Feeding Fish Oil to Rats Accelerates the Metabolism of Hexachlorobenzene

Keizo UMEGAKI1,* and Sachie IKEGAMI2

1 Division of Applied Food Research and 2 Division of Food Science, The National Institute of Health and Nutrition, Shinjuku-ku, Tokyo 162-8636, Japan
(Received November 17, 1997)

Summary This study was conducted to examine the influence of dietary fat on the metabolism and excretion of hexachlorobenzene (HCB), a ubiquitous food contaminant which is metabolized at a low rate. Three groups of rats were fed semi-purified diets containing 10 g/100 g of either soybean oil, lard or fish oil for 2 wk and then given a single dose of HCB by intragastric gavage. The concentrations of HCB and pentachlorophenol (PCP), a major metabolite of HCB, were monitored in the blood for 5 d. Fecal excretion of HCB did not differ among the three groups, indicating no difference in HCB retained in the body among the groups. Concentrations of HCB in blood, liver and brain samples from the lard and fish oil groups, the members of which had a low fat tissue mass, were consistently higher as compared with those in samples from the soybean oil group. The concentration of PCP and the PCP/HCB ratio in the blood were higher in the fish oil group than in the other groups. In addition, the amount of PCP excreted in urine was highest in the fish oil group. The hepatic cytochrome P-450 content in the fish oil group was higher than that in the other groups. These findings indicate that feeding fish oil to rats accelerated HCB metabolism. An increase in hepatic HCB concentration due to a small fat tissue mass and high hepatic cytochrome P-450 content may have played a role in accelerating HCB metabolism in the fish oil group.

Key Words hexachlorobenzene, fish oil, metabolism

Various organochlorine chemicals such as pesticides, herbicides and their intermediate products are present in the environment. These chemicals are lipophilic and tend to accumulate in the fat tissue and remain for a long time without being metabolized. The enhanced excretion of lipophilic chemicals from the body would
be an important way to minimize their biological effects. It has been shown that
tissue mass is involved in the distribution, metabolism and excretion of lipophilic
chemicals such as hexachlorobiphenyl (1, 2), and tetrachlorodibenzofuran (3). We
have shown that the metabolism and excretion of pentachlorobenzene (PECB), a
lipophilic and relatively metabolizable chemical, were markedly increased when fat
tissue mass decreased (4-6). The mechanism was as follows: with the decrease in
the mass of fat tissue in which PECB accumulated, the concentrations of PECB in
the blood and liver increased, and the amount of PECB metabolites formed was therefore increased.

Hexachlorobenzene (HCB) is a ubiquitous environmental pollutant that has
been detected in human fat and milk (7, 8). HCB has been shown to transfer from
mothers to suckling infants in mice and rats (9). HCB is known to have many
harmful effects such as induction of porphyria (10) and hepatic cancer (11). Similar
to PECB, HCB is metabolized to pentachlorophenol (PCP), a major metabolite,
and cytochrome P-450 3A is involved in this metabolism in rats and humans (12,
13). However, HCB is metabolized at a much lower rate than PECB.

To enhance the rate of excretion of HCB from the body, several methods have
been used to date: decreasing fat tissue mass as a result of restricted feeding (14,
and administering mineral oil to increase the rate of fecal excretion of HCB (15).
These methods may be effective in eliminating HCB when large amounts of HCB
have been ingested accidentally, but are not applicable to every day life because
we are constantly exposed to small amounts of HCB from our food and the en-
vironment.

Feeding fish oil to rats has been shown to reduce fat tissue mass (16-18) and
increase the concentration of hepatic drug-metabolizing enzymes (19-21). These
effects of fish oil would result in the enhanced metabolism and excretion of lipophilic
chemicals. In fact, in our previous study, we observed that feeding fish oil to rats
for 2 wk prior to the administration of PECB markedly enhanced PECB metabolism,
thereby decreasing the concentration of PECB residues in the body (22). In this
study, we have determined whether feeding fish oil to rats enhances the metabolism
and excretion of HCB as observed for PECB.

