

Palm and partially hydrogenated soybean oils adversely alter lipoprotein profiles compared with soybean and canola oils in moderately hyperlipidemic subjects¹⁻⁴

Sonia Vega-López, Lynne M Ausman, Susan M Jalbert, Arja T Erkkilä, and Alice H Lichtenstein

ABSTRACT

Background: Partially hydrogenated fat has an unfavorable effect on cardiovascular disease risk. Palm oil is a potential substitute because of favorable physical characteristics.

Objective: We assessed the effect of palm oil on lipoprotein profiles compared with the effects of both partially hydrogenated fat and oils high in monounsaturated or polyunsaturated fatty acids.

Design: Fifteen volunteers aged ≥ 50 y with LDL cholesterol ≥ 130 mg/dL were provided with food for each of 4 diets (35 d/phase) varying in type of fat (partially hydrogenated soybean, soybean, palm, or canola; two-thirds fat, 20% of energy). Plasma fatty acid profiles, lipids, lipoproteins, apolipoprotein A-I, apolipoprotein B, lipoprotein(a), glucose, insulin, HDL subfractions, and indicators of lipoprotein metabolism (HDL-cholesterol fractional esterification rate, cholesteryl ester transfer protein, phospholipid transfer protein, and paraoxonase activities) were measured at the end of each phase.

Results: Plasma fatty acid profiles reflected the main source of dietary fat. Partially hydrogenated soybean and palm oils resulted in higher LDL-cholesterol concentrations than did soybean (12% and 14%, respectively; $P < 0.05$) and canola (16% and 18%; $P < 0.05$) oils. Apolipoprotein B ($P < 0.05$) and A-I ($P < 0.05$) concentrations mirrored the pattern of LDL- and HDL-cholesterol concentrations, respectively. No significant effect on the total-to-HDL cholesterol ratio was observed for palm oil compared with the other dietary fats. HDL3 cholesterol was higher after palm oil than after partially hydrogenated and soybean oils ($P < 0.05$). Differences in measures of glucose and HDL intravascular processing attributable to dietary fat were small.

Conclusion: Palm and partially hydrogenated soybean oils, compared with soybean and canola oils, adversely altered the lipoprotein profile in moderately hyperlipidemic subjects without significantly affecting HDL intravascular processing markers. *Am J Clin Nutr* 2006;84:54–62.

KEY WORDS Cardiovascular disease, *trans* fatty acids, lipoproteins, palm oil, partially hydrogenated soybean oil, LDL cholesterol, HDL cholesterol, insulin, glucose, cholesteryl ester transfer protein, phospholipid transfer protein

INTRODUCTION

The relation between plasma lipid and lipoprotein concentrations and the risk of developing cardiovascular disease (CVD) on the basis of dietary fat type is well documented (1, 2). According to early findings in experimental animals and humans (3, 4), a

population-wide recommendation was made to replace fats of animal origin, which are high in saturated fatty acids, with fats of vegetable origin, which are high in unsaturated fatty acids (1, 2). This recommendation resulted in a gradual shift in the food supply from foods made with animal fats to foods made with a wide range of vegetable oils. Over time, much of the vegetable oil that displaced the animal fat from the diet was in the hydrogenated form (5). Hydrogenation extends the shelf life of the fat and alters its physical properties such that it is more similar to animal fat than vegetable oil in the natural state. However, subsequent work suggested that *trans* fatty acids formed during the hydrogenation process, although unsaturated, resulted in plasma lipid profiles associated with an elevated risk of developing CVD (6–10). This forced a rethinking of the dietary fat recommendations intended to decrease CVD risk.

As a result of early public health recommendations to decrease the intake of saturated fatty acids, the use of palm oil dramatically decreased. Much of the palm oil was displaced with hydrogenated vegetable oils. More recently, because of concerns about the adverse effects of hydrogenated fat and the mandate by the Food and Drug Administration to include *trans* fatty acids on the Nutrition Facts panel of all packaged food by 1 January 2006, the use of palm oil by the food industry has increased (11). Palm oil is favored by food manufacturers over other vegetable oils because of its higher melting point (34.2 °C) and resistance to oxidative changes resulting from its higher content of saturated fatty acids (12).

The aim of the present study was to evaluate the effect of consuming two-thirds of total fat or 20% of energy from palm oil

¹ From the Cardiovascular Nutrition Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA (SV-L, LMA, SMJ, and AHL) and the Department of Clinical Nutrition, University of Kuopio, Kuopio, Finland (ATE).

² Any opinions, findings, conclusion, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the view of the US Department of Agriculture.

³ Supported by the National Institutes of Health, Bethesda, MD (grant HL 54727) and the US Department of Agriculture (agreement no. 58-1950-4-401).

