Guar Gum Reduces Trichloroethylene Accumulation in the Body by Reducing TCE Absorption and Fat Tissue Mass

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Two studies were conducted regarding the effects of guar gum on accumulation and metabolism of trichloroethylene (TCE). In study 1, 6- and 14-weeks-old rats were given a single oral dose of 100 mg of trichloroethylene (TCE). Ten hours after administration of TCE, a marked positive correlation was noted between relative fat tissue weights and TCE distribution in fat tissues. Therefore, a small mass of fat tissue apparently limited TCE accumulation. In study 2, each of four groups of rats was fed one of four diets: cellulose−soybean oil, cellulose−docosahexaenoic acid (DHA), guar gum−soybean oil, or guar gum−DHA for 3 weeks and then all were given TCE as in study 1. The rate of decrease of TCE distributed in fat tissues of groups fed guar gum compared with corresponding groups fed cellulose was greater than the rate of decrease in relative weight of these tissues. TCE absorption by groups fed guar gum decreased 12% compared with TCE absorption of corresponding groups fed cellulose. Therefore, guar gum decreased TCE accumulation in the body by reducing TCE absorption and fat tissue mass.

Keywords: *Trichloroethylene; dietary fiber; fat tissue mass; rats*

INTRODUCTION

1,1,2-Trichloroethylene (TCE) has been widely used as an industrial solvent in a variety of s manufacturing operations. During and after use, TCE may be released into the ground, air, or rivers. Occupational and environmental exposure to TCE has been reported in industrial areas. Recently, high levels of TCE pollution have been found in electronics factories and surrounding areas (*1*). After absorption from the gastrointestinal tract, unmetabolized TCE can be retained in the fat tissue because of its high liposolubility. TCE exposure is known to cause a variety of health hazards. Repeated oral administration of the maximum tolerated dose resulted in hepatotoxicity and neurotoxicity (*1*−*3*). Long-term carcinogenicity studies in rodents have shown that exposure to high doses of TCE results in the induction of tumors in the liver, lung, kidney, and testis (*4*).

The enhanced excretion of lipophilic chemicals from the body would be an important way to minimize their biological effects. It has been shown that fat tissue mass is involved in the distribution, metabolism, and excretion of lipophilic compounds such as pentachlorobenzene (PECB), which is metabolized at a relatively slow rate, and hexachlorobenzene (HCB), which is metabolized at a much slower rate than PECB. We have also observed that the metabolism and excretion of PECB and HCB were markedly increased in rats when they were fed a restricted diet (*5*,*6*), viscous dietary fibers (*7*−*9*), or fish oil (*10*−*12*). This enhanced metabolism and excretion of such lipophilic compounds was not due to the enhancement of the activity of hepatic drug-metabolizing enzymes per se, but due to the small mass of fat tissue that resulted from those treatments (*8*, *11*, *12*). With the decrease of fat tissue mass that accumulates lipophilic compounds, the concentration of lipophilic compounds in the blood and liver increased, and the amount of metabolites formed increased. The role of fat tissue mass is uncertain in the metabolism of rapidly metabolized lipophilic pollutants.

TCE easily crosses the gastrointestinal wall, and it rapidly disappears from the blood as it is exhaled unchanged, transported via the blood stream to be accumulated in fat tissues because of its lipophilic properties, or metabolized. TCE is metabolized at a high rate by the catalytic action of liver microsomal cytochrome P-450 related enzymes and converted to trichloroethanol and trichloroacetic acid (*4*). Nakajima et al. (*13*) reported that TCE is metabolized by a low-Km form of enzyme which is induced by ethanol and a high-Km form of enzyme which is induced by phenobarbital, but no influence on the rate of TCE metabolism was observed by the treatment of methylcholanthrene induced enzymes.

Although TCE is metabolized at a much faster rate (*14*) than PECB (*6*) and HCB (*9*), unmetabolized TCE can be retained in fat tissue because of its high liposolibility (*15*). Therefore, the ingestion of dietary components that reduce fat tissue mass might decrease the amount of TCE residue in the body as has been observed for PECB and HCB. In the first study, we compared the metabolism and accumulation of TCE in the organs and fat tissues of young (6 wk old) rats with that of adult (14 wk old) rats. We investigated whether a small fat tissue mass of young rats compared with a large mass of adult rats could enhance the metabolism and excretion of TCE in rats. In the second study, we determined