MATERIALS AND METHODS

Chemicals. Hexachlorobenzene (HCB), PCP and 2-aminophenol were
purchased from Tokyo Kasei Kogyo, Tokyo, Japan, and uridine diphosphate
(UDP)-glucuronic acid was obtained from Seikagaku Kogyo, Tokyo, Japan. Other
chemicals were purchased from Wako Pure Chemical Industries, Osaka, Japan.
HCB was recrystallized 3 times from methanol before use (purity >99%). Soybean
oil was obtained from Kosakai Pharmaceutical, Tokyo, Japan, lard from Yuro
Chemical, Tokyo, Japan, and fish oil (sardine oil) from Nihon-Yushi, Tokyo, Japan.
Major fatty acid components were: C16: 0 (10%), C18: 1n-9 (23%), C18: 2n-6
(55%), and C18: 3n-3 (10%) in soybean oil; C16: 0 (29%), C18: 1n-9 (14%), C18: 1n-9

J Nutr Sci Vitaminol
Fish Oil Enhances HCB Metabolism in Rats

(42%), and C18:2n-6 (9%) in lard; and C16:0 (9%), C16:1n-7 (10%), C18:1n-9 (10%), C18:2n-6 (2%), C20:5n-3 (28%), and C22:6n-3 (10%) in fish oil. Fish oil was divided into several aliquots in bottles, maintained under a N₂ atmosphere, and stored at –40°C until use. Other dietary components were purchased from Oriental Yeast, Tokyo, Japan.

Animals and diets. Male Sprague-Dawley rats (5 wk old) obtained from Japan Clea, Tokyo, Japan, were housed individually in stainless-steel, wire-bottomed metabolic cages in a constant temperature room (23±1°C) under a 12 h light-dark cycle. After being fed a non-purified commercial diet (CE-2, Japan Clea) for 3 d, the rats were divided into 3 groups of 6 rats each to be fed one of 3 types of semi-purified diet which each included one of the oils. The compositions of the semi-purified diets were: 45% sucrose, 20% casein, 0.3% DL-methionine, 15% cornstarch, 5% cellulose, 3.5% salt mixture (AIN76), 1% vitamin mixture (AIN76), 0.2% choline bitartrate, and 10% of the respective oil. To avoid the oxidation of oil, the diets were freshly prepared every day. The rats had free access to the diets and water for the 19-d experimental period. After 2 wk of consuming a particular diet, rats were orally given a single dose of HCB (105 mg/kg body weight, about 0.5 mL/rat) dissolved in soybean oil. At that time, the body weights of the three groups were 193±2 g for soybean, 190±4 g for lard, and 190±6 g for fish oil (mean±SE). For the analysis of HCB and its metabolite, a blood sample (0.01–0.05 mL) was taken from the tail vein at each time point, and feces was collected for 5 d after HCB administration. On day 5 after the administration of HCB, the rats were anesthetized with pentobarbital and blood was collected by heart puncture. Fat tissues and organs were removed and weighed. All procedures were in accordance with the National Institute of Health and Nutrition Guidelines for the Care and Use of Laboratory Animals.

Analytical methods. Solid tissues were homogenized in 4 volumes of distilled water. Blood (0.01–0.2 mL) was mixed with 0.8–0.99 mL of distilled water. Feces was dried, weighed and pulverized. HCB in the samples was extracted with n-hexane, and PCP was extracted with ethylacetate and methylated with an ethereal solution of diazomethane. HCB and PCP were analyzed on a Hitachi 663-30 gas chromatograph equipped with an electron capture detector as described previously (5).