⁴ Reprints not available. Address correspondence to AH Lichtenstein, Cardiovascular Nutrition Laboratory, JM USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, MA 02111. E-mail: alice.lichtenstein@tufts.edu.

Received March 2, 2006.

Accepted for publication March 2, 2006.

TABLE 1Baseline characteristics of subjects¹

Variable	All subjects (n = 15)	Women (n = 10)	Men (n = 5)
Age (y)	63.9 ± 5.7	66.7 ± 4.4 ^a	58.3 ± 3.5 ^b
BMI (kg/m ²)	26.0 ± 2.4	26.2 ± 2.3	25.6 ± 2.7
Systolic BP (mm Hg)	116 ± 12	120 ± 13	109 ± 5
Diastolic BP (mm Hg)	73 ± 7	74 ± 7	70 ± 7
Plasma lipids, lipoproteins, and apolipoproteins			
TC (mg/dL)	253 ± 30	245 ± 30	270 ± 26
LDL-C (mg/dL)	177 ± 30	167 ± 28	196 ± 28
VLDL-C (mg/dL)	22.2 ± 7.0	21.0 ± 7.4	24.6 ± 6.0
HDL-C (mg/dL)	54 ± 11	57 ± 12	49 ± 8
HDL2-C (mg/dL)	20.2 ± 9.3	22.4 ± 10.0	15.9 ± 6.5
HDL3-C (mg/dL)	33.9 ± 4.9	34.5 ± 5.7	32.7 ± 3.0
TG (mg/dL)	111 ± 38	111 ± 37	110 ± 44
Apo B (mg/dL)	138 ± 23	132 ± 22	150 ± 24
Apo A-I (mg/dL)	174 ± 15	178 ± 16	165 ± 10
AI-LpAI (mg/dL)	48.7 ± 14.4	51.0 ± 15.9	44.3 ± 11.0
AI-LpAII (mg/dL)	125 ± 14	126 ± 14	123 ± 16
Apo A-II (mg/dL)	31.1 ± 6.8	30.1 ± 6.1	33.1 ± 8.4
TC:HDL-C	4.85 ± 1.11	4.42 ± 0.79 ^b	5.70 ± 1.24 ^a
LDL-C:Apo B	1.29 ± 0.08	1.28 ± 0.09	1.32 ± 0.06
HDL-C:Apo A-I	0.310 ± 0.046	0.319 ± 0.050	0.292 ± 0.034
Lp(a) (mg/dL)	12.7 ± 10.7	13.9 ± 13.9	10.4 ± 2.3

¹ All values are $\bar{x} \pm$ SD. Apo, apolipoprotein; AI-LpAI, apo A-I in particles containing only apo A-I; AI-LpAII, apo A-I in particles containing both apo A-I and apo A-II; BP, blood pressure; Lp(a), lipoprotein(a); TC, total cholesterol; LDL-C, LDL cholesterol; VLDL-C, VLDL cholesterol; HDL-C, HDL cholesterol; TG, triacylglycerol. Values in a row with different superscript letters are significantly different, $P < 0.05$ (unpaired *t* test).

compared with the effect of consuming partially hydrogenated soybean oil and oils high in monounsaturated (canola oil) or polyunsaturated (soybean oil) fatty acids on plasma fatty acid profiles, lipid and lipoprotein concentrations, and indicators of glucose homeostasis and HDL metabolism.

SUBJECTS AND METHODS

Study protocol

Fifteen volunteers (5 men and 10 postmenopausal women) aged ≥ 50 y with LDL cholesterol ≥ 130 mg/dL but otherwise apparently healthy were recruited from the greater Boston area. Volunteers were excluded if they had abnormal kidney, liver, thyroid, or cardiac function; had abnormal fasting glucose concentration; were taking medications known to affect blood lipid concentrations; were using dietary supplements; or smoked. All women were postmenopausal and not using hormone replacement therapy. Characteristics of the participants at baseline are summarized in **Table 1**. Except for age and the total-to-HDL cholesterol ratio (total:HDL cholesterol), the baseline characteristics were not significantly different between the men and women (Table 1). The male participants were significantly younger than were the female participants and had a significantly lower total:HDL cholesterol. All study participants gave written consent. The study protocol was approved by the Human Investigation Review Committee of the New England Medical Center and Tufts University.