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Table 1. Compositions of the Experimental Diets[a]

ingredient	diet 1	diet 2			
		cellulose−soybean oil	guar gum−soybean oil	cellulose−DHA	guar gum−DHA
casein	20.0	20.0	20.0	20.0	20.0
DL-methionine	0.3	0.3	0.3	0.3	0.3
cornstarch	15.0	39.75	39.75	39.75	39.75
sucrose	45.0	10.0	10.0	10.0	10.0
dextrin		13.2	13.2	13.2	13.2
soybean oil	10.0	7.0	7.0	3.0	3.0
DHA[b]				4.0	4.0
cellulose	5.0	5.0		5.0	
guar gum			5.0		5.0
AIN mineral mixture[c]	3.5	3.5	3.5	3.5	3.5
AIN vitamin mixture[c]	1.0	1.0	1.0	1.0	1.0
choline bitartrate	0.2	0.25	0.25	0.25	0.25
tert-butylhydroquinone		0.0014	0.0014	0.0014	0.0014

[a] Composition for all ingredients is given in grams per 100 g of diet. [b] Docosahexanoic acid. [c] Mineral mixture and vitamin mixture of diet 1 were based on the AIN-76 formulation and those of diet 2 were based on the AIN-93 formulation.

whether the feeding of guar gum and DHA to rats reduces the TCE absorption in the intestine and enhances the disappearance of TCE from the body in a short period of time, as has been reported for PECB and HCB.

MATERIALS AND METHODS

Materials. TCE was purchased from Wako Pure Chemical Industries, Osaka, Japan. DHA was obtained from Nihon Suisan Co., Tokyo, Japan. Other dietary compounds were purchased from Oriental Yeast Co., Tokyo, Japan. *n*-Hexane of a grade for determining residual pesticides and other chemicals of analytical grade were purchased from Wako Pure Chemical Industries, Osaka, Japan.

Animals and Diets. The compositions of the animal diets are shown in Table 1. Diets 1 and 2 were used in studies 1 and 2, respectively. To avoid the oxidation of fatty acids, DHA was mixed with soybean oil daily, and the blended fats (soybean oil/DHA, 3:4) were added to the fatfree diet immediately before administration of the diet to rats. Therefore, as we reported previously, the (n-6)/(n-3) ratio of cellulose−DHA and guar gum−DHA diets was designed to be 2:1 (*9*).

Male Sprague−Dawley rats obtained from Japan Clea (Tokyo, Japan) were housed individually in stainless steel wire-bottomed cages, in a room with a constant temperature of 23 ± 1 °C and a 12-h light:dark cycle.

To raise adult rats for study 1, 12 rats (5 wk old) were fed a nonpurified commercial diet (CE-2, Japan Clea) for 8 wk. These adult rats and twelve young rats (5 wk old) were then fed diet 1 shown in Table 1. Rats were given free access to the diet and distilled water. After 1 wk of consuming the experimental diet, young and adult rats were divided into two groups each. One group of young rats and one group of adult rats were given by intragastric gavage a single dose of TCE at 100 mg (0.76 mmol) dissolved in 0.5 mL of soybean oil. The other groups to be untreated were given an equal volume of soybean oil. At that time, food was removed and all feeding was discontinued. Blood (25−500 mL) was withdrawn (within 1 min) from the tail vein while rats remained conscious at 1, 2, 4, 6, and 10 h after the administration of TCE. These rats were then anesthetized with ether and blood was removed by heart puncture after the last blood sample was taken. The organs and fat tissues were removed and weighed.

In study 2, rats (4 wk old) were divided into four groups of six rats each. Each group received one of the four diets prescribed under diet 2 shown in Table 1. Rats were given free access to food and distilled water. After 3 wk of consuming the diet, rats were given a single dose of 100 mg of TCE as described in study 1. Blood was taken from tail vein at 1, 2, 4, 6, and 10 h after the administration of TCE. Remaining blood was taken by heart puncture. Organs and fat tissues were removed as in study 1. The small intestine and caecum were dissected and their contents were obtained. All procedures were in accordance with the National Institute of Health and Nutrition Guidelines for the Care and Use of Laboratory Animals.

Analytical Methods. Blood was mixed with 1 mL of distilled water. Organs and the small intestinal and caecal contents were homogenized with 4 vol water. To extract TCE, *n*-hexane was added to the blood mixture and the homogenate. Fat tissue was directly homogenized and extracted with *n*-hexane. Mixing was done by a vortex or homogenizer, and the upper layer was obtained by centrifugation at 600*g* for 5 min. The extracted solution was cleaned by a florisil column and diluted if necessary. TCE was analyzed using a Shimadzu PARVUM QP-5000 gas chromatograpy/mass spectrometer (Shimadzu, Kyoto, Japan). A fused silica capillary column DB-624 (0.25 mm × 60 m) (J & W Scientific, Folsom, CA) was used. The temperature of the column oven and the on-column injector was programmed from 50 °C to 200 °C at 5 °C/min. The GC/MS interface temperature was set at 230 °C. N_2 was used as the carrier gas.

