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Dietary taurine potentiates polychlorinated biphenyl-induced hypercholesterolemia in rats☆

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Abstract

The effect of dietary taurine on cholesterol metabolism and the distribution of lipoprotein-cholesterol in serum of rats fed a diet containing polychlorinated biphenyls (PCB) was examined. Young male Wistar rats (60 g) were fed diets containing 0.2 g/kg diet of PCB and/or 30 g/kg diet of taurine for 15 days. The experiment was performed as the 2 (PCB) × 2 (taurine) factorial design. The addition of PCB elevated serum levels of total- and HDL-cholesterol and apolipoprotein A-I, which is a major apolipoprotein of HDL. Simultaneous supplementation of taurine with PCB amplified the increase of the serum level of total- and HDL-cholesterol. Hepatic concentrations of cholesterol and total lipids were significantly elevated by the supplementation of PCB, and taurine significantly amplified these increases caused by PCB. PCB suppressed hepatic cholesterol 7α-hydroxylase (CYP7A1) gene expression, and taurine induced CYP7A1 gene expression. Taurine also enhanced PCB-induced elevation of malic enzyme mRNA in the liver. These results suggest that taurine enhanced PCB-induced hyper-α-cholesterolemia and that taurine has a role in increasing HDL-cholesterol. © 2001 Elsevier Science Inc. All rights reserved.

Keywords: Taurine; Polychlorinated biphenyls; Cholesterol; Hypercholesterolemia; HDL; Rats

1. Introduction

Taurine, 2-amino ethanesulfonic acid, is the major free intracellular amino acid present in many tissues and has various biological and physiological functions, including cell membrane stabilization [1], antioxidation [2], detoxification [3], osmoregulation [4], neuromodulation [5], and brain and retinal development [6]. Also, taurine plays an important role in lipid metabolism to produce the bile acid conjugates in the liver; that is, taurine increases the utilization of bile acid which is the degrading metabolite of cholesterol and participates in fat absorption [7]. A number of studies concerned with the hypocholesterolemic action of taurine have been conducted using cholesterol-loading animals. Previous studies demonstrated that taurine had a cholesterol-lowering effect in rats and mice [8–11], but not in rabbits [9]. Cholesterol is catabolized to bile acids in the liver and then excreted in the bile after conjugation with glycine or taurine. It is known that the ratios of two types of conjugates with bile acids (glycine conjugates/taurine conjugates; G/T) are different depending on the animal species. G/T ratios in rats and mice are low and, in these animals, taurine is a major precursor of the conjugation of bile acids [12]. Therefore, we consider it pertinent to determine G/T ratio to evaluate the cholesterol-lowering effect of taurine in several species.

On the other hand, the information of the effect of taurine on endogenous type of hypercholesterolemia induced by feeding xenobiotics is limited, as compared with the exogenous type of hypercholesterolemia induced by feeding a high cholesterol diet. Such xenobiotics as polychlorinated biphenyls (PCB) and 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT) are widely distributed in the environment. We occasionally have 2,6-*di*-*tert*-butyl-*p*-cresol (butylated hydroxy toluene; BHT) and barbital derivatives as a food additive and drugs, respectively. We have designated these lipophylic compounds "xenobiotics", which have relatively low molecular weights and induce drug-metaboliz-

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Table 1
The composition of test diets

Ingredient	Control	Taurine	PCB	PCB + Taurine
		g/kg		
Casein[1]	200.0	200.0	200.0	200.0
α-Corn starch[1]	425.3	405.3	425.2	405.2
Sucrose[1]	212.7	202.7	212.6	202.6
Corn oil	50.0	50.0	50.0	50.0
AIN-93G mineral mixture[2]	50.0	50.0	50.0	50.0
AIN-76 vitamin mixture[2]	10.0	10.0	10.0	10.0
Choline choride	2.0	2.0	2.0	2.0
Cellulose	50.0	50.0	50.0	50.0
PCB (Arochlor 1254)[3]	0	0	0.2	0.2
Taurine[4]	0	30.0	0	30.0

[1] Supplied by Oriental Yeast, Tokyo.
[2] Supplied by Nihon Nosan Co. Ltd., Yokohama.
[3] Supplied by Mitsubishi Monsanto Co. Ltd., Tokyo.
[4] Supplied by Taisho Pharmaceutical Co. Ltd., Tokyo.

ing enzymes. The administration of xenobiotics to animals causes many metabolic and pathologic changes [13]: a) induction of hepatic drug metabolizing enzymes [14], b) elevation of serum levels of HDL-cholesterol and apolipoprotein (apo) A-I [15,16], c) accumulation of liver lipids [17,18], d) increase of ascorbic acid concentration in urine and tissues [17,19]. Because PCB is known as the most powerful inducer of these xenobiotic-mediated phenomena, we used PCB for the induction of hypercholesterolemia [20].