Drug-metabolizing enzyme concentration and activities in the liver were assayed as follows. The liver was rinsed with 9 g/L NaCl solution, weighed and homogenized in 50 mmol/L Tris-HCl buffer (pH 7.4) containing 0.25 mol/L sucrose. The homogenate was centrifuged at 10,000 × g at 4°C for 30 min and the supernatant was further centrifuged at 105,000 × g at 4°C for 60 min. The supernatant and pellet were used as the cytosol and microsomal fractions, respectively. For the measurement of cytochrome P-450 concentration, the pellet was washed with 0.1 mol/L phosphate buffer (pH 7.4) and finally resuspended in 0.1 mol/L phosphate buffer (pH 7.4) containing 20% glycerol. The cytochrome P-450 concentration in the pellet was measured by the method of Omura and Sato (23). UDP-glucuronosyl-
transferase activity (EC 2.4.1.17) in the microsomal fraction resuspended in 50 mmol/L Tris-HCl buffer (pH 7.4) was determined by the method of Dutton et al (24) using 2-aminophenol as the substrate. Glutathione S-transferase (EC 2.5.1.18) activity in the cytosol fraction was measured by the method of Habig and Jakoby (25) using 1-chloro-2,4-dinitrobenzene as the substrate. Protein concentration was determined according to the method of Lowry et al (26).

Hepatic lipids were extracted using the method of Folch et al (27). Triglyceride concentration was measured using a triglyceride test kit (Triglyceride Test Wako, Wako Pure Chemical Industries). Phospholipid concentration was measured using the method of Fiske and Subbarow (28), and total cholesterol was measured using the method of Sobel and Fernandez (29).

**Statistical analysis.** Data are presented as means with standard error (SE) for the individual groups. Statistical analysis of the data for the groups was carried out using ANOVA (one-way ANOVA in Tables 1 to 6, repeated-measures ANOVA in Fig. 1) followed by Duncan's multiple range test. These statistical analyses were performed using SAS (SAS Institute, Cary, NC, USA).

**RESULTS**

Body weight and liver weight did not differ among the three groups (Table 1).

**Table 1.** Body weight and tissue weight in rats treated with HCB.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>Body weight (g)</th>
<th>Liver (g/100 g)</th>
<th>Perirenal fat (g/100 g)</th>
<th>Epididymal fat (g/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>240 ± 3.5</td>
<td>5.53 ± 0.11</td>
<td>0.95 ± 0.07a</td>
<td>1.05 ± 0.11a</td>
</tr>
<tr>
<td>Lard</td>
<td>234 ± 6.0</td>
<td>5.54 ± 0.18</td>
<td>0.87 ± 0.08ab</td>
<td>0.92 ± 0.05ab</td>
</tr>
<tr>
<td>Fish oil</td>
<td>227 ± 6.1</td>
<td>5.34 ± 0.16</td>
<td>0.66 ± 0.08b</td>
<td>0.74 ± 0.04b</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats.
Values in the same column not sharing a common superscript letter are significantly different at \( p < 0.05 \).

**Table 2.** Concentration of hepatic lipids in rats treated with HCB.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>Total lipids (g/100 g)</th>
<th>Triglycerides (µmol/g)</th>
<th>Phospholipids (µmol/g)</th>
<th>Cholesterol (µmol/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>4.80 ± 0.23b</td>
<td>23.1 ± 2.2b</td>
<td>63.8 ± 1.7b</td>
<td>3.92 ± 0.08</td>
</tr>
<tr>
<td>Lard</td>
<td>6.89 ± 0.67a</td>
<td>40.9 ± 6.3a</td>
<td>75.0 ± 2.0a</td>
<td>4.39 ± 0.15</td>
</tr>
<tr>
<td>Fish oil</td>
<td>4.87 ± 0.24b</td>
<td>19.0 ± 2.0b</td>
<td>77.2 ± 1.6a</td>
<td>4.10 ± 0.13</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats.
Values in the same column not sharing a common superscript letter are significantly different at \( p < 0.05 \).

*J Nutr Sci Vitaminol*
Table 3. Concentrations and activities of hepatic drug-metabolizing enzymes in rats treated with HCB.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>Cytochrome P-450 (nmol/mg protein)</th>
<th>UDP-glucuronosyl transferase (pmol/mg protein/min)</th>
<th>Glutathione-S transferase (nmol/mg protein/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>0.49 ± 0.02&lt;sup&gt;b&lt;/sup&gt;</td>
<td>349 ± 28</td>
<td>477 ± 42</td>
</tr>
<tr>
<td>Lard</td>
<td>0.57 ± 0.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>307 ± 24</td>
<td>409 ± 23</td>
</tr>
<tr>
<td>Fish oil</td>
<td>0.79 ± 0.04&lt;sup&gt;a&lt;/sup&gt;</td>
<td>294 ± 7</td>
<td>488 ± 37</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats. Values in the same column not sharing a common superscript letter are significantly different at p < 0.05.