Drug-metabolizing enzyme concentrations and activities in the liver were assayed as reported by Umegaki and Ikegami (*12*). Cytochrome P-450 was measured by the method of Omura and Sato (*16*), UDP−glucuronosyltransferase activity was measured by the method of Kuno (*17*), and glutathionetransferase activity was determined by the method of Habig and Jakoby (*18*).

Hepatic lipids were extracted by the methods of Folch et al. (*19*). Triglyceride concentration was measured using a triglyceride test kit (Wako Pure Chemical Industries, Osaka, Japan). Phospholipid concentration was measured by the methods of Fiske and Subbarow (*20*) and total cholesterol was measured by the methods of Sobel and Fernandez (*21*). Protein was determined according to the methods of Lowry et al. (*22*).

Statistical Analysis. The Yukumusu computer program (Yukumusu, Tokyo, Japan) was used for statistical analysis of the data. All results were subjected to ANOVA. Differences in mean values among groups were tested by Duncan's multiple comparison test (Tables 2, 3, 5, and 6 and Figure 2). Student's t test was used for all pairwise comparisons (Table 4 and Figure 1). Differences were considered significant at $p < 0.05$.

RESULTS

Study 1. Average body weights of young and adult rats used in this study were 230.5 ± 2.3 g and 492.0 ± 13.8 g, respectively. Relative weights (g/100 g body weight) of liver, epididymal fat tissue and perirenal fat tissue of young rats were 4.45 ± 0.09 g, 1.10 ± 0.09 g, and 0.82 ± 0.04 g, respectively, and these of adult rats were 3.31 ± 0.11 g, 2.87 ± 0.19 g, and 1.49 ± 0.15 g,

Table 2. Effect of Age on Serum and Liver Lipid Concentrations in Rats with or without Trichloroethylene (TCE) Treatment[a]

	cholesterol	triglyceride	phospholipid	total lipid
serum lipid	(mg/dl)	(mg/dl)	(mg/dl)	
control				
young	70.51 ± 4.95[a]	306.84 ± 38.90[a]	128.17 ± 6.96[a]	
adult	89.69 ± 6.21[b]	412.69 ± 29.01[a]	159.42 ± 10.30[b]	
TCE-treated				
young	77.74 ± 4.45[ab]	360.97 ± 24.45[a]	156.19 ± 7.54[b]	
adult	84.14 ± 6.34[ab]	473.36 ± 44.73[a]	171.96 ± 10.30[b]	
liver lipid	(mg/g)	(mg/g)	(mg/g)	(mg/g)
control				
young	2.46 ± 0.16[a]	35.73 ± 5.19[a]	24.94 ± 1.05[a]	6.41 ± 0.66[a]
adult	2.91 ± 0.41[a]	37.86 ± 10.11[a]	15.93 ± 1.30[c]	7.88 ± 1.27[a]
TCE-treated				
young	2.48 ± 0.15[a]	37.59 ± 5.96[a]	26.49 ± 0.89[a]	7.38 ± 0.78[a]
adult	3.02 ± 0.19[a]	46.06 ± 3.81[a]	21.00 ± 1.25[b]	7.74 ± 0.56[a]

[a] Values are expressed as mean ± SD for 6 rats. Within a row, values not sharing a superscript letter are significantly different at $P < 0.05$.

Table 3. Effect of Age on Drug Metabolizing Enzymes in Rats

	cytochrome P-450 content (nmol/mg prot)	glutathione−*s*-transferase activity (μmol/mg prot/min)	UDP−glucuronyl transferase activity (μmol/mg prot/15min)
control			
young	0.42 ± 0.11[a]	0.48 ± 0.02[a]	0.30 ± 0.03
adult	0.59 ± 0.06[b]	0.39 ± 0.02[a]	0.34 ± 0.02
TCE-treated			
young	0.36 ± 0.01[a]	0.62 ± 0.04[b]	0.27 ± 0.02
adult	0.52 ± 0.05[ab]	0.46 ± 0.02[a]	0.33 ± 0.05

[a] Rats were orally administered TCE at 100 mg (0.76 nmol)/rat after being fed diet 1 for 1 week. Values are expressed as mean ± SD for 6 rats. Within a column, values not sharing a superscript letter are significantly different at $P < 0.05$.

respectively. However, TCE treatment did not influence the body weight and relative weights of the liver and fat tissues in either young or adult rats. In both control and TCE-treated groups, although the body weights and relative weights of epididymal and perirenal fat tissues of adult rats were about 2 times higher than those of young rats, the relative weight of the liver of adult rats was lower than that of young rats.

