Diets Rich in Polyunsaturated Fatty Acids: Effect on Hepatic Metabolism in Rats

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OBJECTIVE: We investigated the effect of diets rich in ω-6 and ω-3 fatty acids on hepatic metabolism.

METHODS: Male Wistar rats, just weaned, were fed ad libitum for 8 wk with one of the following diets: rat chow (C), rat chow containing 15% (w/w) soybean oil (S), rat chow containing 15% (w/w) fish oil (F), and rat chow containing 15% soy bean and fish oil (SF; 5:1, w/w). Casein was added to the fatty diets to achieve the same content of protein (20%) as the control chow. The rats were killed by decapitation, and the hepatic tissue was removed and weighed. Tissue lipid, glycogen, and protein content, in vivo lipogenesis rate, and adenosine triphosphate citrate lyase and malic enzyme activities were evaluated. Plasma total lipids, triacylglycerol, and cholesterol concentrations were assessed.

RESULTS: Body weight gain was higher in F and SF than in C and S rats. Liver weight, lipid content, and lipogenesis rate increased in F and SF rats, although adenosine triphosphate citrate lyase activity decreased. Glycogen concentration decreased in S, F, and SF rats compared with C rats. Plasma total lipids and triacylglycerol concentrations were lower in F and SF than in C rats. Total and high-density lipoprotein cholesterol (HDL-C) plasma levels decreased in F rats, with maintenance of the total:HDL-C ratio. In SF rats, an increase in HDL-C led to a lower total:HDL-C ratio.

CONCLUSIONS: These results indicated that an enrichment of the diet with ω-3 polyunsaturated fatty acids produces hypolipidemia but may cause changes in liver metabolism that favor lipid deposition. They also suggested that the addition of a small amount of eicosapentaenoic and docosahexaenoic polyunsaturated fatty acids to an ω-6–rich diet further improve the circulating lipid profile, in comparison with an ω-3–rich diet, but it does not prevent excess liver lipid accumulation. *Nutrition* 2003;19:144–149. ©Elsevier Science Inc. 2003

KEY WORDS: Diet enriched with ω-3 and ω-6 fatty acids, nutrition, hepatic metabolism

INTRODUCTION

Alterations in dietary fat composition can influence metabolic functions and lead to changes in body weight and/or composition. The ω-3 polyunsaturated fatty acids (PUFAs) have received considerable interest because their consumption has been associated with beneficial health effects. Epidemiologic studies have shown an inverse relation between the incidence of cardiovascular disease and the consumption of fish oil.[1,2]

Available data on the effects of different types of PUFA on body adiposity are controversial. A fish oil–diet elevated body fat and lowered body protein content, whereas a ω-6–rich diet did not induce obesity in rats.[3] In another study, supplementation with ω-3 did not modify the obesity induced in rats by a lard diet.[4] We recently found that enrichment of the diet with ω-3 PUFA decreases adipose tissue lipolysis, whereas ω-6 PUFA increases the uptake of diet-derived lipids by this tissue, both effects favoring fat deposition.[5] Conversely, the consumption of 60% of dietary energy as ω-3 fatty acids during 5 mo upregulated liver uncoupling protein 2 (UCP2) and prevented obesity in mice, whereas the ω-6–rich diet did not produce these effects.[6]

The hypolipidemia caused by ω-3 PUFA diets is well established and has been associated with various hepatic mechanisms such as increased fatty acid oxidation[7–10] and inhibition of de novo fatty acid synthesis secondary to decreased fatty acid synthase gene expression.[11] However, the addition of 5% fish oil to a high carbohydrate diet lowered plasma triacylglycerol levels while stimulating fatty acid synthase activity and liver lipid accumulation.[12] In contrast, addition of fish oil ameliorated the hepatic steatosis induced by a 0.1% cholesterol diet, whereas the ω-6–rich safflower oil did not show the same effect.[13] Reported hepatic effects contributing to the ω-3 PUFA-induced hypolipidemia also included increased uptake of chylomicron remnants[14] and diminished synthesis of apolipoprotein B-48 and very low-density lipoprotein secretion,[15,16] effects potentially leading to liver fat deposition.