All foods and beverages were provided to the study participants. Caloric intake was adjusted, when necessary, to maintain a stable body weight throughout the study period. The diets were designed to have a similar content of total fat, carbohydrate, protein, fiber, and cholesterol. This was confirmed by chemical

analysis (**Table 2**), which was performed by Covance Laboratories (Madison, WI). The same foods were included in each diet. The only difference in the diets was the type of fat added to various mixed foods (partially hydrogenated soybean, soybean, palm, or canola oil). In contrast to the hydrogenated oils used by some in the food industry, which have up to 33% *trans* fatty acids (13), the partially hydrogenated soybean oil used for the present study contained 13.6% of *trans* fatty acids (10). By design, the experimental fat provided two-thirds of the total fat of the diet, which was equivalent to 20% of total energy. This resulted in a dietary intake of *trans* fatty acids of 4.15% of energy (Table 2), a level higher than the 2.6% estimated intakes in the United States (14) and comparable to that of other clinical studies (15–18). The mean (\pm SD) caloric intake of the participants was 2065 \pm 183 kcal in the women and 3050 \pm 737 kcal in the men. Initially, the participants were assigned to a sequence of six 35-d diet phases in a crossover design as described previously (10). After completing that sequence, the participants were given the option to continue for 2 additional phases, palm and canola oils, provided in random order. Previous data from our laboratory indicated that, under the specified study conditions, plasma lipid concentrations at the end of each 5-wk phase were independent of diet order or intervening diet phases (19). Additional diets were included in the original randomization scheme but were not included in the present analysis because they addressed different experimental questions (10, 20).

Fasting (14-h) blood samples were collected into EDTA-containing tubes on 3 separate days during the last week of each diet phase. Plasma was separated by centrifugation at 1100 \times g at 4 °C for 20 min, divided into aliquots, and stored at –80 °C for subsequent analysis.

TABLE 2
Composition of experimental diets¹

Constituent	Partially hydrogenated soybean	Soybean	Palm	Canola
Protein (% of daily energy intake)	17	16	18	15
Carbohydrate (% of daily energy intake)	53	56	52	53
Fat (% of daily energy intake)	30	28	30	32
Saturated fatty acids (% of daily energy intake)	8.56	7.30	14.83	6.38
12:0 (% of daily energy intake)	0.75	0.83	0.78	0.92
14:0 (% of daily energy intake)	0.57	0.63	0.74	0.62
16:0 (% of daily energy intake)	3.91	3.65	11.11	2.84
18:0 (% of daily energy intake)	2.64	1.45	1.59	1.15
Monounsaturated fatty acids (% of daily energy intake)	9.92	8.14	10.91	15.37
18:1 (% of daily energy intake)	7.51	7.20	10.24	13.72
Polyunsaturated fatty acids (% of daily energy intake)	8.13	12.48	3.51	8.74
18:2 (% of daily energy intake)	7.22	10.74	3.26	6.54
18:3 (% of daily energy intake)	0.55	1.67	0.21	2.16
<i>trans</i> Fatty acids (% of daily energy intake)	4.15	0.55	0.60	0.98
Cholesterol (g/1000 kcal)	0.06	0.07	0.06	0.06
Fiber (g/1000 kcal)	13	16	16	16

¹Macronutrients, fiber, cholesterol, and fatty acids were measured by chemical analysis of food.

Biochemical measures

Plasma lipids were measured on all 3 d, and the mean was used for the statistical analysis. VLDL was isolated from plasma by ultracentrifugation at $109\,000 \times g$ at 4 °C for 18 h (21). Triacylglycerol and cholesterol in plasma, VLDL cholesterol, and HDL cholesterol were measured by using a biochromatic analyzer (model CCX, Spectrum; Incstar, Stillwater, MN) with enzymatic reagents (22). The concentrations of HDL cholesterol and the subfractions of HDL2 and HDL3 cholesterol were measured in the supernatant fluid after sequential selective precipitation of apolipoprotein B-containing lipoproteins and then of HDL2 in a separate step by using a modification of the dextran sulfate-magnesium chloride method (23, 24). The concentration of HDL2 cholesterol was calculated by difference. LDL-cholesterol concentrations were calculated by subtracting VLDL- and HDL-cholesterol concentrations from the total cholesterol concentration. Lipid assays were standardized through the Lipid Standardization Program of the Centers for Disease Control and Prevention (Atlanta, GA).

Plasma concentrations of apolipoprotein A-I and apolipoprotein B were measured by immunoturbidimetric assays with a Spectrum CCX analyzer (Incstar) (25, 26). Concentrations of apolipoprotein A-II and apolipoprotein A-I in particles without apolipoprotein A-II were measured by an electroimmunodiffusion technique by using commercially available agarose gels with polyclonal apolipoprotein A-II antibodies incorporated into the gels (Laboratoires Sebia, Lisses, France) (27). Concentrations of apolipoprotein A-I in particles containing both apolipoprotein A-I and apolipoprotein A-II were calculated by difference. Lipoprotein(a) was measured as previously described (Terumo Medical, Elkton, MD) (28). Plasma lipid subfractionation and measurement of fatty acids of these subfractions were performed as previously described (29) in a subset of 10 volunteers from whom adequate sample was available.

