 a.m. The basal diet was composed of casein 25%, α -corn starch 40%, sucrose 20%, corn oil 5%, cellulose powder 4%, salt mixture 4%[5], and vitamin mixture 2% (Oriental Yeast Co., Ltd.). The chemicals including 0.02%-0.05% PCB, 0.3% caffein, 0.05% DDT, 0.3% flavone, 0.3% chloretone and 0.3% BHA were added to the basal diet as shown in tables. Deionized water and the diets were available ad libitum. After feeding the test diets containing the chemicals mentioned above for 14 to 15 days, the diets were removed from the cages at 8:00 a.m. and the animals were lightly anesthetized with ether and killed

between 1:00 p.m. and 3:00 p.m.

Analysis of the elements was performed using a polarized Zeeman atomic absorption spectrophotometer (Model 180—60, Hitachi, Ltd.) as described previously[6]. Serum cholesterol was measured by the method of Pearson *et al*[7]. Student's t-test was used to statistically analyze the data.

Table 1. Effect of dietary addition of PCB on the levels of trace elements in liver of rats

Group		Control	0.02% PCB	0.05% PCB
Liver wt.	% of body wt.	4.99 ± 0.59[a]	6.24 ± 0.73[b]	8.07 ± 0.88[b]
Fe	μg/g tissue	69 ± 15	66 ± 10	54 ± 10
	μg/100g body wt.	344 ± 71	415 ± 105	434 ± 64
Zn	μg/g tissue	25 ± 3	23 ± 2	22 ± 2
	μg/100g body wt.	123 ± 12	143 ± 10[b]	178 ± 17[b]
Cu	μg/g tissue	3.0 ± 0.5	3.8 ± 0.5[b]	4.6 ± 0.7[b]
	μg/100g body wt.	14.6 ± 2.0	24.0 ± 3.2[b]	37.2 ± 8.8[b]
Mn	μg/g tissue	2.2 ± 0.5	1.7 ± 0.2	1.6 ± 0.5
	μg/100g body wt.	10.7 ± 2.7	10.6 ± 1.7	12.9 ± 1.7
Mo	μg/g tissue	0.49 ± 0.07	0.55 ± 0.10	0.45 ± 0.10
	μg/100g body wt.	2.4 ± 0.5	3.5 ± 0.7[b]	4.0 ± 0.4[b]
Ni	μg/g tissue	0.11 ± 0.10	0.11 ± 0.05	0.10 ± 0.07
	μg/100g body wt.	0.55 ± 0.47	0.72 ± 0.20	0.78 ± 0.50
Cr	μg/g tissue	67 ± 34	48 ± 17	61 ± 20
	μg/100g body wt.	0.34 ± 0.20	0.56 ± 0.15	0.49 ± 0.17
Co	μg/g tissue	92 ± 27	135 ± 37[b]	112 ± 17
	μg/100g body wt.	0.46 ± 0.15	0.86 ± 0.27[b]	0.90 ± 0.15[b]

a) Values represent mean ± S. D. of six rats.
b) Significantly different from control group ($p<0.05$).

RESULTS

Table 1 describes the effects of dietary addition of 0.02% and 0.05% PCB on liver levels of eight trace elements. In this experiment, dietary PCB caused no influence on the growth (Data not shown). PCB intake caused significant increase in liver concentration of copper and there was a good correlation between dietary level of PCB and liver level of copper. Liver concentration of cobalt was also significantly increased by dietary 0.02% PCB, but not by dietary 0.05% PCB. Concentrations of other elements such as iron, zinc, manganese, molybdenum, chromium and nickel were not significantly influenced by PCB intake, although when expressed as per 100g body weight, the contents of iron, zinc, and molybdenum were significantly increased by PCB because of liver enlargement due to the chemical.

Kidney and tibia levels of iron, zinc, and copper were presented in Table 2. Kidney copper was increased by PCB, but kidney iron and zinc were not influenced. Tibia zinc was significantly increased by PCB intake, while tibia iron was depressed by the chemical. Dietary 0.02% and 0.05% PCB also

Table 2. Effect of dietary addition of PCB on the levels of iron, zinc, and copper in kidney and tibia of rats

Tissue	Tissue wt.	Fe	Zn	Cu
	% of body wt.	μg/g tissue	μg/g tissue	μg/g tissue
Kidney				
control	0.86 ± 0.02[a]	59 ± 12	24 ± 2	4.9 ± 0.5
0.02% PCB	0.86 ± 0.07	60 ± 12	24 ± 2	5.2 ± 0.5
0.05% PCB	0.91 ± 0.05[b]	63 ± 12	24 ± 2	8.7 ± 3.7[b]
Tibia				
control	0.15 ± 0.02	57 ± 5	103 ± 10	ND[c]
0.02% PCB	0.15 ± 0.02	54 ± 5	114 ± 5[b]	ND
0.05% PCB	0.14 ± 0.02	46 ± 2[b]	128 ± 12[b]	ND

a) Values represent mean ± S. D. of six rats.
b) Significantly different from control group ($p < 0.05$).
c) Not determined.

caused 39% and 80% increase in serum levels of copper, respectively.

Table 3 shows the influence of dietary xenobiotics including PCB, caffein, DDT, flavone, chloretone and BHA on tissue copper and serum cholesterl. Dietary addition of PCB, caffein, DDT, and flavone caused a significant increase in liver concentration of copper, but dietary chloretone and BHA did not. Kidney copper significantly increased with the intake of PCB, caffein, DDT, chloretone, and BHA. All the chemicals examined here caused an increase in serum copper and cholesterol. Serum level of copper generally correlated with serum cholesterol ($r=0.84$, $P<0.05$).