The effect of ω-6 PUFAs on circulating lipids is less clear. A sunflower diet maintained plasma and liver triacylglycerol concentrations similar to those of rats fed a chow diet.[17] A corn oil diet did not modify the plasma lipid levels induced by a lard diet.[18] Plasma triacylglycerol levels were similar, whereas total liver lipid was higher with a safflower than with a beef tallow diet.[19] In another study, the plasma concentration of triacylglycerols de-

This research was supported by FAPESP, CAPES and CNPq.

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0899-9007/03/$30.00
PII S0899-9007(02)00909-7

creased progressively with the decrease in the ω-6:ω-3 ratio of the diet.[20]

Thus, the consequences of the consumption of diets rich in ω-3 or ω-6 on circulating and liver lipids have not been determined. We investigated these aspects in rats fed diets enriched with fish or soy oil and evaluated the effects of a combination of these oils.

MATERIALS AND METHODS

Animals

The Experimental Research Committee of the Federal São Paulo University approved all the procedures involving animals. We used male Wistar rats supplied by the animal care facility of the Physiology Department of the São Paulo Federal University. Immediately after weaning (30 d of life), the animals were assigned to one of four groups, with 24 rats in each group, according to diet composition. All groups were maintained at a temperature of 23 ± 1°C in a temperature-controlled room with a 12-h light, 12-h dark cycle (lights on at 7:00 AM) and received diets ad libitum for 8 wk. After treatment, eight rats from each group were used to measure lipogenesis rate, enzyme activities, and liver glycogen content. Another set of eight rats from each group was used to measure ^{14}C-triolein uptake by the liver and the absorption of ^{14}C-labeled lipid by the intestinal tract (percentage of administered dose). Another set of eight rats from each group was kept for 12 h without food and used for plasma metabolite measurements.

Preparation of Diets

The groups were given one of the following diets. The control group (C) received commercial rat chow (Nuvilab CR-1, Paraná, Brazil) consisting of 20% protein and 4% fat. The soy group (S) received commercial rat chow plus ω-6 PUFA, prepared by adding 15% (w/w) soybean oil to the chow. The fish group (F) received commercial rat chow plus ω-3 PUFA, prepared by adding 15% (w/w) fish oil (Sigma Chemical Co., St. Louis, MO, USA) to the chow. The soy plus fish group (SF) received commercial rat chow plus PUFAs, prepared by adding 15% (w/w) soybean oil and fish oil (ratio = 5:1).

Casein was added to the lipid diets to achieve 20% protein. The C diet contained 4.15 kcal/g, and the PUFA-rich diets contained 4.90 kcal/g, with 33% of total calories from lipids. The proportion of the different types of fatty acids was analyzed in the Adolfo Lutz Laboratory, São Paulo (Table I). A detailed preparation of the diets was described previously.[21]

Food was given fresh each day, and 24-h body weight gains were recorded.

TABLE I.

FATTY ACID COMPOSITION OF STUDY DIETS

Fatty acid*	C	S	F	SF
12:0	0.60	—	—	—
14:0	2.07	—	8.85	1.50
16:0	20.44	12.22	21.33	13.77
18:0	5.12	3.18	4.63	3.43
16:1ω7	—	—	11.18	1.90
18:1ω9	27.37	25.11	17.13	23.78
18:2ω6	41.00	55.11	11.10	47.63
18:3ω3	2.91	4.35	—	3.61
20:1ω9	—	—	3.38	0.57
20:5ω3	—	—	14.04	2.39
22:6ω3	—	—	8.10	1.38
Saturated	28.23	15.40	34.81	18.70
Monounsaturated	27.37	25.11	31.69	26.25
Polyunsaturated	43.91	59.46	33.24	55.01
ω-6	41.0	55.11	11.10	47.63
ω-3	2.91	4.35	22.14	7.38
ω-6:ω-3	14.00	12.70	0.50	6.45

* Grams per 100 g of fat.

