A High Cholesterol, (n-3) Polyunsaturated Fatty Acid Diet Induces Hypercholesterolemia More Than a High Cholesterol, (n-6) Polyunsaturated Fatty Acid Diet in Hamsters¹,²

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ABSTRACT This study was designed to study the effects of (n-3) polyunsaturated fatty acids (PUFA) on plasma and liver lipids, particularly lipoprotein cholesterol concentrations, in hamsters. Diets rich in (n-3) PUFA (21 g/100 g fatty acid) or (n-6) PUFA (37.4 g/100 g fatty acid) with or without 5 g/kg cholesterol (C) supplements were given for 4 wk to male hamsters weighing 70-90 g. The VLDL- and (IDL + LDL)-cholesterol concentrations were 114 and 128% higher in hamsters fed the (n-3) PUFA + C diet than in those fed the (n-6) PUFA + C diet. However, these differences were not observed when cholesterol was not supplemented. Hamsters fed the (n-3) PUFA diet had significantly lower plasma and hepatic triglyceride concentrations than those fed the (n-6) PUFA diet. Concentrations were comparable in hamsters fed (n-6) PUFA + C and (n-3) PUFA + C. Hepatic cholesterol esters were significantly lower, while hepatic microsomal acyl-CoA:cholesterol acyltransferase activity and VLDL cholesterol esters were significantly higher in hamsters fed the (n-3) PUFA + C diet than in those fed the (n-6) PUFA + C diet. Our results demonstrate that elevation of VLDL- and (IDL + LDL)-cholesterol in hamsters by (n-3) PUFA, compared with (n-6) PUFA, is dependent on dietary cholesterol supplementation and may be due to decreased catabolism of these lipoproteins. J. Nutr. 126: 1759-1765, 1996.

INDEXING KEY WORDS:
• (n-3) polyunsaturated fatty acids
• hypercholesterolemia • hamsters
• dietary cholesterol

Epidemiological studies (Bang et al. 1971, Kromhout et al. 1985) have suggested that consumption of fish oil is beneficial in lowering the risk of coronary heart diseases. This was attributed mainly to the biological effects of the long-chain [n-3] polyunsaturated fatty acids (PUFA), that is, eicosapentaenoic acid [EPA] and docosahexaenoic acid (DHA) in fish oil [Dyerberg 1986, Kagawa et al. 1982]. These fatty acids may modify the formation of prostaglandins and leukotrienes, and may also modify the metabolism of lipoproteins, thus decreasing the risk of coronary heart disease [Drevon 1992].

Many published reports have demonstrated that the (n-3) PUFA are potent in lowering plasma triglyceride concentrations. The hypotriglyceridemic effect of these fatty acids is considered to be due to their adaptive effects on inhibition of hepatic triglyceride synthesis and secretion [Lang and Davis 1990, Noslen et al. 1986, Wong et al. 1984], and is perhaps also due to stimulation of fatty acid oxidation [Wong et al. 1984, Yamazaki et al. 1987]. However, their effect on plasma cholesterol, especially LDL-cholesterol, has been inconsistent. Abbey et al. [1990] have shown that EPA attenuated the elevation of plasma and LDL-cholesterol by an atherogenic diet in marmosets. Parks and