Plasma glucose concentrations were measured by a colorimetric assay (Roche Laboratories, Nutley, NJ). Plasma insulin was measured by using a human insulin-specific radioimmunoassay

kit (Linco Research, St Louis, MO) that uses the double-antibody and polyethylene glycol technique (30). Homeostatic model assessment (HOMA) was calculated as follows (31, 32):

$$\text{HOMA} = \text{glucose (mmol/L)} \times [\text{insulin } (\mu\text{U/mL})/22.5] \quad (1)$$

Cholesteryl ester transfer protein (CETP) activity and the HDL cholesterol fractional esterification rate (FER_{HDL}) were measured in plasma after the removal of endogenous VLDL and LDL by phosphotungstate and magnesium chloride precipitation, as previously indicated (33, 34). CETP activity was measured as previously described (35).

Phospholipid transfer protein (PLTP) activity in plasma was quantified by assessing the transfer of radioactively labeled phosphatidylcholine in phosphatidylcholine-liposomes to HDL3 (36–38). Paraonase (EC 3.1.8.1) activity was measured by using Paraon (diethyl-*p*-nitrophenyl phosphate; Sigma Chemicals, St Louis, MO) as a substrate, as previously reported (39).

Statistical analyses

Baseline characteristics of the male and female participants were compared by using an unpaired *t* test. A repeated-measures analysis of variance was performed to test the effects of palm, partially hydrogenated soybean, soybean, and canola oils on plasma lipids, lipoproteins, apolipoproteins, and markers of HDL metabolism and glucose homeostasis. Tukey's test was used to perform post hoc analysis. Before statistical analysis, variables with a skewed distribution [triacylglycerol, lipoprotein (a), HOMA, and CETP activity] were log-transformed to achieve normality. For plasma fatty acids, the analysis was conducted on ranked data because no transformation would normalize the data. Untransformed data are presented in the text and tables as means \pm SDs. Analyses were conducted at the 0.05 α level. Statistical analyses were conducted by using SAS version 8.2 (SAS Institute Inc, Cary, NC).

TABLE 3

Selected serum fatty acid profiles in the cholesteryl ester, triacylglycerol, and phospholipid fractions at the end of each experimental diet phase¹