C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

Experimental Procedure

MEASUREMENTS OF LIPOGENESIS RATE. Rats were killed by decapitation 1 h after the intraperitoneal administration of 3 mCi of ^3H_2O. Livers were removed and weighed. Aliquots, 500 mg, were saponified, and the fatty acids were extracted according to the method of Stansbie et al.[22] Tissue lipogenesis rate was expressed as micromoles of ^3H_2O incorporated into lipid each hour per gram of tissue.[23] Lipid content was measured according to the method of Oller do Nascimento and Williamson.[24]

ENZYME ACTIVITIES. Aliquots (~1 g) of liver were used to measure enzyme activities. Malic enzyme activity was measured according to the method of Newsholme and Williams[25] and expressed as micromoles per minute per 100 mg of tissue. Adenosine triphosphate citrate (ATP-cit) lyase activity was measured as described by Corrigan and Rider[26] and expressed as micromoles per minute per 100 mg of tissue. Tissue protein content was determined according to the method of Lowry.[27]

MEASUREMENT OF ^{14}C-LABELED LIPID ABSORPTION FROM INTESTINE AND ACCUMULATION IN LIVER. The rats received an intragastric load of [1-^{14}C] triolein (~0.5 g; 0.3 μCi/rat). After 4 h, the rats were killed by decapitation. The entire intestinal tract and samples (~1 g) of the liver were removed and weighed. The intestinal tract was homogenized with H_2O (1:1 w/v) in a Waring blender. Three milliliters (mL) of 30% KOH was added to the intestinal tract homogenates (2 to 3 g) and liver samples. The lipids were saponified and extracted according to the method of Stansbie et al.[22] The extracted fatty acids were dissolved in 5 mL of scintillation liquid, and the radioactivity was measured for determination of the ^{14}C-labeled lipid accumulated in the tissue and the amount of ^{14}C-labeled lipid remaining in the intestinal tract. The absorption of ^{14}C-labeled lipid was determined by subtracting the radioactivity remaining in the intestinal tract from the amount administered.

LIVER GLYCOGEN. Liver glycogen was purified by ethanol extraction and alkali digestion and hydrolyzed, and glucose was determined according to the anthrone method of Johann and Lentini.[28]

PLASMA METABOLITES. Plasma was obtained by centrifugation and aliquots used to measure triacylglycerols, total lipids, cholesterol, and high-density lipoprotein cholesterol (HDL-C). For these measurements, we used commercial kits from Labtest Diagnostic S.A. (LAGOA Santa, MG, Brazil).

Statistical Analysis

The results are expressed as means ± standard of the mean. Intergroup comparisons were performed by one-way analysis of variance followed by Duncan's test. Significance was set at $P \leq 0.05$.

TABLE II.