Fig. 1. Effect of dietary fats on concentrations of HCB (a), PCP (b) and the ratio of PCP/HCB (c) in blood over time. Rats were orally administered HCB on day 0 after being fed the respective diets for 2 wk, and then fed the same diet for a further 5 d. Each point and vertical bar indicate the mean and SE for six rats per group. At a given time point, values not sharing a common letter are significantly different (p < 0.05).
However, the fat tissue weight in the fish oil group was lower than that in the soybean oil group. The concentration of hepatic lipids, especially triglycerides, in the lard group was higher than that in the other groups (Table 2). Differences in hepatic drug-metabolizing enzyme activity are shown in Table 3. The cytochrome P-450 concentration in the fish oil group was higher than that in the other groups. The activities of UDP-glucuronosyl-transferase and glutathione S-transferase did not differ among the three groups.

Changes in the concentrations of HCB and PCP, a major metabolite of HCB, and the ratio of PCP/HCB in the blood after HCB administration are shown in Fig. 1. The concentration of PCP was less than 1% of the parent compound throughout the experimental period. In the fish oil group, concentrations of both HCB and PCP in the blood and the ratio of PCP/HCB were consistently higher than those in the soybean oil group. In the lard group, the concentration of HCB in the blood was higher, but that of PCP and the ratio of PCP/HCB in the blood did not differ compared with those in the soybean oil group. The concentrations of HCB in the liver, kidneys and brain on day 5 after HCB administration were higher in the fish oil and lard groups than in the soybean oil group (Table 4). The concentration of HCB in the fat tissues was 20 to 40 times higher than that in the brain, liver, and kidneys (Table 5). The concentration of HCB in the epididymal

Table 4. Concentrations of HCB in the brain, liver and kidneys.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>Brain (nmol/g)</th>
<th>Liver (nmol/g)</th>
<th>Kidneys (nmol/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>16 ± 1.3\textsuperscript{b}</td>
<td>56 ± 9.1\textsuperscript{b}</td>
<td>28 ± 2.1\textsuperscript{b}</td>
</tr>
<tr>
<td>Lard</td>
<td>23 ± 1.7\textsuperscript{a}</td>
<td>99 ± 1.4\textsuperscript{a}</td>
<td>38 ± 2.1\textsuperscript{a}</td>
</tr>
<tr>
<td>Fish oil</td>
<td>25 ± 2.0\textsuperscript{a}</td>
<td>93 ± 4.7\textsuperscript{a}</td>
<td>43 ± 1.2\textsuperscript{a}</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats.
Values in the same column not sharing a common superscript letter are significantly different at \( p < 0.05 \).

Table 5. Concentrations of HCB in fat tissues.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>Perirenal (nmol/g)</th>
<th>Perirenal (nmol/tissue)</th>
<th>Epididymal (nmol/g)</th>
<th>Epididymal (nmol/tissue)</th>
<th>Subcutaneous (nmol/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>859 ± 56</td>
<td>1,943 ± 152\textsuperscript{a}</td>
<td>557 ± 59\textsuperscript{b}</td>
<td>1,493 ± 102</td>
<td>734 ± 60</td>
</tr>
<tr>
<td>Lard</td>
<td>807 ± 116</td>
<td>1,612 ± 209\textsuperscript{ab}</td>
<td>911 ± 57\textsuperscript{a}</td>
<td>1,970 ± 171</td>
<td>843 ± 64</td>
</tr>
<tr>
<td>Fish oil</td>
<td>980 ± 41</td>
<td>1,329 ± 183\textsuperscript{b}</td>
<td>1,032 ± 53\textsuperscript{a}</td>
<td>1,665 ± 119</td>
<td>736 ± 63</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats.
Values in the same column not sharing a common superscript letter are significantly different at \( p < 0.05 \).
Fish Oil Enhances HCB Metabolism in Rats

Table 6. The amount of HCB and its metabolite PCP excreted in feces and urine, respectively, during the experimental period.