The hypercholesterolemia caused by PCB was shown to be influenced by dietary nutrients such as protein [17] and sulfur-containing amino acids (S-AA). The supplementation of methionine and cystine to a low soy protein isolate diet containing PCB significantly increased the serum cholesterol levels as compared with those of rats fed non-supplemented diet [21,22]. These study also demonstrated that S-AA changed serum level of cholesterol mainly in HDL [23]. Moreover, we recently reported that dietary taurine elevated serum level of HDL-cholesterol in normocholesterolemic rats [24]. Since the treatment of xenobiotics magnified the change of HDL metabolism, we speculated that dietary taurine might increase serum level of HDL-cholesterol in hypercholesterolemic rats induced by xenobiotics.

In the present study, we explored the effect of supplementation of taurine to a diet containing PCB on serum total- and HDL-cholesterol, apo A-I and liver cholesterol. And we here found a new role of taurine increasing HDL-cholesterol in rats.

2. Materials and methods

2.1. Experimental design

Young male rats of the Wistar strain weighing about 60 g (Japan SLC, Hamamatsu, Japan) were maintained at 24°C with a 12-h light (0700–1900 h) and dark cycle. To accustom the animals to experimental conditions, they were initially fed a casein diet (control diet, 200 g/kg diet) for 2 days *ad libitum*, then divided into four groups. The composition of the control diet was (in g per kg diet) (Table 1): casein, 200; mineral mixture (AIN-93G [25]; Nihon Nosan, Yokohama, Japan), 50; corn oil, 50; vitamin mixture (AIN-76™ [26]; Nihon Nosan, Yokohama, Japan), 10; choline chloride, 1.5; and a mixture of sucrose and α-corn starch (1:2, in weight) to make a kg diet. For the experimental diets, PCB (0.2 g/kg diet; Arochlor 1254, Mitsubishi Monsant Co., Ltd., Tokyo, Japan) and/or taurine (30 g/kg diet; Taisho Pharmaceutical Co., Ltd., Tokyo, Japan) were supplemented to the basal diet at the expense of carbohydrate. The rats were individually housed and given free access to the experimental diets and water for 15 days. The rats were killed by decapitation at 1000 after 16 h of starvation on the last day of the experimental period, and blood was collected from the cervical wound. The experimental procedures used

Table 2
Effect of taurine (30 g/kg diet) body weight gain, food intake, liver weight and liver lipids in rats fed a diet containing polychlorinated biphenyls (PCB, Arochlor 1254, 0.2 g/kg diet) for 15 days[1]

	Control	Taurine	PCB	PCB + Taurine	ANOVA[2]		
					PCB	Taurine	Interaction
Final body weight, g	137 ± 5.3	137 ± 4.2	141 ± 3.6	138 ± 4.0	NS	NS	NS
Body weight gain, g/15 days	73.7 ± 3.4	74.1 ± 2.6	77.8 ± 2.8	75.1 ± 3.0	NS	NS	NS
Food intake, g on day 14	14.7 ± 0.5	15.7 ± 1.3	13.9 ± 0.3	14.8 ± 1.0	NS	NS	NS
Liver weight, g/100 g body weight	3.51 ± 0.07	3.45 ± 0.04	5.06 ± 0.08[3]	7.07 ± 0.20[4]	0.01	0.01	0.01
Liver lipids							
Total lipids, mg/g liver	50.2 ± 2.6	47.0 ± 1.8	122 ± 7.7[3]	166 ± 15[4]	0.01	0.05	0.05
Cholesterol, μmol/g liver	6.09 ± 0.33	6.04 ± 0.49	17.9 ± 3.1[3]	28.5 ± 2.0[4]	0.01	0.05	0.01

[1] Values are means ± SEM, n = 6.
[2] Statistical significance of differences among values were analyzed by two-way ANOVA. When the interaction was significant ($P < 0.05$), Student's t test was performed. NS: not significant ($P > 0.05$).
[3] The values differed significantly ($P < 0.001$) from the value of control group.
[4] These values differed significntly ($P < 0.001$) from the value of PCB group.