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⁴ Abbreviations used: ACAT, acyl-CoA:cholesterol acyltransferase, DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; [n-3] PUFA diet, [n-3] polyunsaturated fatty acid diet; [n-6] PUFA diet, [n-6] polyunsaturated fatty acids diet, [n-3] PUFA + C diet, [n-3] polyunsaturated fatty acid diet supplemented with 0.5% cholesterol, [n-6] PUFA + C diet, [n-6] polyunsaturated fatty acid diet supplemented with 0.5% cholesterol, SFA, saturated fatty acids.
Crouse (1992) reported a 20–30% reduction of total and LDL-cholesterol by a fish oil diet in African green monkeys. The same diet had no effect on total and LDL-cholesterol in cynomolgus monkeys [Parks and Gebre 1991]. On the contrary, Field et al. (1987) observed significantly increased total- and LDL-cholesterol in rabbits fed a menhaden oil diet. Human feeding trials showed that fish oil resulted in a decrease in or no effect on LDL-cholesterol in most normolipidemic subjects [Illingworth et al. 1984, Nestel 1986]. However, Sullivan et al. (1986) showed that fish oil raised both LDL- apo B and cholesterol in hypertriglyceridemic subjects. Several other studies also revealed elevations of LDL-cholesterol by fish oil (Demke et al. 1988, Harris et al. 1988, Sanders et al. 1985). The effects of fish oil on plasma lipids and lipoprotein metabolism in humans has been reviewed by Harris (1989). It is not clear what factor[s] causes the conflicting results. In our previous study [Lin et al. 1995], we found that hamsters ingesting a diet containing 10% sardine oil had significantly lower plasma total-, VLDL- and LDL-cholesterol than hamsters ingesting diets containing 10% soybean oil or 10% coconut oil; however, when the same diets were supplemented with 5 g/kg cholesterol, the fish oil group had higher plasma total-, VLDL- and LDL-cholesterol concentrations than the other two diet groups. In that study, however, the proportions of the dietary saturated, monounsaturated and polyunsaturated fatty acids were not the same in the three test groups. Therefore, we could not conclude with certainty that the cholesterol induced hypercholesterolemic effect of fish oil was due to its larger concentration of (n-3) PUFA.

In this study we tried to determine whether the role of (n-3) PUFA in modifying plasma cholesterol concentrations in hamsters is different from that of (n-6) PUFA. The hamsters were fed diets containing 15% fat rich in either (n-3) or (n-6) PUFA, and the amounts of PUFA, monounsaturated fatty acids (MUFA) and saturated fatty acids (SFA) were comparable in the two groups. The (n-3) PUFA diet contained 15.5 g of EPA plus DHA/100 g dietary fatty acids, whereas in the (n-6) PUFA diet, linoleic acid replaced these fatty acids. Each diet group was further divided into two groups fed diets with or without 5 g/kg cholesterol. The results indicated clearly that the cholesterol-induced hypercholesterolemic effect of fish oil was due mainly to its high concentration of EPA and DHA.

**MATERIALS AND METHODS**

*Diets and animals.* Male golden Syrian hamsters (Animal Center, National Taiwan University, College of Medicine, Taipei, Taiwan) weighing 70–90 g were housed in colony cages (6 per cage) and subjected to a 12-h light cycle (0700–1900 h). All animal experimen-

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>(n-6) PUFA</th>
<th>(n-3) PUFA</th>
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<tr>
<td>8:0</td>
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<td>2.6</td>
</tr>
<tr>
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<td>6.5</td>
<td>8.8</td>
</tr>
<tr>
<td>16:0</td>
<td>11.7</td>
<td>12.8</td>
</tr>
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<td>—</td>
<td>3.6</td>
</tr>
<tr>
<td>18:0</td>
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<td>—</td>
<td>1.4</td>
</tr>
<tr>
<td>20:4[n-6]</td>
<td>—</td>
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<td>22:5[n-3]</td>
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<td>22:6[n-3]</td>
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<td>MUFA</td>
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<td>19</td>
</tr>
<tr>
<td>P/S, g/g</td>
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<td>1</td>
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</tbody>
</table>

1 Abbreviations used: PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids; MUFA, monounsaturated fatty acid; P/S, polyunsaturated fatty acids/saturated fatty acids.