<table>
<thead>
<tr>
<th>Dietary fat</th>
<th>HCB in feces (μmol/5 d)</th>
<th>PCP in urine (nmol/5 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>15.0 ± 1.3</td>
<td>8.1 ± 2.5&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lard</td>
<td>14.4 ± 1.6</td>
<td>5.2 ± 1.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fish oil</td>
<td>15.0 ± 2.7</td>
<td>12.3 ± 1.2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 rats.
Values in the same column not sharing a common superscript letter are significantly different at p < 0.05.

fat was higher in the fish oil and lard groups than in the soybean oil group, but the HCB concentration in subcutaneous and perirenal fat did not differ among the three groups. Due to the changes of fat tissue mass, the whole amount of HCB existing in the epididymal fat was not higher in the fish oil group than in the soybean oil group, and that in the perirenal fat was lower in the fish oil group.

The cumulative fecal excretion of HCB during the experimental period is shown in Table 6. The amount of HCB excreted in feces was about 20% of the dose administered, and did not differ among the three groups. Urinal excretion of PCP was only 0.01% of the estimated amount of HCB absorbed. The amount of PCP excreted in the urine in the fish oil group was higher than that in the lard group, and tended (p = 0.15) to be higher than that in the soybean oil group.

DISCUSSION

In a previous study, we observed that feeding fish oil to rats markedly enhanced PECB metabolism and its excretion from the body (22). In this study, we investigated whether the same beneficial effect of fish oil feeding was observed with respect to HCB, which is a ubiquitous environmental pollutant detectable in human milk and fat (7, 8). Both PECB and HCB have been shown to be metabolized to PCP (12, 13), but HCB is very slowly metabolized. In fact, after the administration of either PECB or HCB to rats, about 50% of the PECB and 0.1% of HCB were metabolized to PCP (22) (Fig. 1). It might be difficult to detect a significant decrease in HCB concentration within 5 d, the time period used in this study and the previous study performed with PECB. Den Besten et al (13) has reported that the HCB metabolite formed was enhanced with a high dose of HCB when compared with a low dose of HCB. Koss and Koransky (30) have shown that after the administration of 14C-labeled HCB to rats, the urine contained mainly their metabolites and very little HCB. According to these findings, the analysis of PCP levels in the blood and urine after the administration of a high dose of HCB is an effective and suitable way to evaluate how dietary fish oils affect the metabolism and excretion of HCB.
The amount of HCB excreted in feces within 5 days was only 20% of the dose administered, indicating that about 80% of the HCB administered to rats was retained in the body (Table 6). This result was consistent with that of Ingebrigtsen et al (31), who investigated 14C-labeled HCB absorption in rats. No group differences in the amounts of HCB excreted in feces suggested that HCB retained in the body did not differ among the three groups. In contrast, the amount of PCP excreted in urine was higher in the fish oil group than in the other groups (Table 6). In addition, blood PCP concentration and the ratio of PCP/HCB in the fish oil group were consistently higher than those in the other groups (Fig. 1). These findings indicated that the metabolism of HCB was accelerated in rats fed fish oil. The data were consistent with those of a similar experiment conducted using PECB (22).

Feeding fish oil to rats has been shown to increase the mixed-function oxidase system; increasing cytochrome P-450 content and related enzyme activities (19–21). Consistent with these reports, feeding rats fish oil resulted in an increase in cytochrome P-450 concentration (Table 3). It has been shown that cytochrome P-450 3A is involved in the transformation of HCB to PCP (12, 13). In this study, we only determined the total concentration of cytochrome P-450 in the liver. Therefore, it is unclear whether fish oil intake significantly induced the activity of cytochrome P-450 involved in HCB metabolism. However, as evaluated by the changes in PCP concentration in the blood and urine, the increase in cytochrome P-450 in the fish oil group may be a cause of the accelerated metabolism of HCB. Interestingly, the induction of cytochrome P-450 by phenobarbital in rats has been reported to be enhanced by fish oil feeding (32). This finding led us to speculate that the induction of cytochrome P-450, which is specific for HCB metabolism, was also enhanced in the fish oil group.