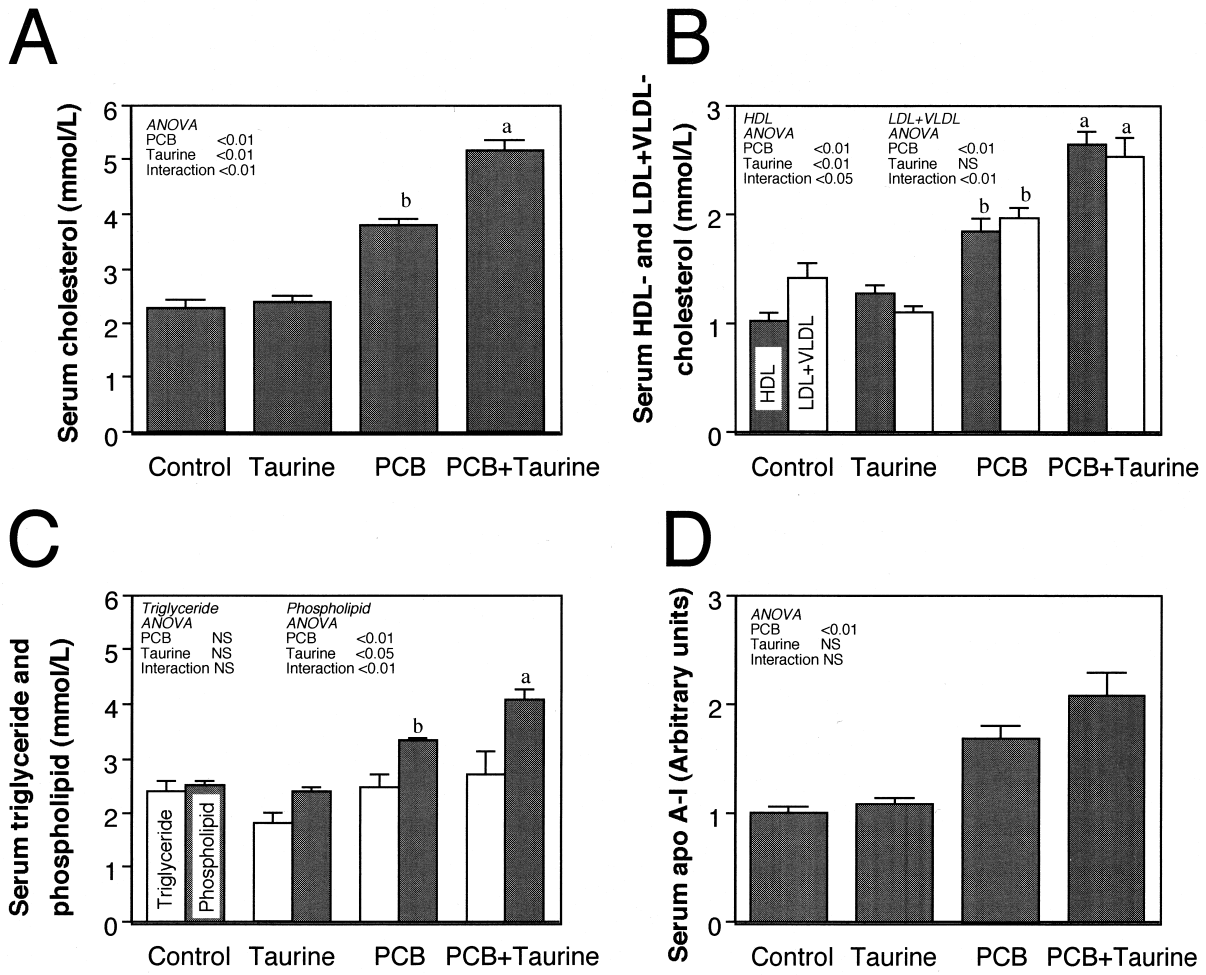

Fig. 1. Effect of dietary taurine on (A) serum total cholesterol, (B) serum HDL-cholesterol and LDL+VLDL-cholesterol, (C) serum triglyceride and phospholipid, and (D) serum apo A-I level in rats fed PCB. Rats were killed at 1000 after 16 h-starvation. Values are means and SEM for six rats in each dietary group. Statistical significance of differences among values was analyzed by two-way ANOVA. When the interaction (PCB × Taurine) was signigicant, Student's t-test was performed. Results of ANOVA are inset in each graph. Superscript b indicates that the values differed significantly from Control group using Student's t test ($P < 0.01$). Superscript a indicate that the values differed significantly from PCB group using Student's t test ($P < 0.01$).

in this study met the guidelines of the Animal Care and Use Committee of the University of Shizuoka.