**TABLE 1**

**Fatty acid composition of the test diets**

**t**al procedures followed the *Guide for the Care and Use of Laboratory Animals*, National Science Council, Taiwan. The hamsters were divided into four groups and assigned to one of the four semisynthetic diets: (n-6) PUFA diet, (n-3) PUFA diet, (n-6) PUFA supplemented with cholesterol to 5 g/kg diet [(n-6) PUFA + C], and (n-3) PUFA supplemented with cholesterol to 5 g/kg diet [(n-3) PUFA + C]. The experimental diet contained (g/kg diet): casein, 200; fat, 150; vitamin mix (AIN-76, ICN, Aurora, OH), 10; mineral mix (AIN-76, ICN), 40; methyl cellulose, 40, and cornstarch to 1000 g. The dietary fat mixtures were prepared with various ratios of soybean oil (Taiwan Sugar, Taiwan), coconut oil (President Natural Industrial, Taiwan) and sardine oil (President Natural Industrial). The fatty acid composition of each diet was determined by capillary gas chromatography (Hewlett-Packard, Avondale, PA) [Welz et al. 1990] and is shown in Table 1. The test diets had similar fatty acid compositions with the polyunsaturated fatty acid/saturated fatty acid ratio set to be 1.0, except that 18 g linoleic acid/100 g fatty acids in the (n-6) PUFA diet was replaced by (n-3) PUFA, mainly EPA and DHA, in the (n-3) PUFA diet. The cholesterol concentration of the sardine oil was determined, and the dietary cholesterol level was adjusted to be the same for all groups. All diets were supplemented with 0.005 g DL-α-tocopherol/kg and stored in the dark at −20°C. Hamsters were given free access to the experimental diets and tap water for 4 wk. After food was
withheld for 14 h (from 1900 to 0900 h), the animals were decapitated. Blood was collected in tubes with EDTA and chilled on ice. Livers were excised immediately. A portion of the liver (2 g) was taken to prepare the microsomal fraction before storing at −70°C.

**Lipoprotein isolation and lipid analysis.** Plasma was isolated by low speed centrifugation at 4°C. VLDL, IDL + LDL and HDL were isolated from plasma by ultracentrifugation at d < 1.006 kg/L, d: 1.006–1.063 kg/L and d: 1.063–1.21 kg/L, respectively. The ultracentrifugation was carried out using a Beckman TL 100 ultracentrifuge equipped with a TLA 100.3 rotor (Beckman, Palo Alto, CA). The lipid composition of the isolated lipoproteins was assayed colorimetrically using Cholesterol Enzymatic CHOP-PAP, Free Cholesterol Enzymatic PAP and Triglycerides Enzymatic PAP kits (BioMerieux, Marcy l’Etoile, France). Protein was determined by the method of Lowry et al. (1951).

**Hepatic lipids analysis.** Liver lipids were extracted by the method of Folch et al. (1957). Liver triglyceride was determined by the method of Soloni (1971), and unesterified and esterified cholesterol were determined by gas chromatography on a capillary column (Brown et al. 1975).

**Measurement of acyl-CoA:cholesterol acyltransferase (ACAT) activity in hepatic microsomes.** A 2-g portion of liver was homogenized in 10 mL of ice-cold potassium phosphate buffer [0.1 mol/L, pH 7.4] containing 1 mmol/L dithiothreitol and 10 mmol/L nico- tinamide. The homogenate was centrifuged at 12,000 × g for 15 min. The resulting supernatant was further centrifuged at 105,000 × g for 60 min to obtain the microsomal pellet (Erickson et al. 1980). The microsomes were suspended in the same buffer and stored at −70°C until use. Hepatic microsomal ACAT (EC 2.3.1.26) activity was assayed by the method of Bilheimer (1985). Briefly, 180 μL of reaction mixture containing 100 μg of microsomal protein, 50 μL of fatty acid-free bovine serum albumin (1 mg), 100 μL of cholesterol solution [52 nmol of cholesterol in 0.3% Triton WR-1339] and potassium phosphate buffer was preincubated at 37°C for 30 min; the reaction was initiated by the addition of 20 μL of 14C-oleoyl-coenzyme A (CoA) solution (0.1 mmol/L, 83.3 kBq/mmol). The reaction was carried out for 10 min and stopped by the addition of 4 mL of chloroform/methanol (2:1, v/v). Ten milligrams of cholesteryl oleate containing 0.83 kBq of 3H-cholesteryl oleate was added as a carrier and internal standard. Then, 0.8 mL of 0.12 mol/L KCl was added and the mixture was mixed well by vortex. The chloroform layer was separated, and the cholesteryl ester was separated by a thin-layer chromatography plate as described above. The cholesteryl ester spot was scraped off individually and placed in a scintillation vial for counting.

**Statistical analysis.** Data were analyzed by two-way ANOVA using a SAS program (SAS Version 6.08, SAS Institute, Cary, NC). Differences between mean values were evaluated by the Newman-Keuls multiple range test (Steel and Torrie 1980) and were considered significant at P < 0.05. Some data were logarithmically transformed before ANOVA due to heterogenous variance.