DAILY FATTY ACID INTAKE OF RATS FED THE STUDY DIETS FOR 8 WK*

Fatty acid†	C	S	F	SF
12:0	2.1 ± 0.1	—	—	—
14:0	7.2 ± 0.4^{a}	—	109.8 ± 10.5^{b}	19.8 ± 3.0^{c}
16:0	71.5 ± 4.1^{a}	153.8 ± 14.5^{b}	264.7 ± 25.4^{c}	181.8 ± 27.3^{b}
18:0	17.9 ± 1.0^{a}	40.0 ± 3.8^{b}	57.5 ± 5.5^{c}	45.3 ± 6.8^{b}
16:1ω7	—	—	138.7 ± 13.3^{a}	25.1 ± 3.8^{b}
18:1ω9	95.8 ± 5.5^{a}	315.9 ± 29.9^{b}	214.7 ± 20.6^{c}	313.8 ± 47.1^{bc}
18:2ω6	143.5 ± 8.2^{a}	693.3 ± 65.6^{b}	137.8 ± 13.2^{a}	628.7 ± 94.3^{b}
18:3ω3	10.2 ± 0.6^{a}	54.7 ± 5.2^{b}	—	47.6 ± 7.1^{b}
20:1ω9	—	—	41.9 ± 4.0^{a}	7.5 ± 1.1^{b}
20:5ω3	—	—	174.3 ± 16.7^{a}	31.5 ± 4.7^{b}
22:6ω3	—	—	98.4 ± 9.4^{a}	18.2 ± 2.7^{b}
Saturated	98.7 ± 5.5^{a}	193.8 ± 18.4^{b}	432.0 ± 41.3^{c}	246.9 ± 37.0^{b}
Monounsaturated	95.8 ± 5.5^{a}	315.9 ± 29.9^{b}	180.6 ± 17.3^{c}	346.4 ± 51.9^{b}
Polyunsaturated	153.7 ± 8.9^{a}	748.0 ± 71.1^{b}	410.5 ± 39.4^{c}	726.0 ± 108.9^{b}
ω-6	143.5 ± 8.2^{a}	693.3 ± 65.6^{b}	137.8 ± 13.2^{a}	628.7 ± 94.3^{b}
ω-3	10.2 ± 0.6^{a}	54.7 ± 5.2^{b}	272.7 ± 26.1^{c}	97.3 ± 14.6^{d}
Total lipid	354.0 ± 20.0^{a}	1246.4 ± 121.6^{b}	1215.0 ± 120.0^{b}	1315.8 ± 198.9^{b}
ω-6:ω-23	14.0	12.7	0.5	6.4
Saturated:unsaturated	0.40	0.18	0.73	0.25

* Values are mean ± standard error of the mean. Values in the same row with different superscript letters are significantly different from one another at $P < 0.05$ (Duncan's test).
† Milligrams per 100 g of body weight.
C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

RESULTS

Fat intake, Body Weight Gain, and Intestinal Lipid Absorption

As shown in Table II, total lipid intake was similar among the S, F, and SF diets. Animals fed the F diet ingested a higher amount of saturated and ω-3 PUFAs than those fed the S and SF diets. Accordingly, the ω-6:ω-3 ratio was lower but the saturated:unsaturated ratio was higher in the F diet as compared with the other lipid diets. Body weight gain was higher in the S, F, and SF groups than in the C group and in the F and SF groups than in the S group (Fig. 1). Compared with the C group, the absorption of ^{14}C-labeled lipid by the intestinal tract was greater in the S and SF groups (Fig. 2).

Liver Metabolites

Absolute liver weight increased in the SF compared with the C and S groups. In the F group, absolute and relative liver weights were higher than in the C, S, and SF groups. Liver lipid content was higher in the F than in the C and S groups and higher in the SF than in the F group. Protein content was not affected by fat enrichment of the diet, although glycogen concentration decreased in the S, F, and SF groups compared with the C group. Lower glycogen

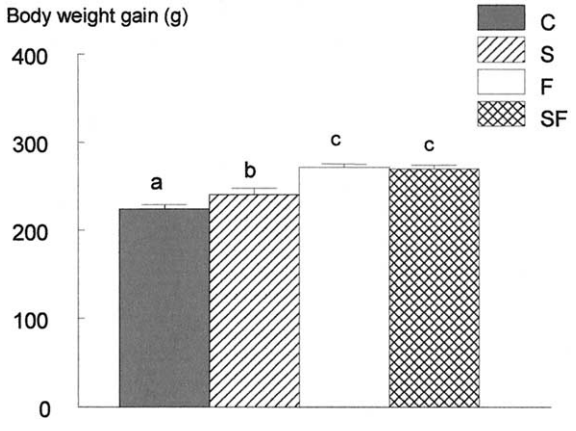

FIG. 1. Effects of dietary fat on body weight gain in rats fed C, S, F, or SF during 8 wk. Values are means ± standard error of the mean. Bars with different letters are significantly different from one another at $P < 0.05$ as determined by Duncan's test. C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