	Partially hydrogenated soybean	Soybean	Palm	Canola
Triacylglycerols (molar %)				
14:0	2.33 ± 0.56	2.27 ± 0.71	2.50 ± 0.54	2.10 ± 0.54
16:0	23.34 ± 2.55 ^b	21.95 ± 2.68 ^b	29.36 ± 3.04 ^a	21.75 ± 2.97 ^b
18:0	3.28 ± 0.93	2.80 ± 0.81	3.15 ± 0.50	2.66 ± 0.45
18:1c	32.04 ± 3.51 ^b	27.98 ± 3.64 ^c	35.53 ± 2.02 ^a	38.15 ± 2.94 ^a
18:1t	4.52 ± 0.59	3.53 ± 1.88	3.12 ± 1.26	3.17 ± 1.41
18:2n-6c	23.73 ± 3.72 ^b	29.76 ± 4.94 ^a	16.93 ± 4.26 ^c	21.44 ± 3.12 ^b
18:2t	2.60 ± 0.43 ^a	1.73 ± 0.58 ^{a,b}	1.47 ± 0.36 ^{b,c}	1.56 ± 0.60 ^{b,c}
18:3n-6	0.51 ± 0.21 ^{a,b}	0.74 ± 0.30 ^a	0.46 ± 0.11 ^b	0.53 ± 0.16 ^{a,b}
18:3n-3	1.31 ± 0.55 ^b	2.91 ± 0.50 ^a	0.86 ± 0.23 ^c	2.57 ± 1.00 ^a
20:4n-6	1.37 ± 0.29	1.53 ± 0.61	1.25 ± 0.39	1.35 ± 0.48
20:5n-3	0.21 ± 0.08 ^b	0.39 ± 0.17 ^a	0.22 ± 0.09 ^b	0.35 ± 0.16 ^{a,b}
22:6n-3	0.51 ± 0.16	0.61 ± 0.24	0.52 ± 0.17	0.55 ± 0.23
Phospholipid (molar %)				
14:0	0.52 ± 0.11	0.54 ± 0.05	0.52 ± 0.08	0.60 ± 0.13
16:0	29.65 ± 0.90 ^b	29.97 ± 1.03 ^b	33.17 ± 0.74 ^a	29.84 ± 0.54 ^b
18:0	13.64 ± 0.90 ^a	13.59 ± 1.07 ^a	12.21 ± 0.90 ^c	13.05 ± 1.02 ^b
18:1c	7.68 ± 1.44 ^b	6.97 ± 1.26 ^c	9.21 ± 1.37 ^a	9.75 ± 1.84 ^a
18:1t	2.84 ± 0.42 ^a	1.86 ± 0.65 ^{b,c}	1.73 ± 1.15 ^c	2.22 ± 1.32 ^b
18:2n-6c	22.22 ± 1.90 ^b	24.65 ± 2.40 ^a	20.83 ± 1.90 ^c	20.95 ± 2.10 ^c
18:2t	0.98 ± 0.17 ^a	0.70 ± 0.27 ^{a,b}	0.72 ± 0.40 ^b	0.76 ± 0.44 ^b
18:3n-6	0.13 ± 0.05	0.13 ± 0.04	0.19 ± 0.09	0.14 ± 0.04
18:3n-3	0.21 ± 0.03 ^b	0.34 ± 0.04 ^a	0.16 ± 0.02 ^c	0.39 ± 0.09 ^a
20:4n-6	9.01 ± 1.44	8.72 ± 1.29	8.21 ± 1.34	8.93 ± 1.19
20:5n-3	0.63 ± 0.15 ^b	0.76 ± 0.20 ^{a,b}	0.66 ± 0.25 ^b	0.94 ± 0.26 ^a
22:6n-3	3.74 ± 0.50	3.50 ± 0.47	3.34 ± 0.61	3.38 ± 0.38
Cholesteryl ester (molar %)				
14:0	0.77 ± 0.18 ^{a,b}	0.70 ± 0.18 ^b	0.98 ± 0.33 ^a	0.80 ± 0.15 ^{a,b}
16:0	11.30 ± 0.60 ^b	11.15 ± 0.74 ^b	13.83 ± 1.88 ^a	12.97 ± 3.25 ^b
18:0	0.98 ± 0.23	0.85 ± 0.26	1.11 ± 0.84	1.31 ± 1.74
18:1c	13.90 ± 2.20 ^b	11.66 ± 2.13 ^c	17.95 ± 2.17 ^a	18.18 ± 3.05 ^a
18:1t	1.89 ± 1.69	1.51 ± 1.06	1.88 ± 1.76	1.54 ± 0.86
18:2n-6c	56.73 ± 2.86 ^b	60.61 ± 3.02 ^a	49.58 ± 5.85 ^c	50.27 ± 6.63 ^c
18:2t	2.48 ± 0.73 ^a	1.83 ± 0.59 ^{a,b}	2.30 ± 1.19 ^{a,b}	1.71 ± 0.55 ^b
18:3n-6	0.82 ± 0.28 ^{a,b}	0.75 ± 0.28 ^b	0.97 ± 0.30 ^a	0.82 ± 0.30 ^b
18:3n-3	0.52 ± 0.05 ^c	0.83 ± 0.24 ^b	0.44 ± 0.05 ^c	1.11 ± 0.14 ^a
20:4n-6	6.70 ± 1.23	6.47 ± 1.23	6.08 ± 1.30	6.65 ± 1.32
20:5n-3	0.55 ± 0.13 ^c	0.71 ± 0.16 ^b	0.59 ± 0.16 ^{b,c}	0.98 ± 0.26 ^a
22:6n-3	0.50 ± 0.10	0.50 ± 0.09	0.45 ± 0.10	0.59 ± 0.42

¹ All values are $\bar{x} \pm SD$. $n = 10$. Values in a row with different superscript letters are significantly different, $P < 0.05$ (repeated-measures ANOVA with post hoc Tukey's test).

RESULTS

Fatty acid profiles in the plasma lipid subfractions (triacylglycerols, phospholipids, and cholesteryl ester) showed, for the most part, those of the predominant oil in the diet (Table 3). Consistent with the fatty acid composition of the different oils, the proportion of palmitic acid (16:0) in all plasma lipid fractions was higher after consumption of the diet enriched with palm oil than the diets enriched with partially hydrogenated soybean oil, soybean oil, or canola oil ($P < 0.05$). Differences in other plasma saturated fatty acids between diet phases were modest and were likely attributable to the ability of humans to synthesize saturated fatty acids (data not shown). Oleic acid (18:1c) was higher in all lipid subfractions ($P < 0.05$ for all) after the participants consumed the diets enriched with canola oil and palm oil than after the diets enriched with soybean oil or partially hydrogenated soybean oil. Linoleic acid (18:2n-6c) was highest in all 3 lipid

subfractions ($P < 0.05$ for all) after the participants completed the diet phase with soybean oil, reflecting the composition of the experimental fats. A small effect of the higher intake of linolenic acid (18:3n-3) oils on eicosapentaenoic acid (20:5n-3; EPA) but not arachidonic acid (20:4n-6) or docosahexaenoic acid (22:6n-3; DHA) was observed in the phospholipid and cholesteryl ester lipid subfractions as well. The proportion of *trans* fatty acids was highest after the participants consumed the diet enriched with partially hydrogenated soybean oil. This was more pronounced in the triacylglycerol and phospholipid fractions than in the cholesteryl ester fraction ($P < 0.05$ for all). As anticipated from the fatty acid profile of the experimental fats, no significant differences in the proportion of *trans* fatty acids were observed between the diets enriched with palm, soybean, and canola oils.