**RESULTS**

**Plasma and lipoprotein lipids.** Dietary cholesterol significantly raised VLDL-, (IDL + LDL)- and HDL-cholesterol concentrations and the ratio of(IDL + LDL)/HDL in hamsters fed both (n-6) and (n-3) PUFA (Table 2). VLDL- and (IDL + LDL)-cholesterol concentrations were not significantly different in the (n-3) and (n-6) PUFA groups. However, VLDL- and (IDL + LDL)-cholesterol concentrations in the hamsters ingesting the (n-3) PUFA + C diet were significantly higher (P < 0.05) than in those ingesting the (n-6) PUFA + C diet. The HDL-cholesterol concentration was significantly lower in the (n-3) PUFA group compared with the (n-6) PUFA group with 14% less HDL cholesterol.
Two-way ANOVA,
P  
FA2 <0.05 <0.001 NS  
Cholesterol <0.001 <0.001 <0.05  
FA*Cholesterol NS NS <0.05  

1 Values are means ± sem (n = 6). Within a column, values with different superscript letters are significantly different at P < 0.05.  
2 FA = fatty acid; NS = not significant, P > 0.05.

6) PUFA group, but was not significantly different between the (n-3) and (n-6) PUFA + C groups. The (n-3) PUFA diet also tended to result in a higher ratio of [IDL + LDL] / HDL compared with the (n-6) PUFA diet (P = 0.07). The difference was significant (P < 0.01) when cholesterol was given.

Compared with the (n-6) PUFA group, the (n-3) PUFA group had 42 and 54% lower plasma- and VLDL-triglyceride concentrations, respectively (Table 3). Supplemen-
tal cholesterol raised plasma- and VLDL-triglyceride concentrations in both the (n-3) and (n-6) PUFA groups. The (n-3) PUFA + C group had 20 and 33% lower plasma triglyceride (P = 0.06) and VLDL-triglyceride (P < 0.05) concentrations, respectively, compared with the (n-6) PUFA + C group (Table 3). The data indicated that the hypotriglyceremic effect of (n-3) PUFA was reduced by dietary cholesterol feeding.

Hepatic lipids. Cholesterol feeding caused hepatic accumulation of esterified cholesterol, with only modest increases in unesterified cholesterol, in both the (n-3) and (n-6) PUFA groups [Table 4]. Esterified cholesterol concentration was significantly less in the (n-3) PUFA + C group than in the (n-6) PUFA + C group. In contrast to cholesterol accumulation, hepatic triglyceride concentration was decreased by cholesterol feeding in hamsters ingesting the (n-6) PUFA diet but not in hamsters ingesting the (n-3) PUFA diet (Table 4).

Hepatic microsomal ACAT activity. To test whether the lower concentration of hepatic esterified cholesterol in the (n-3) PUFA + C group was due to a decrease in ACAT activity, ACAT activity of the isolated hepatic microsomes was measured. An unexpected finding was that while having a lower esterified cholesterol concentration, the microsomal ACAT activity of the (n-3) PUFA + C group was significantly higher than that of the (n-6) PUFA + C group [(101.2.8 ± 170.9 vs. 608.8 ± 136.2 pmol/ [mg protein · min]; P < 0.05).

Composition of VLDL. The composition of VLDL is shown on a weight percent basis in Table 5. Hamsters fed the (n-3) PUFA diet had a significantly higher proportion of esterified cholesterol and a lower proportion of triglyceride in VLDL compared with those fed the (n-6) PUFA diet. The differences were more striking between the cholesterol-fed groups. The unesterified and esterified cholesterol and phospholipid concentrations of VLDL of the (n-3) PUFA + C group were 150, 69 and 34% higher than that of the (n-6) PUFA + C group, respectively, and triglyceride concentration of VLDL from the (n-3) PUFA + C group was only 40% of that of the (n-6) PUFA + C group.