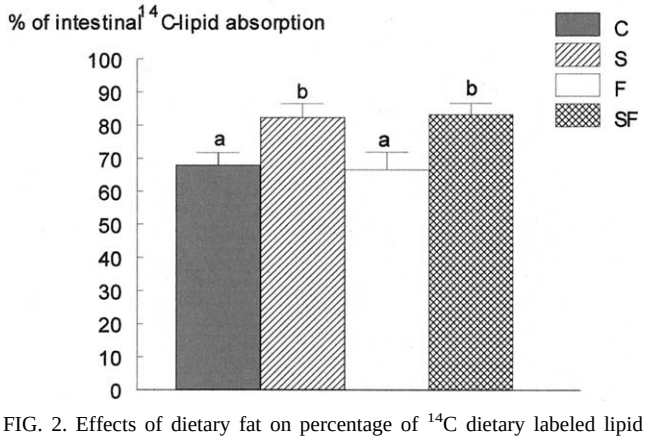

FIG. 2. Effects of dietary fat on percentage of ^{14}C dietary labeled lipid intestinal absorption in rats fed C, S, F, or SF during 8 wk. Values are means ± standard error of the mean. Bars with different letters are significantly different from one another at $P < 0.05$ as determined by Duncan's test. C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

TABLE III.

EFFECTS OF DIETARY FAT ON LIVER WEIGHT, LIPID, PROTEIN AND GLYCOGEN CONTENT IN RATS FED THE STUDY DIETS FOR 8 WK*

	C ($n = 8$)	S ($n = 8$)	F ($n = 8$)	SF ($n = 8$)
Absolute tissue weight (g)	11.76 ± 0.48[a]	11.51 ± 0.50[a]	14.95 ± 0.35[b]	13.22 ± 0.43[c]
Relative tissue weight (g/100 g BW)	3.85 ± 0.15[a]	3.47 ± 0.24[a]	4.45 ± 0.10[b]	3.91 ± 0.15[a]
Lipid content (mg/100 mg)	3.53 ± 0.24[a]	3.22 ± 0.32[a]	5.31 ± 0.27[b]	6.44 ± 0.28[c]
Protein content (mg/g)	184.4 ± 4.8[a]	195.2 ± 3.6[a]	189.2 ± 6.8[a]	189.0 ± 6.7[a]
Glycogen content (mg/100 mg)	4.11 ± 0.18[a]	3.57 ± 0.09[b]	3.31 ± 0.15[b]	2.52 ± 0.13[c]

* Values are means ± standard error of the mean. Values in the same row with different superscript letters are significantly different from one another at $P < 0.05$ (Duncan's test).
BW, body weight; C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

concentration was detected in the SF group when compared with C, S, and F groups (Table III).

Lipogenesis Rate, Lipogenesis Enzymes, and Dietary Lipid Accumulation in Liver

The F and SF diets increased the in vivo lipogenesis rate in the liver, whereas the activity of ATP-cit lyase enzyme decreased. No significant differences in the malic enzyme activity and the percentage of diet-derived lipid accumulation were observed across groups (Table IV).

Plasma Metabolites

The F group exhibited lower plasma total lipids, cholesterol, and HDL-C concentrations than did the C, S, and SF groups.

Plasma triacylglycerol and total lipid levels of the F and SF groups were lower than those of the C group. The enrichment of diet with soybean oil (S and SF) increased HDL-C compared with the C and F diets. SF significantly decreased the ratio of total cholesterol to HDL-C as compared with C, S, and F diets (Table V).