As already reported by others (16–18), perirenal and epididymal fat tissue mass in the fish oil group were lower than those in the other groups (Table 1). This decrease in fat tissue mass may also contribute to the accelerated metabolism of HCB in the fish oil group, as observed by us with PECB (4-6), by Ahotupa and Mantyla (1) and Birnbaum (2) with hexachlorobiphenyl and by Decad et al (3) with tetrachlorodibenzofuran. When the fat tissue mass is low, the distribution of HCB in the body changes, and the mobilization of HCB accumulated in the fat tissue into blood is increased due to the high lipolytic activity in the fat tissue (17). As a result, the concentrations of HCB in the blood and liver increase, and the metabolite of HCB formed by the hepatic drug-metabolizing enzymes is accelerated. In this study, the concentrations of HCB in the blood and liver were the highest in the fish oil group, which could be an important factor for enhanced HCB metabolism in the liver. Although the concentration of HCB in the fat tissue was not lower in the fish oil group than in the other groups, the whole amount of HCB existing in perirenal fat tissue was lower in the fish oil group due to the decrease of fat tissue mass in the fish oil group (Table 5). Different changes in fat tissue mass and HCB concentration due to the feeding of various fats may be associated with the different characteristics of fat tissues such as lipolytic activity and the
content of triglyceride.

In the lard group, the fat tissue mass was lower and HCB concentrations in the blood and liver higher than those in the soybean oil group (Table 1). This finding in the lard group was consistent with that obtained for the fish oil group in terms of the relation between small fat tissue mass and high HCB concentration in the blood. However, the concentration of PCP and ratio of PCP/HCB in the blood of the lard group were comparable to that in the soybean oil group (Fig. 1), and the amount of PCP excreted in the urine of the lard group was the lowest among the three groups (Table 6). These results indicated that the metabolism of HCB was suppressed in the lard group. As the concentration of hepatic fats, especially triglycerides, was high in the lard group (Table 2), the degree of interaction of HCB with the hepatic drug-metabolizing enzymes might have been reduced, resulting in the impaired metabolism of HCB. We have observed similar findings using PECB (22, 33). These findings in the lard group suggest that both the decrease in fat tissue mass and the interaction of HCB with hepatic drug-metabolizing enzymes were responsible for the increase of HCB metabolism in the fish oil group.

To reduce the concentration of HCB accumulated in the body, several methods have been applied to date: mobilization of HCB accumulated in fat tissue by food deprivation or restricted feeding (14), and the enhancement of fecal elimination of HCB by treatment with mineral oil (15). Food deprivation and restricted feeding have been shown to induce the redistribution of HCB stored in fat tissue, resulting in an increase in HCB concentration in other tissues such as the brain (34, 35). In this study, the concentration of HCB in the brain, liver and kidneys in the fish oil and lard groups was consistently higher than that in the same tissues in the soybean oil group (Table 4). Accordingly, feeding with fish oil may enhance HCB toxicity in the case of accidental exposure to large concentrations of HCB. However, humans are consistently exposed to HCB in small amounts from their food and the environment. Cabral et al (11) have shown that HCB at high concentrations induced hepatic cancer in rats, but not at low concentrations. With regard to these findings, the accelerated excretion of HCB as a result of the use of a dietary component (i.e., fish oil) may be a practical way to minimize the toxicity of HCB during continuous exposure at low levels. The dietary fish oil level in our study was 10%, which was comparable to other studies (16–18, 21, 32). However, the calculated intake of the fish oil is extremely high; it is about 4 g/d/rat, and estimated to be about 200–250 g/d/human. Inuit people consume large amounts of fish oil, but that has been reported to be about 14 g/d (36). It is also noted that the feeding of excess fish oil may cause oxidative stress in the body. Accordingly, further detailed studies, such as dose-response and long-time feeding experiments, will be needed to apply the present findings to humans.

This work is supported by the Environmental Agency, Japan and by a Grant-in-Aid for Fundamental Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan (08680072).

Vol 44, No 2, 1998
REFERENCES


Fish Oil Enhances HCB Metabolism in Rats