**DISCUSSION**

This study was designed to compare the effects of (n-3) PUFA with those of (n-6) PUFA, with or without dietary cholesterol, on various plasma cholesterol fractions in hamsters. It was demonstrated that the effects of (n-3) PUFA on plasma lipids were different in the presence or absence of 5 g/kg of dietary cholesterol (Table 2). Significantly higher levels of VLDL- and [IDL + LDL]-cholesterol were observed in the (n-3) PUFA + C group than in the (n-6) PUFA + C group. The results support our earlier observations [Lin et al. 1995] made in a hamster experiment using coconut, soybean or sardine oil as the sole source of fat in each of 3 cholesterol-supplemented diets. The sardine oil diet induced significantly higher plasma-, VLDL-, and [IDL + LDL]-cholesterol concentrations than either the coconut or soybean oil diets in hamsters. Recently, Surette et al. [1992] observed 90% greater VLDL- and LDL-cholesterol concentrations in hamsters ingesting a (n-3) PUFA
TABLE 5

Effects of (n-3) polyunsaturated fatty acids (PUFA) on VLDL unesterified cholesterol (UC), esterified cholesterol (EC), triglyceride (TG), phospholipid (PL) and protein concentrations in hamsters fed diets with or without supplemental cholesterol (C)₁

<table>
<thead>
<tr>
<th>Group</th>
<th>UC</th>
<th>CE</th>
<th>TG</th>
<th>PL</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mmol/100 g</td>
<td>g/100 g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[n-6] PUFA</td>
<td>7.0 ± 0.3₄</td>
<td>15.0 ± 1.5₄</td>
<td>77.5 ± 1.7₃</td>
<td>16.3 ± 0.4₄</td>
<td>11.4 ± 0.6₅</td>
</tr>
<tr>
<td>[n-3] PUFA</td>
<td>8.3 ± 0.5₅</td>
<td>26.1 ± 0.5₅</td>
<td>69.7 ± 1.8₅</td>
<td>16.9 ± 0.₆₅</td>
<td>13.8 ± 1.₆₅</td>
</tr>
<tr>
<td>[n-6] PUFA + C</td>
<td>11.4 ± 0.₃₅</td>
<td>35.1 ± 2.₃ₕ</td>
<td>68.9 ± 1.₈₅</td>
<td>17.₉ ± 0.₄₅</td>
<td>9.₀ ± 0.₈₃₅</td>
</tr>
<tr>
<td>[n-3] PUFA + C</td>
<td>28.₄ ± 2.₃ₕ</td>
<td>5₉.₃ ± ₃.₃ₕ</td>
<td>4ₕ.₅ ± 2.₂ₕ</td>
<td>2₄.₀ ± 1.₂ₕ</td>
<td>10.₉ ± 0.₃₄ₕ</td>
</tr>
</tbody>
</table>

Two-way ANOVA, P

FA² | <0.001   | <0.001   | <0.001   | <0.001   | <0.001   |
Cholesterol | <0.001   | <0.001   | <0.001   | <0.001   | <0.001   |
FA·Cholesterol | <0.001   | <0.001   | <0.05    | <0.01    | NS       |

1 Values are mean ± SEM (n = 6). Within a column, values with different superscript letters are significantly different at P < 0.05.
2 FA = fatty acid; NS = not significant, P > 0.05.

Diet containing 0.1% cholesterol compared with those consuming an oleic acid–rich diet. We also have observed higher VLDL- and [IDL + LDL]-cholesterol concentrations in hamsters fed an [n-3] PUFA–rich diet supplemented with 5 g/kg cholesterol compared with those fed a saturated fatty acid–rich diet supplemented with 5 g/kg cholesterol (unpublished data). These studies demonstrated that fish oil has a hypercholesterolemic effect in hamsters in the presence of dietary cholesterol.

Another interesting observation we made in this study was that hamsters of the [n-3] PUFA + C group had significantly lower hepatic cholesteryl ester concentrations than hamsters of the [n-6] PUFA + C group (Table 4). This observation is consistent with published reports in hamsters and rabbits fed menhaden oil and cholesterol [Field et al. 1987, Surette et al. 1992]. Although the [n-3] PUFA + C group had lower hepatic cholesteryl esters, it had higher hepatic microsomal ACAT activity compared with the [n-6] PUFA + C group. This result is in agreement with the study of Field et al. [1987]. They further pointed out that it was the composition of microsomal fatty acids but not the microsomal cholesterol concentration which regulates ACAT activity. It has been reported that EPA and DHA are poor substrates for ACAT in vitro [Rustan et al. 1988a]; however, Jones et al. [1990] reported a higher esterification rate of cholesterol in the liver of menhaden oil–fed hamsters compared with those fed corn or olive oil.