2.2. Biochemical analyses

The serum lipids (total cholesterol, HDL-cholesterol, phospholipid and triglyceride) were enzymatically determined by using a commercial kit (Cholesterol C-test, HDL-cholesterol-test, phospholipid-test and Triglyceride G-test; Wako Pure Chemical, Osaka, Japan). Cholesterol level in VLDL plus LDL fractions was obtained after subtracting HDL-cholesterol level from total cholesterol level. Liver lipids were extracted by the method of Folch et al. [27], and then the concentrations of cholesterol were determined by the method of Peason et al. [28] Hepatic total lipids were determined gravimetrically. Serum apo A-I was analyzed by non-reducing sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) according to the method of Walsh et al. [29].

Total RNA was isolated from the liver according to the method described by Chomcynski and Sacchi [30], and 15 μg of total RNA was subjected to Northern blot hybridization. The cDNA clones of rat apo A-I [31], rat cholesterol 7α-hydroxylase (CYP7A1) [32], rat malic enzyme [33], and mouse apo E [34] were labeled with Megaprime DNA labeling system (Amersham, Tokyo, Japan) for hybridization. Specific hybridization was quantified with an image analyzer (BAS 2000II, Fuji Film, Tokyo, Japan). Because the apo E mRNA level was not affected by any treatment [20,33,35], we used it as a normalization standard.

2.3. Agarose gel electrophoresis of serum lipoproteins

Agarose gel electrophoresis was carried out by using Corning Universal Film from Corning (Palo Alto, CA). After the agarose gel was run, lipoprotein-cholesterol was stained with Co-Cholest-A (Nippon Chemiphar, Tokyo, Japan).

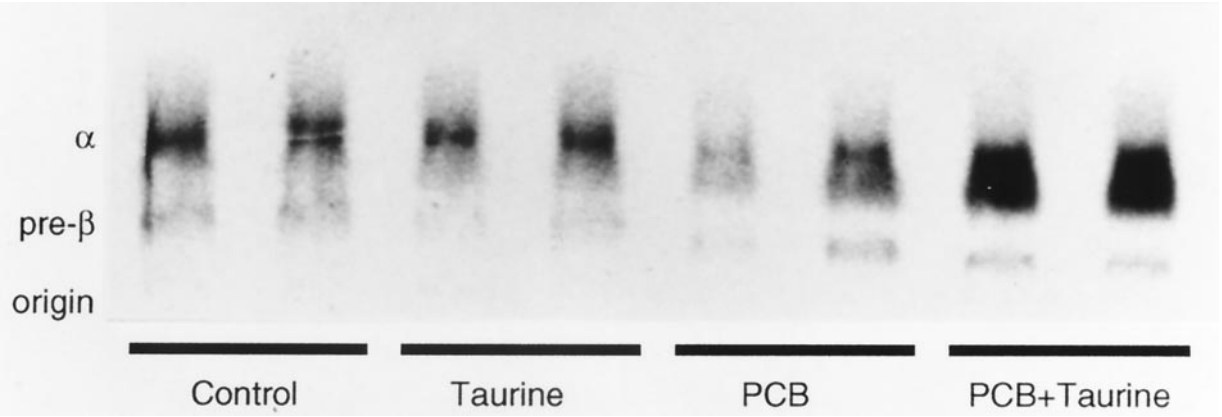

Fig. 2. Agarose gel electrophoresis of serum lipoproteins from control rats fed the control diet (Control), rats fed taurine (Taurine), rats fed PCB (PCB), and rats fed PCB plus taurine (PCB+Taurine). Lipoprotein-cholesterol was stained enzymatically using Co-Cholest-A.

2.4. Statistical analysis

Statistical significance of the differences among values was analyzed by two-way analysis of variance (ANOVA). When interaction (PCB × taurine) was significant ($P < 0.05$), Student's t test was performed.

3. Results

Body weight gains and food intake of rats fed the diets supplemented with taurine and/or PCB did not differ from those of Control group fed the control diet (Table 2). In rats that were not treated with PCB, dietary addition of taurine had no effect on relative liver weight. However, the treatment of PCB to the control diet significantly increased the weight of liver (Student's t test; Control group vs PCB group, $P < 0.001$), and taurine further increased liver weights (Student's t test; PCB group vs PCB+taurine group, $P < 0.001$).