Table 2 shows the lipid components of the serum and liver. In the control group, the serum cholesterol concentration of young rats was lower than that of adult rats. The serum phospholipid concentration of young rats in the control group was lower than that of the other three groups. However, serum cholesterol, triglyceride, and phospholipid concentrations were not markedly different among the adult rats in the control group and both the young and adult rats in the TCE-treated group. In both the control and TCE-treated groups, the liver phospholipid concentration of young rats was higher than that of adult rats. However, liver cholesterol, triglyceride, and total lipid concentrations were not markedly different among these four groups.

Hepatic drug-metabolizing enzyme activity is shown in Table 3. Cytochrome P-450 concentration of adult rats in the control group was higher than that of young rats in both the control and TCE-treated groups. Glutathione−*s*-transferase activity of young rats in the TCE-treated group was higher than that of other three groups. No remarkable difference in UDP−glucuronyltransferase activity was observed among these four groups.

Changes in the concentration of TCE (nmol/mL/100 g body weight) in the blood up to 10 h after TCE administration are shown in Figure 1. TCE peak concentrations in the blood of young and adult rats were

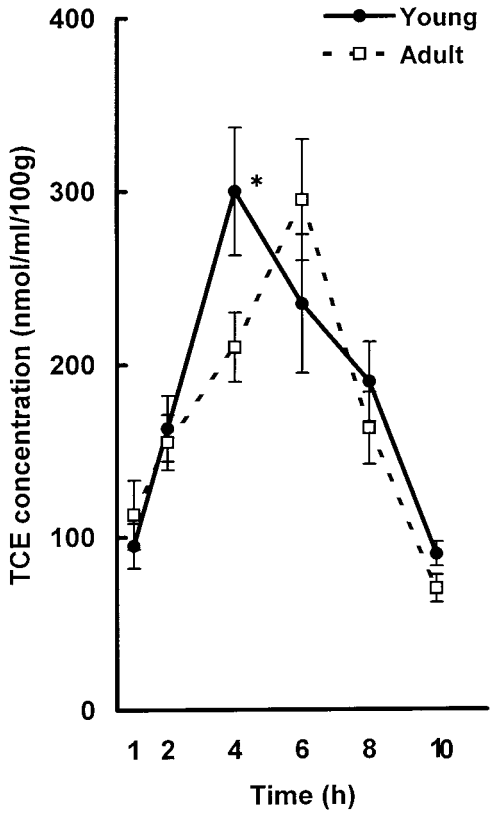

Figure 1. Changes in TCE concentration in the blood of young and adult rats. Rats were orally administered 100 mg (0.76 mmol) of TCE at h 0 after being fed diet 1 for 1 wk. TCE concentrations represent nmol of TCE/mL blood/100 g of body weight. Values are means for six rats per group. *Significant difference was observed between the groups of young and old rats.

Table 4. Effect of Age on the Distribution of Trichloroethylene (TCE) in Organs and Fat Tissues in Rats 10 h after TCE Administration[a]

group	young	adult	young/adult
organ			
liver	0.0137 ± 0.0041[a]	0.0032 ± 0.0019[b]	4.28
kidney	0.0014 ± 0.0004[a]	0.0003 ± 0.0001[b]	4.67
brain	0.0008 ± 0.0003[a]	0.0005 ± 0.0002[b]	1.60
fat tissue			
epididymal	0.2524 ± 0.0799[a]	0.6762 ± 0.2752[b]	0.37
perirenal	0.2263 ± 0.0882[a]	0.4224 ± 0.1879[b]	0.54

[a] Values are expressed as the ratio of TCE content in organ or fat tissue per orally administered TCA 100 mg (0.76 mmol). Values are mean±SD for 6 rats. Within a row, values not sharing a superscript letter are significantly different at $P<0.05$.

reached at 4 and 6 h, respectively. However, no significant difference was observed between the young and adult rats in terms of the actual TCE peak concentrations reached.