Table 3. Effects of dietary xenobiotics on tissue levels of copper and cholesterol in rats

Group	Gains in body wt. (g/14 days)	Liver wt. (% of body wt.)	Liver Cu (μg/g tissue)	Kidney wt. (% of body wt.)	Kidney Cu (μg/g tissue)	Seum Cu (μg/100 ml)	Serum cholesterol (mg/100 ml)
Control	102 ± 10[a]	4.68 ± 0.34	3.3 ± 0.5	0.88 ± 0.07	4.0 ± 0.2	97[c]	62 ± 12
0.05% PCB	94 ± 5	7.40 ± 0.37[b]	5.3 ± 0.5[b]	1.02 ± 0.07[b]	12.4 ± 6.9[b]	130	129 ± 20[b]
0.3% Caffein	59 ± 7[b]	4.70 ± 0.37	4.4 ± 0.2[b]	1.06 ± 0.10[b]	16.0 ± 5.4[b]	144	96 ± 12[b]
0.05% DDT	95 ± 12	6.17 ± 0.57[b]	4.3 ± 0.5[b]	1.17 ± 0.51[b]	5.8 ± 1.5[b]	119	87 ± 27[b]
0.3% Flavone	62 ± 15	7.25 ± 0.61[b]	4.2 ± 0.5[b]	1.27 ± 0.12[b]	4.5 ± 0.7	136	138 ± 20[b]
0.3% Chloretone	111 ± 12	5.46 ± 0.29[b]	3.9 ± 0.7	1.07 ± 0.05[b]	4.4 ± 0.2[b]	123	116 ± 20[b]
0.3% BHA	101 ± 3	5.29 ± 0.32[b]	3.4 ± 0.2	0.95 ± 0.05	13.7 ± 3.4[b]	117	113 ± 12[b]

a) Values represent mean ± S. D. of 5 to 6 rats.
b) Significantly different from control group ($p < 0.05$).
c) Pooled samples.

DISUCUSSION

The present study demonstrated that dietary addition of PCB and other six xenobiotics raised tissue copper. During our study, Dubick and Keen also reported an increase in tissue copper of rats fed phenytoin[8]. Thus, it seems likely that these effects could be widely observed for a variety of xenobiotics.

It has been shown that the activity of liver microsomal drug-metabolizing enzymes in animals given xenobiotics correlated with serum cholesterol and urinary ascorbic acid[2]. The present study demonstrated that serum cholesterol significantly correlated with serum copper when the animals were fed xenobiotics. Although the physiological significance of these metabolic interrelationship is unknown, it is tempting to postulate that inducers of drug-metabolizing enzymes might generally have potential functions to raise serum cholesterol and copper. It has been reported that hypercholesterolemia could be induced by feeding the diet deficient in copper[9]. These facts together with the present study emphasize an importance of the metabolic interrelationship between copper and cholesterol.

Carter and Koo reported a raised serum zinc of rats fed PCB[10]. The present study also showed an increase in tibia zinc by PCB intake (Table 2). Turk and Hietman reported an increase in zinc absorption by feeding PCB to chick[11]. It is therefore conceivable that an increment in tissue zinc might be attributable to its enhanced absorption by PCB intake.

REFERENCES

1. Kato, N., Okada, T., Takenaka, Y. and Yoshida, A. (1977):Ameliorative effect of dietary ascorbic acid on PCB toxicity in guinea pigs. Nutr. Rep. Int., 15, 125–130.
2. Kato, N. and Yoshida, A. (1979): Effects of some fat-soluble chemicals on plasma cholesterol and urinary ascorbic acid in rats. Agric. Biol. Chem., 43, 191–192.
3. Innami, S. (1985): Interaction between toxicity of pollutants and nutrition. J. Jap. Soc. Nutr. Food Sci., 38, 1–13.
4. Yagi, N., Kimura, M. and Itokawa, Y. (1976): Sodium, potassium, magnesium and calcium levels in polychlorinated biphenyl (PCB) poisoned rats. Bull. Environ. Contamin. Toxicol. 16, 516–519.
5. Ebihara, K., Imamura, Y. and Kiriyama, S. (1979): Effect of dietary mineral composition on nutritional equivalency of amino acid mixture and casein in rats. J. Nutr., 109, 2106–2116.
6. Gunshin, H., Yoshikawa, M., Doudou, T. and Kato, N. (1985): Trace elements in human milk, cow's milk and infant formula. Agric. Biol. Chem., 49, 21–26.
7. Pearson, S., Stern, S. and McGavack, T. H. (1953): A rapid, accurate method for the determination of total cholesterol in serum. Anal. Chem., 25, 813–814.
8. Dubick, M. A. and Keen, C. L. (1985): Alterations in tissue trace element and ascorbic acid metabolism in phenytoin fed rats and mice. J. Nutr., 115, 1481–1487.
9. Lei, K. Y. (1977): Cholesterol metabolism in copper deficient rats. Nutr. Rep. Int., 15, 597–605.
10. Carter, J. W. and Koo, S. I. (1984): Effect of dietary Aroclor 1254 (PCBs) on serum levels of lipoprotein cholesterol and tissue distribution of zinc, copper and calcium in Fisher rats. Nutr. Rep. Int., 29, 223–232.
11. Turk, D. E. and Hietman, K. G. (1976): Ingested polychlorinated biphenyl (Aroclor 1242) and growth, calcium and zinc absorption, and intestinal ultrastructure in chicks. Poultry Sci., 55, 672–678.