The concentrations of total- and HDL-cholesterols and phospholipid in the serum were significantly higher in PCB group than in Control group (Student's t test, $P < 0.001$) (Figure 1A, B, C). In the PCB-treated groups, the addition of taurine significantly amplified the increase of total- and HDL-cholesterols and phospholipid in the serum (Student's t test, PCB group vs PCB+taurine group, $P < 0.001$). In our previous study (Mochizuki et al. 1998), dietary addition of taurine increased serum level of HDL-cholesterol in normocholesterolemic rats. Although dietary taurine tended to increase serum level of HDL-cholesterol in normocholesterolemic rats (Figure 1B), it was not significant in this experiment (Student's t test, Control group vs Taurine group, $P > 0.05$). Serum triglyceride level was not affected by the supplementation of PCB and/or taurine (Figure 1C). As reported previously [16], serum apo A-I concentrations were significantly elevated by dietary PCB (ANOVA, $P < 0.01$) (Figure 1D). Dietary taurine tended to increase serum level of apo A-I, but it was not significant (ANOVA, $P > 0.05$).

Agarose gel electrophoretograph of serum lipoprotein-cholesterol is shown in Figure 2. As we demonstrated before [15,18], α-migrating lipoprotein-cholesterol was increased by PCB. Taurine further amplified the PCB-induced increase in the α-lipoprotein-cholesterol.

Hepatic concentration of total lipids and cholesterol were significantly elevated by PCB (Student's t test; Control group vs PCB group, $P < 0.001$), and taurine significantly amplified these increases caused by PCB (Student's t test; PCB group vs PCB+taurine group, $P < 0.001$) (Table 1). Hepatic levels of mRNA for apo A-I, CYP7A1 and malic enzyme were then measured (Figure 3). Hepatic level of apo A-I mRNA was increased by PCB (ANOVA, $P < 0.05$) (Figure 3A) [20]. The dietary addition of taurine tended to increase apo A-I mRNA level in rats fed PCB like serum apo A-I level (Figure 1D and 3A). CYP7A1 mRNA level in the liver was lower in rats fed PCB than in rats that were not treated with PCB (ANOVA, $P < 0.05$) (Figure 3B). Dietary taurine increased CYP7A1 mRNA level (ANOVA, $P < 0.05$), as reported recently [11]. As we demonstrated before [20,36], NADPH-generating enzymes, which are thought as lipogenic enzymes, were induced by PCB in the liver. Although the increase in malic enzyme mRNA by PCB was not significant (Student's t test, Control group vs. PCB group, $P > 0.05$), the increased mRNA level by PCB was amplified by dietary taurine ($P < 0.01$) (Figure 3C).

4. Discussion

The hypocholesterolemic effects of taurine are observed in the rats with hypercholesterolemia induced by feeding a high cholesterol diet, and this hypocholesterolemic action of taurine is mainly due to the enhancement of cholesterol degradation and the excretion of bile acid [10,11,37]. The reduction was found in the fractions of VLDL and LDL. On the other hand, we recently demonstrated that taurine increased the serum HDL-cholesterol concentration without any change in total cholesterol level in normocholester-

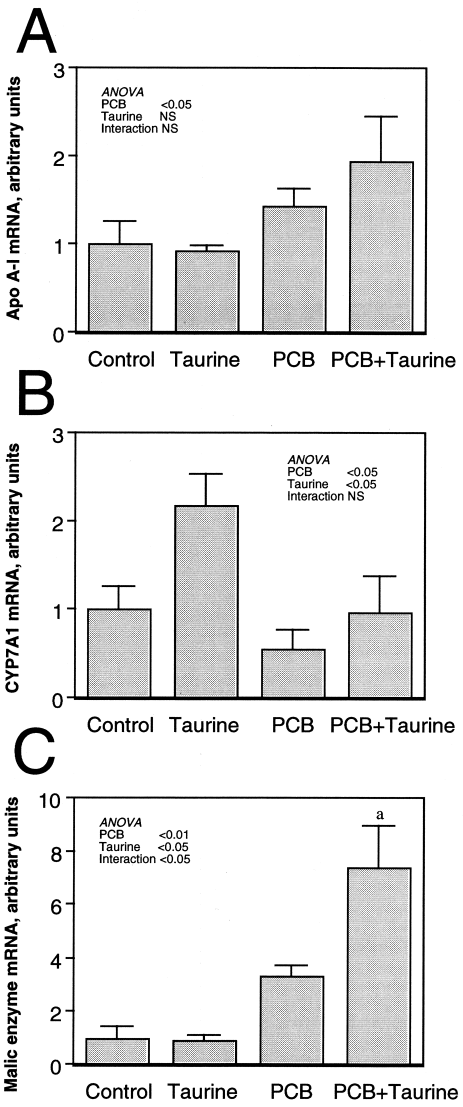

Fig. 3. Effect of dietary taurine on hepatic gene expression of apo A-I (A), CYP7A1 (B) and malic enzyme (C) in rats fed PCB. Rats were killed at 1000 after 16 h-starvation. Values are means and SEM for six rats in each dietary group. Statistical significance of differences among values was analyzed by two-way ANOVA. When the interaction (PCB × Taurine) was significant, Student's t-test was performed. Results of ANOVA are inset in each graph. Superscript a indicates that the value differed significantly ($P < 0.01$) from PCB group using Student's t test.

olemic rats [24]. That study suggested that taurine might regulate HDL-cholesterol metabolism.