The ratio of TCE content in organs and fat tissues to the orally administered TCE (100 mg/rats) are shown in Table 4. In both young and adult rats, a large amount of TCE was concentrated in fat tissues. The distribution of TCE in the liver, kidney, and brain in young rats was 4.3, 4.7, and 1.6 times higher than that of adult rats, respectively. However, the distributions of TCE in epididymal and perirenal fat tissues of young rats were respectively 37% and 54% those of adult rats. In young rats, the amount of TCE found in epididymal and perirenal fat tissues was respectively 18 and 17 times higher than that in the liver. On the other hand, in adult rats, the amount of TCE found in epididymal and perirenal fat tissues was respectively 211 and 132 times higher than that in the liver. Therefore, it was evident that the ratio of TCE distributed in fat tissues was higher in adult rats than in young rats.

As shown in Figure 2, a marked positive correlation was noted between the relative fat tissue weight and the distribution of TCE in both epididymal ($r = 0.99$, $p < 0.05$) and perirenal ($r = 0.91$, $p < 0.05$) fat tissues.

Study 2. Body weights of cellulose−soybean oil, cellulose−DHA, guar gum−soybean oil, and guar gum−DHA diet groups were 238.3 ± 7.1 g, 282.2 ± 3.7 g, 258.3 ± 4.7 g, and 247.0 ± 6.4 g, respectively. Therefore, body weight in both guar gum groups was about 90% of that in the corresponding cellulose groups.

Relative weights of epididymal fat tissue of cellulose−soybean oil, cellulose−DHA, guar gum−soybean oil, and guar gum−DHA groups were 0.86 ± 0.14 g, 0.88 ± 0.05 g, 0.45 ± 0.05 g, and 0.52 ± 0.06 g, respectively, and these of perirenal fat tissue were 0.71 ± 0.03 g, 0.69 ± 0.05 g, 0.50 ± 0.05 g, and 0.55 ± 0.06 g, respectively. Therefore, relative weights of the epididymal fat tissue of guar gum−soybean oil and guar gum−DHA group were 52% and 59% of those of the corresponding cellulose groups, respectively, and these of the perirenal fat tissue were 70% and 80% of those of the corresponding cellulose groups. Therefore, the decrease of fat tissue weight was larger than that of body weight.

Changes in the concentration of TCE (nmol/mL/100 g body weight) in the blood up to 10 h after TCE administration are shown in Figure 3. TCE peak concentrations in blood of cellulose−soy bean oil, cellulose−DHA, and guar gum−soy bean oil groups were reached at 2 h, and that of guar gum−DHA was reached at 4 h after administration TCE. However, TCE concentration in the blood was not markedly different among these four groups during 10 h.

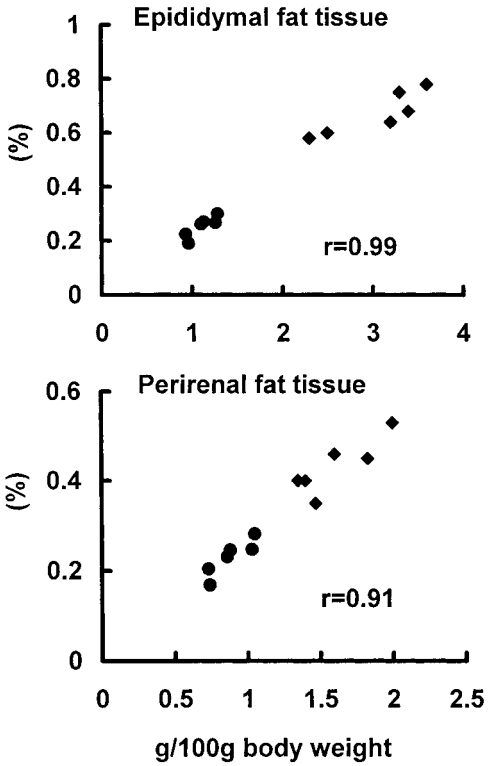

Figure 2. Correlation between the relative fat tissue weight (g/100 g of body weight) and distribution of TCE (%, the rate of TCE content in fat tissue/orally administered TCE) in epididymal ($r = 0.99$, $p < 0.001$) and perirenal ($r = 0.91$, $p < 0.001$) fat tissues. Each point represents one rat (●, young rats; ◆, adult rats).