Although the hepatic cholesteryl ester concentration was lower, the VLDL cholesteryl ester proportion was significantly higher in the [n-3] PUFA + C fed hamsters. Fungwe et al. [1992] demonstrated that cholesterol feeding resulted in increased hepatic secretion of VLDL particles in rats. It is possible that secretion of VLDL was stimulated in hamsters consuming the [n-3] PUFA + C diet. However, this possibility can be excluded, because both human and animal studies [Hollingworth et al. 1984, Nestel et al. 1984, Wong et al. 1984] have shown decreased synthesis and secretion of VLDL due to fish oil feeding. Consequently, the increase of VLDL- and [IDL + LDL]-cholesterol concentrations in the [n-3] PUFA + C group was most likely due to decreased catabolism of these lipoproteins. Several human and animal studies [Parks et al. 1990, Suzukioka et al. 1995] have recently reported that fish oil feeding induced changes in lipoprotein composition and particle size. Our data showed dramatic differences in VLDL composition of hamsters fed [n-3] PUFA + C relative to those fed [n-6] PUFA + C (Table 5). The differences in VLDL composition may lead to differences in composition and particle size of LDL. Nigon et al. [1991] demonstrated that larger or smaller LDL particles had a lower LDL-receptor binding affinity than medium-sized LDL particles and might have a slower turnover rate. Therefore, the changes in composition and particle size of lipoproteins in hamsters consuming [n-3] PUFA + C diet may induce the elevation of VLDL- and LDL-cholesterol concentrations. This possibility is currently under investigation.

Another possible mechanism for elevation of LDL-cholesterol by dietary fish oil may be through down-regulation of the LDL-receptor. Wong and Nestel [1986] showed that EPA reduced LDL-receptor number in Hep G2 cells. Surette et al. [1992] also showed that fish oil suppressed hepatic LDL-receptor activity in hamsters. Recently, Spady et al. [1995] further demonstrated that the [n-3] PUFA–induced suppression of hepatic receptor-dependent LDL transport in hamsters was due to downregulation of LDL-receptor mRNA. However, in rats, hepatic LDL-receptor protein and mRNA were unaffected by the [n-3] PUFA diet compared with the [n-6] PUFA diet (Spady et al. 1995). The suppression of hepatic receptor-dependent LDL transport may result in less cholesterol accumulation in the liver.

The hypotriglyceridemic effect of [n-3] PUFA has been attributed to decreased synthesis and secretion of VLDL by the liver [Lang and Davis 1990, Rustan et al. 1988b]. However, in hamsters, the effect was decreased...
by dietary cholesterol (Table 3). The explanation might be that cholesterol stimulates synthesis and secretion of triglyceride and VLDL [Fungwé et al. 1992 and 1993, Liu et al. 1995] which negates the hypotriglyceridemic effect of (n-3) PUFAs. In contrast to the results in rats [Fungwé et al. 1992, Liu et al. 1995], dietary cholesterol failed to stimulate hepatic triglyceride accumulation in hamsters. In rats, dietary cholesterol reduced the rate of fatty acid oxidation and increased the rate of triglyceride biosynthesis [Fungwé et al. 1993, Liu et al. 1995]. The increased availability of triglyceride may be required for the formation of VLDL as a vehicle to transport the excess cholesteryl esters out of the liver. Whether dietary cholesterol also stimulates hepatic triglyceride synthesis in hamsters remains to be determined.

Although there have been many observations of the beneficial effects of fish oil on plasma lipids and eicosanoid metabolism, there have also been many feeding trials with normal or hyperlipidemic subjects which showed a hypercholesterolemic effect of fish oil [Harris 1989]. In this study we showed that (n-3) PUFAs raised VLDL- and LDL-cholesterol concentrations of hamsters when 5 g/kg of cholesterol was supplemented in the diet. We also observed significantly higher LDL-cholesterol concentration in rats fed the (n-3) PUFAs + C (10 g/kg diet) diets compared with those fed the (n-6) PUFAs + C diet (Lu et al. 1995), therefore, the phenomenon seems not to be specific to hamsters.

LITERATURE CITED


[n-3] PUFA–INDUCED HYPERCHOLESTEROLEMIA IN HAMSTERS 1765