Administration of xenobiotics to rats causes an increase in serum level of cholesterol, urinary ascorbic acid, and the activity of liver microsomal mixed function oxidase system [13,17]. Dietary PCB, a powerful xenobiotic, markedly increased serum level of HDL-cholesterol and apo A-I [16]. Changes in serum cholesterol level induced by PCB was modified by dietary manipulation [21,23]. We showed that supplementation of methionine to soy protein isolate (SPI) enhanced PCB-induced hyper-α-cholesterolemia, although methioinine alone tended to increase HDL-cholesterol level [22]. Since HDL-cholesterol level was increased in rats fed PCB, alteration of HDL-cholesterol by dietary manipulation was emphasized in rats fed PCB [22]. Therefore, we supposed that regulation of HDL-cholesterol metabolism by dietary taurine could be pursued by using xenobiotic-treated rats.

We used soy protein as a protein source in previous studies [21–23]. As the sulfur-containing amino acid (S-AA) such as methionine is the first limiting amino acid in SPI, we in this study examined the effect of taurine on cholesterol metabolism using casein for the protein source. In general, the excess administration of S-AA to animals caused a severe toxicity [38]. However, taurine is an end-product of S-AA metabolism. Also it is known that taurine is a non-essential amino acid for animals, except for cats. Therefore, in this study, we supplemented a considerable amount of taurine (30g/kg diet) to the control diet, because toxicity of excessive taurine was not detected [10,11]. The results in the present study showed that dietary addition of taurine further enhanced the increase of serum level of total- and HDL-cholesterol caused by feeding the PCB diet, as the same manner reported by Oda et al. [21] who used methionine and cystine.

It was suggested that the hypercholesterolemia induced by PCB was caused by a significant enhancement of hapatic cholesterol synthesis, accompanied by the induction of the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase [20,39]. On the other hand, it was reported that dietary PCB reduced the activity of CYP7A1, the rate limiting enzyme in the conversion of cholesterol to bile acids in the liver, and thereafter depressed the excretion of fecal bile acids [22]. Therefore, the supplementation of taurine to a diet containing PCB might affect the activities of HMG-CoA reductase and CYP7A1 for cholesterol metabolism, and also might cause the changes in the excretion of bile acids in feces. Although HMG-CoA reductase activity was not measured in the present study, it was shown that taurine increased this enzyme activity in the spontaneously hypertensive rats [37]. Moreover, we found tendency of the enhancement of cholesterol biosynthesis by taurine in rats fed phenobarbital, another xenobiotic [40]. Therefore, we speculated that the enhancement of cholesterol biosynthesis by taurine might be responsible for the increase of serum level of cholesterol. Dietary PCB reduced CYP7A1 mRNA level (Figure 3B). Although CYP7A1 mRNA levels were increased by taurine in both control and PCB groups, the degree of the induction of CYP7A1 gene expression was lower in rats fed PCB than in control rats. This smaller induction of CYP7A1 by taurine might be also explain the increase of serum level of cholesterol by taurine in rats fed PCB.

As our previous report [16], the treatment of PCB increased serum level of apo A-I, which is a major apolipoprotein of HDL. In rats fed PCB, taurine increased the serum level of HDL-cholesterol, and tended to increase serum level of apo A-I (Figure 1). Hepatic apo A-I mRNA level was also increased by PCB, and taurine tended to

increase the level of apo A-I mRNA in the liver (Figure 2). Although the effect of taurine on hepatic apo A-I gene expression was not so great, taurine would stimulate apo A-I gene expression in the liver [24].

The addition of taurine to a diet containing PCB increased not only serum level of cholesterol but also liver lipid (Table 1). It was demonstrated that PCB elevated lipogenic enzyme activities and their gene expression [36]. PCB-induced fatty liver might be caused by the increased synthesis of liver lipid not by the impairment of VLDL secretion [18]. A lipogenic enzyme, malic enzyme, was induced by PCB, and the induction was significantly amplified by dietary taurine (Figure 3c). These suggested that dietary taurine enhanced the increased lipid synthesis by PCB in the liver.