Outcome measures were considered as 2 experimental questions. To assess the effect of hydrogenation, data generated at the

TABLE 4Plasma lipids, lipoproteins, and apolipoproteins at the end of each diet phase¹

Variable	Partially hydrogenated soybean	Soybean	Palm	Canola
TC (mg/dL)	235 ± 31 ^a	220 ± 27 ^b	240 ± 36 ^a	210 ± 25 ^b
LDL-C (mg/dL)	162 ± 28 ^a	145 ± 24 ^b	165 ± 35 ^a	140 ± 23 ^b
VLDL-C (mg/dL)	25.0 ± 9	25.4 ± 12	24.7 ± 11.3	22.2 ± 12
HDL-C (mg/dL)	48 ± 9	49 ± 9	50 ± 8	48 ± 8
HDL2-C (mg/dL)	16.1 ± 7.4 ^{a,b}	16.9 ± 6.4 ^a	15.1 ± 6.4 ^{a,b}	13.4 ± 4.6 ^b
HDL3-C (mg/dL)	32.2 ± 4.4 ^b	32.4 ± 3.7 ^b	35.0 ± 3.2 ^a	34.4 ± 4.0 ^{a,b}
TG (mg/dL)	129 ± 54	123 ± 56	120 ± 63	120 ± 60
Apo B (mg/dL)	131 ± 23 ^{a,b}	123 ± 21 ^{b,c}	136 ± 27 ^a	121 ± 22 ^c
Apo A-I (mg/dL)	158 ± 18 ^b	161 ± 13 ^b	169 ± 15 ^a	159 ± 16 ^b
AI-LpAI (mg/dL)	44.3 ± 12.9	47.0 ± 14.5	46.7 ± 11.4	45.6 ± 10.3
AI-LpAII (mg/dL)	114 ± 14	117 ± 16	121 ± 12	114 ± 10
Apo A-II (mg/dL)	32.4 ± 7.4	34.1 ± 9.1	33.7 ± 7.4	34.3 ± 6.5
TC:HDL-C	4.99 ± 1.05 ^a	4.61 ± 1.17 ^{a,b}	4.89 ± 1.06 ^{a,b}	4.54 ± 1.06 ^b
LDL-C:Apo B	1.21 ± 0.10	1.18 ± 0.10	1.22 ± 0.11	1.17 ± 0.09
HDL-C:Apo A-I	0.304 ± 0.040	0.306 ± 0.041	0.296 ± 0.028	0.299 ± 0.031
Lp(a) (mg/dL)	13.3 ± 11.6	12.5 ± 9.3	11.1 ± 7.8	13.9 ± 10.2

¹ All values are $\bar{x} \pm$ SD. Apo, apolipoprotein; AI-LpAI, apo A-I in particles containing only apo A-I; AI-LpAII, apo A-I in particles containing both apo A-I and apo A-II; Lp(a), lipoprotein(a); TC, total cholesterol; LDL-C, LDL cholesterol; VLDL-C, VLDL cholesterol; HDL-C, HDL cholesterol; TG, triacylglycerol. Statistical analysis of TG and Lp(a) was conducted on log-transformed data. Values in a row with different superscript letters are significantly different, $P < 0.05$ (repeated-measures ANOVA with post hoc Tukey's test).

end of the diet phases with soybean, partially hydrogenated soybean, and palm oils were compared. To evaluate the effect of degree of saturation, data generated at the end of the diet phases with soybean, palm, and canola oils were compared.

Palm, partially hydrogenated soybean, and soybean oils

Total cholesterol concentrations at the end of the diet phase with soybean oil were significantly lower than after the diet phases with partially hydrogenated soybean oil and palm oil (7% and 9%, respectively; $P < 0.05$ for both; **Table 4**). Similarly, LDL-cholesterol concentrations were 12% and 14% higher after the diet phases with partially hydrogenated soybean oil and palm oil than at the end of the diet phases with soybean oil, respectively ($P < 0.05$ for both). No significant difference was observed between palm oil and partially hydrogenated soybean oil or soybean oil on concentrations of triacylglycerol, VLDL cholesterol, HDL cholesterol, or HDL subfractions with the exception of HDL3 cholesterol, which was highest after the participants consumed the diet enriched with palm oil ($P < 0.05$). Total:HDL cholesterol was not significantly different at the end of the dietary phases in a comparison of the partially hydrogenated soybean, soybean, and palm oil phases. Similar to the response in LDL cholesterol, palm oil consumption resulted in apolipoprotein B concentrations that were 11% higher ($P < 0.05$) than at the end of the soybean oil phase (Table 4). In accordance with the response of HDL cholesterol, apolipoprotein A-I concentrations were 7% and 5% higher after the palm oil phase than after the diet phases with partially hydrogenated soybean oil and soybean oil, respectively ($P < 0.05$; Table 4). The lack of statistical differences in the LDL cholesterol-to-apolipoprotein B and HDL cholesterol-to-apolipoprotein A-I ratios suggests little effect of dietary fat type on particle composition. No significant differences in lipoprotein(a) concentrations or the distribution of apolipoprotein A-I in particles containing only apolipoprotein A-I or both apolipoprotein A-I and apolipoprotein A-II were observed

as a result of consumption of diets enriched in palm, partially hydrogenated soybean, and soybean oils.