The ratios of the TCE content in organs and fat tissues to the dose of TCE administered are shown in Table 5. A large amount of TCE was accumulated in fat tissues. The ratios of the TCE content in the liver and kidney to the dose administered were lower in the guar gum−DHA group than other three groups. The distributions of TCE in the epididymal fat tissue of the guar gum−soybean oil and guar gum−DHA group were respectively 50% and 34% of those in the corresponding cellulose groups. The amounts of TCE in the perirenal fat tissue of the guar gum−soybean oil and guar gum−DHA groups were respectively 57% and 60% those of the corresponding cellulose groups. Therefore, the decrease of TCE distribution in the epididymal and perirenal fat tissues between the guar gum groups and the corresponding cellulose groups was larger than the decrease of the relative weight of these fat tissues. A marked positive correlation was noted between the relative fat tissue weight and the distribution of TCE in epididymal ($r = 0.98$, $p < 0.05$) and perirenal ($r = 0.97$, $p < 0.05$) fat tissues.

The ratios of the total amounts of TCE in the contents of the intestine and caecum to the dose administered are shown in Table 6. Total amount of TCE in the caecal contents of those four groups was higher than that in the intestinal contents. Although the amount of TCE in the intestinal content was not markedly different among these four groups, the amount of TCE in caecal content of both guar gum groups was higher than that of both cellulose groups. The total amounts of TCE in the intestine and caecum of the cellulose−soybean oil, cellulose−DHA, guar gum−soybean oil, and guar gum−DHA groups were about 4.8%, 3.9%, 17.3%, and 15.8%, respectively, and the amounts of absorbed TCE by these

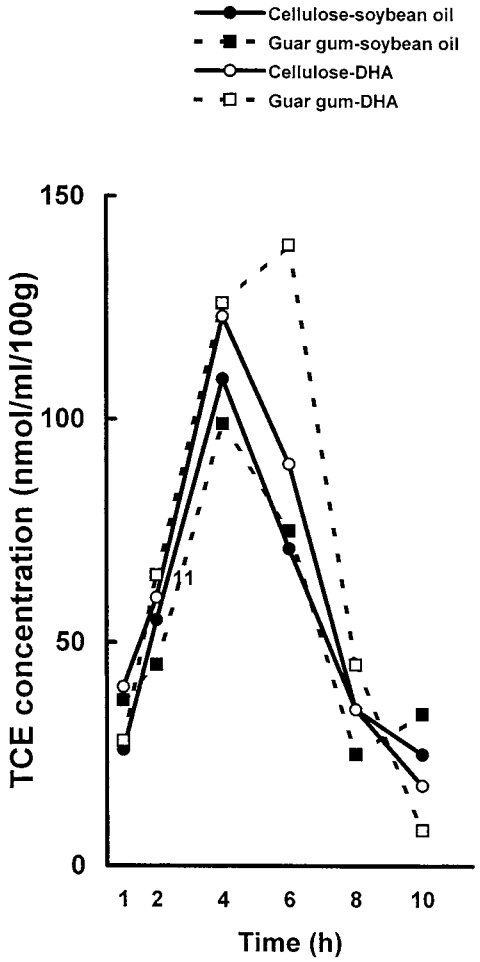

Figure 3. Effect of guar gum and DHA on TCE concentration in the blood. Rats were orally administered 100 mg (0.76 mmol) of TCE at h 0 after being fed the respective diets for 3 weeks. TCE concentrations represent nmol of TCE/mL blood/100 g of body weight. Values are means for six rats per group.

groups were 95.2%, 96.1%, 82.7%, and 84.2%, respectively. Therefore, the amount of absorbed TCE in these guar gum groups was about 12% lower than that in these corresponding cellulose groups.

DISCUSSION

In studies 1 and 2, we expressed TCE values in the organs, the fat tissues, and the contents of intestine and caecum as the ratio of TCE contents per orally administered TCE. TCE values in blood represented nmol per mL of blood per 100 g body weight. Therefore, to simplify the experiments, all rats used in studies 1 and 2 were given same amount of TCE. We found that TCE easily crossed the gastrointestinal wall and its peak concentration in blood was reached at 2 to 4 h after administration, after which it disappeared rapidly from the blood, being exhaled unchanged or accumulated in organs and fat tissues via the blood stream and metabolization (Figures 1 and 3). Similar findings were observed by Hobata et al. (*23*) using dogs and D'Souza et al. (*24*) using rats. Although a large amount of TCE was distributed in fat tissues because of its lipophilic property, the ratio of TCE content in the epididymal and perirenal fat tissue to the dose administered TCE in adult rats was respectively 2.7 and 1.9 times higher than that in young rats (Table 4). On the other hand, relative weights of the epididymal and perirenal fat tissue of adult rats were also 2.7 and 1.8 times higher than those of young rats, respectively. Furthermore, in epididymal and perirenal fat tissues, a marked positive correlation was observed between the relative weight of fat tissue and the distribution of TCE in it (Figure 2). Therefore, it was considered from these values that the total amount of TCE that accumulated in these fat tissues paralleled the relative fat tissue mass. Namely, when the fat tissue is small its capacity to store lipophilic chemicals is reduced.