In conclusion, we here first demonstrated that taurine had a significant hyper-α-cholesterolemic action. On the other hand, dietary taurine reduced serum level of VLDL- and LDL-cholesterol in rats fed a high cholesterol diet [10,11]. Therefore, the treatment of taurine would have a beneficial effect on some diseases relating to the serum level of cholesterol such as atherosclerosis.

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References

[1] Pasantes-Morales, H., Wright, C. E., and Gaull, G. E, Taurine protection of lymphoblastoid cells from iron-ascorbate-induced damage, Biochem Pharmacol, 34, 2205–2207 (1985).
[2] Nakamura, T., Ogasawara, M., Nemoto, M., and Yoshida, T, The protective effect of taurine on the biomembrane against damage produced by oxygen radicals, Biol Pharm Bull, 16, 970–972 (1993).
[3] Huxtable, R. J, Physiological actions of taurine, Physiol Rev, 72, 101–163 (1992).
[4] Thurston, J. H., Hauhart, R. E., and Dirgo, J. A, Taurine: A role in osmotic reglulation of mammalian brain and possible clinical significance, Life Sci, 26, 1561–1568 (1980).
[5] Kuriyama, K, Taurine as a neuromodulator, Fed Proc, 39, 2680–2684 (1980).
[6] Sturman, J. A, Nutritional taurine and central nervous system development, Ann NY Acad Sci, 477, 196–213 (1986).
[7] Yamanaka, Y., Tsuji, K., and Ichikawa, T, Stimulation of chenodeoxycholic acid excretion in hypercholesterolemic mice by dietary taurine, J Nutr Sci Vitaminol, 32, 287–296 (1986).
[8] Gandhi, V. M., Cherian, K. M., and Mulky, M. J, Hypolipidemic action of taurine in rats, Ind J Exp Biol, 30, 413–417 (1992).
[9] Herrmann, R. G, Effect of taurine, glycine and sitosterols on serum and tissue cholesterol in the rat and rabbit, Circuration Res, 7, 224–227 (1959).
[10] Mochizuki, H., Takido, J., Oda, H., and Yokogoshi, H, Improving effect of dietary taurine on marked hypercholesterolemia induced by a high-cholesterol diet in streptozotocin-induced diabetic rats, Biosci Biotechnol Biochem, 63, 1984–1987 (1999).
[11] Yokogoshi, H., Mochizuki, H., Nanami, K., Hida, Y., Miyachi, F., and Oda, H, Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet, J Nutr, 129, 1705–1712 (1999).
[12] Stephan, Z., Armstrong, M., and Hayes, K, Bile lipid alterations in taurine-depleted monkeys, Am J Clin Nutr, 34, 204–210 (1981).
[13] Conney, A. H. and Burns, J. J, Stimulatory effect of foreign compounds on ascorbic acid biosynthesis and on drug-metabolizing enzymes, Nature, 184, 363–364 (1959).
[14] Poland, A. and Knutson, J. C, 2, 3, 7, 8-Tetrachlorodibenzo-*p*-dioxin and related halogenated aromatic hydrocarbons, Annu Rev Pharmacol Toxicol, 22, 517–554 (1982).
[15] Oda, H., Matsushita, N., Hirabayashi, A., and Yoshida, A, Hyperlipoproteinemia in rats fed polychlorinated biphenyls, J Nutr Sci Vitaminol, 36, 117–122 (1990).
[16] Oda, H. and Yoshida, A, Effect of feeding xenobiotics on serum high density lipoprotein and apolipoprotein A-I in rats, Biosci Biotechnol Biochem, 58, 1646–1651 (1994).
[17] Kato, N., Tani, T., and Yoshida, A, Effect of dietary level of protein on liver microsomal drug-metabolizing enzymes, urinary ascorbic acid and lipid metabolism in rats fed PCB-containing diets, J Nutr, 110, 1686–1694 (1980).
[18] Oda, H., Matsushita, N., Hirabayashi, A., and Yoshida, A, Cholesterol-rich very low density lipoproteins and fatty liver in rats fed polychlorinated biphenyls, Biosci Biotechnol Biochem, 58, 2152–2158 (1994).
[19] Horio, F. and Yoshida, A, Effect of some xenobiotics on ascorbic acid metabolism in rats, J Nutr, 112, 416–425 (1982).
[20] Oda, H., Suzuki, Y., Shibata, T., and Yoshida, A, Glucocorticoid-dependent induction of HMG-CoA reductase and malic enzyme gene expression by polychlorinated biphenyls in rat hepatocytes, J Nutr Biochem, 10, 644–653 (1999).
[21] Oda, H., Matsuoka, S., and Yoshida, A, Effects of dietary methionine, cystine and potassium sulfate on serum cholesterol and urinary ascorbic acid in rats fed PCB, J Nutr, 116, 1660–1666 (1986).
[22] Oda, H., Okumura, Y., Hitomi, Y., Ozaki, K., Nagaoka, S., and Yoshida, A, Effect of dietary methionine and polychlorinated biphenyls on cholesterol metabolism in rats fed a diet containing soy protein isolate, J Nutr Sci Vitaminol, 35, 333–348 (1989).
[23] Oda, H., Fukui, H., Hitomi, Y., and Yoshida, A, Alteration of serum lipoprotein metabolism by polychlorinated biphenyls and methionine in rats fed a soybean protein diet, J Nutr, 121, 925–933 (1991).
[24] Mochizuki, H., Oda, H., and Yokogoshi, H, Increasing effect of dietary taurine on the serum HDL-cholesterol concentration in rats, Biosci Biotechnol Biochem, 62, 578–579 (1998).
[25] Reeves, P. G., Nielssen, F. H., and Fahey, G. C. Jr, AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutritioin ad hoc writing committee on the reformulation of the AIN-76A rodent diet, J Nutr, 123, 1939–1951 (1993).
[26] American Institute of Nutrition (1977), Report of the American Institute of Nutrition ad hoc committee on standards for nutritional studies, J Nutr, 107, 1340–1348.
[27] Folch, J., Lee, M., and Sloane-Staley, G. H, A simple method for the isolation and purification of total lipids from animal tissues, J Biol Chem, 226, 497–509 (1957).
[28] Peason, S., Stern, S., and McGavack., T. H, A rapid, accurate method for the determination of total cholesterol in serum, Anal Chem, 25, 813–814 (1953).
[29] Walsh, A., Ito, Y., and Breslow, J. L, High levels of human apolipoprotein A-I in transgenic mice result in increased plasma levels of small high density lipoprotein (HDL) particles comparable to human HDL3, J Biol Chem, 264, 6488–6494 (1989).
[30] Chomczynski, P. and Sacchi, N, Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction, Anal Biochem, 162, 156–159 (1987).