Indicators of HDL metabolism and glucose homeostasis were not significantly different when palm oil was compared with partially hydrogenated soybean oil and soybean oil (**Table 5**). The diet with partially hydrogenated soybean oil resulted in a significantly higher concentration of insulin and HOMA value than did the diet with soybean oil ($P < 0.05$). No significant differences in insulin concentration and HOMA values were observed at the end of the diet phases with partially hydrogenated soybean oil and palm oil. Mean plasma glucose concentrations were not significantly different between the diet phases. At the end of the diet phases with partially hydrogenated soybean, soybean, and palm oils, systolic blood pressures were 119 ± 15 , 123 ± 14 , and 120 ± 12 mm Hg and diastolic blood pressures were 76 ± 8 , 77 ± 8 , and 72 ± 9 mm Hg, respectively, and were not significantly different.

Palm, soybean, and canola oils

Total and LDL-cholesterol concentrations were significantly higher after the participants consumed the palm oil diet than either the soybean oil (9% and 14% higher, respectively; $P < 0.05$) or canola oil (14% and 18% higher, respectively; $P < 0.05$) diets (Table 4). No significant effect on concentrations of VLDL cholesterol, HDL cholesterol, or triacylglycerols was observed for fat type. Although HDL-cholesterol concentrations were not significantly different, significant differences were observed in both the HDL2 and HDL3 subfractions. HDL2 cholesterol was 26% higher after the consumption of soybean oil than canola oil ($P < 0.05$). HDL3 cholesterol was 8% higher after the palm oil phase than after the soybean oil phase ($P < 0.05$). Apolipoprotein A-I concentrations were significantly higher after the participants consumed the diet enriched with palm oil than after the diets enriched with soybean (5%; $P < 0.05$) or canola (6%; $P < 0.05$) oils. These differences appeared to be primarily in the



TABLE 5

Markers of HDL and glucose metabolism at the end of each diet phase¹

	Partially hydrogenated soybean	Soybean	Palm	Canola
FER _{HDL} (%/h)	18.1 ± 3.9	18.4 ± 6.0	20.4 ± 5.9	19.7 ± 6.4
CETP (nmol · h ⁻¹ · L ⁻¹)	14.3 ± 4.5	14.6 ± 5.4	16.3 ± 5.1	13.7 ± 3.5
PLTP (μmol · h ⁻¹ · L ⁻¹)	5707 ± 2136	5343 ± 2356	5515 ± 1777	5544 ± 1312
Paraoxonase (μmol/min)	306 ± 234	330 ± 233	297 ± 208	288 ± 177
Insulin (μU/mL)	11.51 ± 4.16 ^a	9.62 ± 3.76 ^b	10.54 ± 3.78 ^{a,b}	9.31 ± 3.48 ^b
Glucose (mg/dL)	89.9 ± 8.0	87.6 ± 7.7	90.6 ± 10.8	88.3 ± 8.5
HOMA	2.56 ± 0.97 ^a	2.05 ± 0.79 ^b	2.36 ± 0.92 ^{a,b}	2.00 ± 0.71 ^b

¹ All values are $\bar{x} \pm SD$. $n = 15$. CETP, cholesteryl ester transfer protein; FER_{HDL}, HDL-cholesterol fractional esterification rate; HOMA, homeostatic model assessment; PLTP, phospholipid transfer protein. Statistical analysis of CETP activity and HOMA was conducted on log-transformed data. Values in a row with different superscript letters are significantly different, $P < 0.05$ (repeated-measures ANOVA with post hoc Tukey's test).

apolipoprotein A-I and A-II particles, although the differences in this lipoprotein subfraction were not statistically significant. Consistent with the differences in LDL cholesterol, apolipoprotein B concentrations were significantly higher at the conclusion of the diet phase with palm oil than after the diet phases with soybean (11%; $P < 0.05$) and canola (12%; $P < 0.05$) oils. These differences resulted in LDL cholesterol:apolipoprotein B and HDL cholesterol:apolipoprotein A-I that were not significantly different at the end of each diet phase, suggesting a lack of difference in particle composition. No significant differences in total:HDL cholesterol were observed between the diets enriched with palm, canola, and soybean oils. No significant differences in lipoprotein(a) concentrations were observed from diets enriched in palm, soybean, and canola oils.