Umegaki et al. (*11*) reported that the triglyceride concentration in the liver of rats fed lard was higher than those in rats fed soybean oil or fish oil, and a marked positive correlation was noted between pentachlorobenzene (PECB) and triglyceride concentration in liver. Therefore, we measured triglyceride, phospholipid, cholesterol, and total lipid concentrations in the serum and liver (Table 2), but in both control and TCE-treated groups these lipid component concentrations were not markedly different between the young and adult rats. However, in this study, the distribution of TCE in the liver of young rats was 4.3 times higher than that of adult rats (Table 4). These findings indicate that the smaller fat tissue mass of young rats compared with that of adult rats limited the accumulation of TCE in these tissues of young rats and thereby extra TCE was accumulated in the liver and other organs.

In TCE-treated rats, phospholipid concentration in serum of young rats and in liver of adult rats was higher than that of control rats (Table 2). TCE was reported to be hepatotoxic and oral administration of TCE resulted in hepatocellular swelling in mice (*25*). However, further study will be necessary to clarify the causes.

To examine the contribution of hepatic drug-metabolizing enzymes on the difference of TCE amounts in the liver, other organs, and fat tissues, we measured cytochrome P-450 content and the activities of UDP−glucuronyltransferase and glutathione−*s*-transferase in liver (Table 3). Although glutathione−*s*-transferase activity of TCE-treated young rats was significantly higher than that of control rats, no significant difference was observed in adult rats. It was considered that the treatment of TCE increased the activity of the enzyme in young rats because the distribution of TCE in the liver of young rats was 4.3 times higher than that of adult rats (Table 4). However, in TCE-treated groups, although glutathione−*s*-transferase activity was slightly higher in young rats than adult rats, no significant difference in cytochrome P-450 content and UDP−glucuronyltransferase activity was observed between the young and adult rats. Therefore, it was naturally considered that these drug-metabolizing enzymes do not contribute much to the difference of the TCE metabolization rate between the young and adult rats. However, it was considered that, in young rats, the small size of the fat tissue mass limited the accumulation of TCE in it and increased the amount of TCE in the liver and accelerated the TCE metabolism by hepatic drug-metabolizing enzyme. We have already reported that the metabolism and excretion of the lipophilic and relatively metabolizable PECB and stable HCB were markedly increased in rats by the feeding of viscous dietary fiber and fish oil (11,12,14). This enhanced metabolism and excretion of PECB and HCB were not due to the enhancement of the activity of hepatic drug-

Table 5. Effect of Guar Gum and Docosahexanoic Acid (DHA) on the Distribution of Trichloroethylene (TCE) in Organs and Fat Tissues[a]

group	cellulose−soybean oil	guar gum−soybean oil	soybean oil guar./cellu.	cellulose−DHA	guar gum−DHA	DHA guar./cell.
organ						
liver	0.0224 ± 0.0037[a]	0.0198 ± 0.0062[a]	0.88	0.0202 ± 0.0033[a]	0.0149 ± 0.0007[b]	0.74
kidney	0.0027 ± 0.0002[a]	0.0026 ± 0.0003[a]	0.96	0.0028 ± 0.0002[a]	0.0021 ± 0.0000[b]	0.75
brain	0.0010 ± 0.0001	0.0012 ± 0.0001	1.20	0.0012 ± 0.0001	0.0014 ± 0.0003	1.17
fat tissue						
epididymal	0.2374 ± 0.0652[a]	0.1182 ± 0.0321[b]	0.50	0.2628 ± 0.0514[a]	0.0986 ± 0.0189[b]	0.34
perirenal	0.1613 ± 0.0317[a]	0.0924 ± 0.0209[b]	0.57	0.1581 ± 0.0371[a]	0.0947 ± 0.0438[b]	0.60

[a] Rats were orally administered TCE at 100 mg (0.76 nmol)/rat after being fed diet 2 for 3 weeks. Values are expressed as % of TCE content in organ or fat tissue per orally administered TCE. Values are mean ± SD for 6 rats. Within a row, values not sharing a superscript letter are significantly different at $P < 0.05$.