DISCUSSION

In the present study, feeding rats with PUFA-rich diets significantly increased body weight gain, in agreement with previous reports.[5,29,30] This indicated that a greater food efficiency occurred in the lipid groups and, as reported previously, PUFA-rich diets decreased food intake.[5] This finding has been ascribed to lower energy expense of lipid deposition from dietary fat than from dietary carbohydrate.[31] Moreover, it has been previously shown[5,32] that the increase in total carcass lipid content was similar across the lipid diet groups, whereas the presence of ω-3 PUFA also increased carcass protein content. This finding may explain the greater body weight gain of the S and SF groups.

In accordance with our findings, hepatomegaly has been observed in rats fed a diet rich in fish oil and accompanied by a low ratio of milligrams of DNA per gram of liver[33] and an increase in hepatocyte cytoplasms.[34] As suggested by Agius et al.,[35] liver size evolution occurs in parallel with changes in glycogen content during a fasted-to-fed transition. Although liver glycogen content in the S, F, and SF groups was lower in our study, the lipid content increased in the F and SF groups, suggesting that the hepatomegaly may be caused, at least in part, by lipid accumulation. Hill et al.[18] suggested that the hepatomegaly in rats fed a diet enriched with fish oil might be caused by a high metabolic activity in the liver.

The hepatic lipid accumulation was accompanied by a decrease in plasma total lipids and triacylglycerol and cholesterol concentrations in the F and SF groups. Brown et al.[15] found a decreased capacity of rat liver to transport triacylglycerol out of the hepatocyte after a diet rich in fish oil and associated this finding with decreased synthesis and presecretory degradation of apolipoprotein B-48 and, hence, a decreased secretion of very low-density lipoprotein apolipoprotein B-48. These metabolic changes also might explain the increase in the accumulation of labeled lipids in liver in the F and SF groups, as determined by the amount of ^3H_2O incorporated into lipid, despite a decrease in ATP-cit enzyme activity in this tissue. Decreased malic and ATP-cit enzyme activities in the livers of rats treated with PUFA-rich diets has been reported.[36] In contrast, increased fatty acid synthase activity and lipid content were observed in livers of rats fasted and re-fed with a diet supplemented with 5% menhaden oil.[12]

TABLE IV.

EFFECTS OF DIETARY FAT ON LIVER ACCUMULATION OF ^{14}C-LABELED DIETARY LIPID, LIPOGENESIS RATE, MALIC ENZYME ACTIVITY, AND ATP CITRATE LYASE ENZYME ACTIVITY IN RATS FED THE STUDY DIETS FOR 8 WK*

	C ($n = 8$)	S ($n = 8$)	F ($n = 8$)	SF ($n = 8$)
Lipogenesis rate (μM ^3H_2O incorporated into lipid/h/g tissue)	2.53 ± 0.20[a]	2.90 ± 0.18[a]	4.29 ± 0.24[b]	3.97 ± 0.45[b]
Malic enzyme activity (μM of substrate/min/g tissue)	0.28 ± 0.01[a]	0.30 ± 0.03[a]	0.27 ± 0.03[a]	0.36 ± 0.06[a]
ATP-cit enzyme activity (μM of substrate/min/g tissue)	0.86 ± 0.10[a]	0.40 ± 0.03[b]	0.19 ± 0.04[c]	0.22 ± 0.03[c]
Dietary fatty accumulation (% ^{14}C lipid accumulated/g tissue/h	4.85 ± 0.66[a]	4.46 ± 0.48[a]	5.88 ± 0.60[a]	4.82 ± 0.59[a]

* Values are means ± standard error of the mean. Values in the same row with different superscript letters are significantly different from one other at $P < 0.05$ (Duncan's test).
ATP-cit, adenosine triphosphate citrate; C, control diet; F, fish oil diet; S, soybean diet; SF, soybean plus fish oil diet.

TABLE V.