[31] Boguski, M. S., Elshoubagy, N., Taylar, J. M., and Gordon, J. I, Comparative analysis of repeated sequences in rat apolipoproteins A-I, A-IV, and E, Proc Natl Acad Sci USA, 82, 992–996 (1985).
[32] Noshiro, M., Nishimoto, M., Morohashi, K., and Okuda, K, Molecular cloning of cDNA for cholesterol 7α-hydroxylase from rat liver microsomes. Nucleotide sequence and expression, FEBS Lett, 257, 97–100 (1989).
[33] Oda, H., Nozawa, K., Miyachi, F., Shimizu, A., Iwasaki, Y., and Kakinuma, A, High responsiveness to thyroid hormone of adult rat primary hepatocytes cultured on EHS-gel, Biosci Biotechnol Biochem, 61, 1590–1592 (1997).
[34] Horiuchi, K., Tajima, S., Menju, M., and Yamamoto, A, Structure and expression of mouse apolipoprotein E gene, J Biochem, 106, 98–103 (1989).
[35] Kawamura, A., Yoshida, Y., Kimura, N., Oda, H., and Kakinuma, A, Phosphorylation/dephosphorylation steps are crucial for the induction of CYP2B1 and CYP2B2 gene expression by phenobarbital, Biochem Biophys Res Commun, 264, 530–536 (1999).
[36] Hitomi, Y., Wakayama, M., Oda, H., and Yoshida, A, Liver-specific induction of NADPH-generating enzymes by polychlorinated biphenyls in rats, Biosci Biotechnol Biochem, 57, 1134–1136 (1993).
[37] Murakami, S., Nara, Y., and Yamori, Y, Taurine accelerates the regression of hypercholesterolemia in stroke-prone spontaneously hypertensive rats, Life Sci, 58, 1643–1651 (1996).
[38] Sauberlich, H. E, Studies on the toxicity and antagonism of amino acids for weanling rats, J Nutr, 75, 61–71 (1961).
[39] Kato, N., Tani, T., and Yoshida, A, Effect of dietary PCB on hepatic cholesterogenesis in rats, Nutr Rep Inter, 21, 107–112 (1980).
[40] Mochizuki, H., Takido, J., and Yokogoshi, H, Effect of dietary taurine on endogenous hypercholesterolemia in rats fed on phenobarbital-containing diets, Biosci Biotechnol Biochem, 63, 1298–1300 (1999).