Table 6. Effect of Guar Gum and Docosahexanoic Acid (DHA) on Trichloroethyrene (TCE) Levels in Contents of Intestine and Caecum[a]

group	cellulose−soybean oil	guar gum−soybean oil	cellulose−DHA	guar gum −DHA
intestine	0.882 ± 0.217	0.855 ± 0.285	1.305 ± 0.439	0.632 ± 0.156
caecum	3.947 ± 1.773[a]	16.447 ± 4.454[b]	2.632 ± 0.877[a]	15.136 ± 4.505[b]

[a] Values are expressed as % of TCE in the intestinal and caecal contents per orally administered TCE at 100 mg (0.76 mmol). Values are mean ± SD for 6 rats. Within a row, values not sharing a superscript letter are significantly different at $P < 0.05$.

metabolizing enzyme per se, but were due to the small mass of fat tissue that resulted from the treatment.

In study 2, we investigated whether the same beneficial effect of guar gum and DHA feeding would be observed with respect to TCE. As shown in Table 5, we found that the amounts of TCE residue in organs and fat tissues were remarkably lower in groups fed the guar gum−soybean oil or guar gum−DHA diet than in those fed the cellulose−soybean or cellulose−DHA diet. Also, the relative weight of fat tissues was lower in both groups of rats fed the diet containing guar gum than in those fed the diet containing cellulose. These results are consistent with our previous reports that concentrations of highly lipophilic compounds in the fat tissues decrease with food restriction, starvation, or feeding viscous dietary fiber or fish oil to rats reduces the mass of fat tissue (5, 6, 14, 26, 27). However, feeding DHA did not give comparable results with feeding fish oil rich in DHA. Namely, feeding of DHA to rats did not reduce the fat tissue mass and the accumulation of TCE in it. The cause was considered to be that we used blended fats (DHA/soybean oil, 4:3) and designed the rate (n-6)/(n-3) to be 2:1 to avoid essential fatty acid deficiency.

In this study, the amount of TCE absorbed into blood of the cellulose−soybean oil, cellulose−DHA, guar gum−soybean oil, and guar gum−DHA was 95.2%, 96.1%, 82.7%, and 84.2%, respectively. However, there are many reports that administered TCE is easily absorbed into the blood and disappears from the blood rapidly, being exhaled unchanged or distributed in the fat tissues and organs (*15*, *23*, *24*, *28*, *29*). Therefore, although the amount of absorbed TCE into the blood of cellulose groups during 10 h was about 12% higher than that corresponding guar gum groups, respectively, no significant difference was observed in the blood TCE concentration among these four groups (Figure 3).

However, the dramatic decrease of TCE accumulation in fat tissues of the rats fed guar gum could not be explained only by changes in the decreased amount of TCE that crosses the gastrointestinal wall. In a previous paper (*14*), we observed a similar phenomenon in rats fed a diet containing Na-alginate and fish oil. The accumulation of TCE in fat tissue was significantly lower in rats given Na-alginine−soybean or cellulose−fish oil diet than in rats given cellulose−soybean oil diet, and was accompanied by fat tissue of a relatively smaller mass. It is widely recognized that fat tissue has an important role in the storage of drugs or organochlorine chemicals in the body. Our results suggested that the TCE metabolism and excretion might be accelerated in rats with small fat tissue mass such as the young rats and the rats fed guar gum. The possible mechanism was considered as follows. The amount of TCE distributed in fat tissues was lower in rats with small fat tissue mass than in rats with large fat tissue mass. As a result, the distribution of TCE in the liver and other organs increased via the blood stream, and metabolism by the hepatic drug-metabolizing enzyme in liver and exhaled in breath was accelerated.

In study 1, we found that the amount of TCE distributed in fat tissues of the adult rats with a bigger fat tissue mass was higher than that in young rats. As a result, the distribution of TCE in the liver of the adult rats was lower than that in young rats. Therefore, the metabolism of TCE by the hepatic drug-metabolizing enzyme was reduced in adult rats with a bigger fat tissue mass. In study 2, the amount of TCE which crossed the gastrointestinal wall in the groups of rats fed guar gum was decreased by about 12% compared with that of the corresponding groups fed cellulose. However, the decrease of TCE accumulation in the fat tissue of rats fed guar gum could not be explained only by the amount of TCE remaining in the intestines. Therefore, we concluded that this might be related to the small mass of the fat tissues in rats fed guar gum. As shown in the result of study 1, the small mass of the fat tissues limited the accumulation of TCE in fat tissues and accelerated TCE metabolism in the liver.

ABBREVIATIONS USED

TCE, trichloroethylene; DHA, docosahexaenoic acid; PECB, pentachlorobenzene; HCB, hexachlorobenzene.

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