EFFECTS OF DIETARY FAT ON PLASMA TOTAL LIPIDS, TRIACYLGLYCEROLS, TOTAL CHOLESTEROL, AND HDL-C CONCENTRATIONS OF RATS FED THE STUDY DIETS FOR 8 WK*

	C (n = 8)	S (n = 8)	F (n = 8)	SF (n = 8)
Total lipids (mg/dL)	347.87 ± 17.3[a]	378.14 ± 16.4[a]	253.90 ± 20.6[b]	306.63 ± 12.9[c]
Triacylglycerols (mg/dL)	127.69 ± 12.98[a]	102.36 ± 7.90[ab]	94.81 ± 8.61[b]	87.21 ± 7.82[b]
Total cholesterol (mg/dL)	71.41 ± 5.79[a]	71.11 ± 6.64[a]	37.71 ± 4.23[b]	59.70 ± 4.33[a]
HDL-C (mg/dL)	40.78 ± 2.04[a]	49.70 ± 3.95[b]	26.23 ± 2.43[c]	49.98 ± 2.49[b]
Total cholesterol:HDL-C	1.78 ± 0.17[a]	1.45 ± 0.12[a]	1.42 ± 0.10[a]	1.20 ± 0.07[b]

* Values are means ± standard error of the mean. Values in the same row with different superscript letters are significantly different from one other at $P < 0.05$ (Duncan's test).
C, control diet; F, fish oil diet; HDL-C, high-density lipoprotein cholesterol; S, soybean diet; SF, soy bean plus fish oil diet.

The lower absorption of dietary ^{14}C-labeled lipid, observed in the present study, likely contributed to the hypolipidemic effect of the fish oil. Triacylglycerols from fish oil may be hydrolyzed less efficiently by pancreatic lipases than other triacylglycerols.[37] The digestion and absorption of fish oil reportedly were lower than those of corn oil.[38] However, an unaltered intestinal absorption of dietary fish oil has been described.[39]

The type of fat consumed in the diet has been shown to modify the fatty acid composition of chylomicron remnants and their uptake by the liver.[40,41] In a perfused rat liver preparation, the removal of [^{3}H]triacylglycerol chylomicron remnants was lower when the chylomicrons were derived from rats given a bolus of palm oil as opposed to fish oil.[14] Conversely, in the present study, the type of dietary fatty acid previously consumed failed to affect the hepatic in vivo accumulation of ^{14}C-labeled lipid derived from an intragastric ^{14}C-triolein load. We previously showed that, in the epididymal white adipose tissue, such lipid accumulation is higher in F rats than in C rats,[5] suggesting that a considerable amount of ω-3 fatty acids from chylomicrons was taken by this tissue, thus leaving a diminished amount for hepatic uptake. Also, chronic treatment with an ω-3 PUFA-rich diet may stimulate fatty acid oxidation in the liver because Hill et al.[18] found that a diet enriched with fish oil can increase liver metabolic activity.

The F diet decreased plasma total cholesterol and HDL-C levels, in agreement with previous reports.[42,43] The hypocholesterolemic effect of the F diet has been ascribed in part to a higher binding affinity of low-density lipoprotein to liver plasma membranes in comparison with saturated diets.[43]

Interestingly, the SF diet, although it induced a less pronounced decrease in total cholesterol, increased HDL-C levels, leading to a lower ratio of total cholesterol to HDL-C. The lowering effect on plasma triacylglycerol also was slightly stronger in the SF than in the F group. Thus, the mixed diet seemed to have a more beneficial effect on the circulating lipid profile than did the F diet enriched with ω-3.

One important difference in composition between the F and SF diets, aside from the ω-3 content, was the higher level of saturated fatty acids in the F diet. Chylomicrons from saturated fatty acids have been shown to generate less circulating HDL-C than those from ω-3 and ω-6.[40]

These results indicated that an enrichment of the diet with ω-3 PUFAs produces hypolipidemia but may change liver metabolism in favor of lipid deposition. These data also suggested that the addition of small amounts of eicosapentaenoic and docosahexaenoic PUFAs to an ω-6–rich diet can improve the circulating lipid profile, in comparison with an ω-3–rich diet, but does not prevent excess liver lipid accumulation.

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