No significant effect of the different dietary fats on plasma FER_{HDL}, CETP, PLTP, or paraoxonase activities (Table 5) was observed. Similarly, insulin and glucose concentrations and HOMA values were not significantly different between diet phases. At the end of the diet phases with soybean, palm, and canola oils, systolic blood pressures were 123 ± 14 , 120 ± 12 , and 120 ± 13 mm Hg and diastolic blood pressures were 77 ± 8 , 72 ± 9 , and 72 ± 9 mm Hg, respectively, and were not significantly different.

DISCUSSION

It is now recognized that the type of dietary fat has a greater effect on CVD risk than does the amount of fat, and that this is, at least in part, due to the hypercholesterolemic effect of *trans* and saturated fatty acids (9, 10), which are both associated with an elevated CVD risk (7, 40, 41). Accordingly, the Food and Drug Administration has ruled that the *trans* fatty acid content of packaged foods marketed in the United States must appear on the Nutrition Facts panel by 1 January 2006. As a consequence, because of similar functional characteristics the questions arises as to whether palm oil would be a preferable substitute for partially hydrogenated fat. The present study was designed to compare the effects of palm, partially hydrogenated soybean, canola, and soybean oils on CVD risk factors.

The results suggest that, compared with canola oil or soybean oil, both partially hydrogenated soybean oil and palm oil elevate concentrations of LDL cholesterol and apolipoprotein B to a similar extent in moderately hypercholesterolemic persons. Consistent with the results of the present study, palm oil was reported to have a hypercholesterolemic effect similar to that of other

saturated fats when compared with oils rich in monounsaturated or polyunsaturated fatty acids (42–46), including high oleic or linoleic acid safflower oils (42), sunflower oil (45), and high oleic acid sunflower oil (46). However, some reports have questioned this observation in humans (12, 47–50). Palm oil has a relatively low proportion of lauric (12:0) and myristic (14:0) acids and a high proportion of palmitic acid compared with other tropical oils (ie, coconut and palm kernel oils) (12). In isolation, palmitic acid is less cholesterolemic than are lauric and myristic acids (15, 51–54). Nonetheless, regardless of the potential differential effects of individual saturated fatty acids, relative to those of either soybean or canola oil, palm oil has an adverse effect on plasma lipoprotein profiles. Exceptions to this observation are usually attributable to differences in the study population, eg, focusing on normocholesterolemic adolescent males rather than on persons who may be more responsive to dietary intervention such as moderately hypercholesterolemic persons (47).

Previous data on the effects of *trans* fatty acid-containing fats compared with saturated fats on the lipoprotein profile are consistent with the present observations (44, 55). Consumption of a palm oil-based margarine or partially hydrogenated soybean oil-based margarine resulted in comparable LDL-cholesterol concentrations, both of which were higher than with a margarine high in polyunsaturated fatty acids (44). A study that compared a solid fat high in lauric acid with one rich in *trans* fatty acids reported a smaller hypercholesterolemic effect of saturated fatty acids than of *trans* fatty acids (55). Although no differences in LDL-cholesterol concentrations were reported, the higher total cholesterol concentrations after consumption of the high lauric acid fat were caused by higher HDL-cholesterol concentrations.

The present intervention resulted in small changes in the cholesterol content of HDL subfractions. These results are not consistent with previous observations in which consumption of saturated fat as butter resulted in higher concentrations of HDL2 cholesterol than with consumption of hydrogenated fat (56). However, the fatty acid composition of the individual fats used is different from those previously studied. Moreover, the implications of these findings are the subject of debate. Although an inverse association between CVD risk and HDL3 cholesterol was documented (57), it was also suggested that the redistribution of cholesterol in HDL subfractions does not provide additional cardioprotective effect compared with an increase in HDL cholesterol (58–60). The differences in total:HDL cholesterol


observed are consistent with a previous meta-analysis (15). Mensink et al (15) calculated $\approx 0.14-0.15$ higher total:HDL cholesterol for diets high in soybean oil than for those high in palm oil and partially hydrogenated fat. It should be noted that the statistical power for this study was based on LDL cholesterol, not on total:HDL cholesterol.

Plasma fatty acid profiles reflect short-term dietary intake of fatty acids (61, 62) and can provide an indication of dietary compliance. The fatty acid profile in the plasma lipid fractions (triacylglycerols, phospholipids, and cholesteryl ester), for the most part, reflected the compositional differences of the experimental fats. Consistent with previous reports, the dietary fatty acid composition was reflected more strongly in the triacylglycerol and phospholipid subfractions than in the cholesteryl ester subfraction (29, 63). A higher percentage of plasma EPA, but not of DHA or arachidonic acid, occurred after consumption of the linolenic acid-rich oils (soybean or canola) than of the other fats. This finding was somewhat unexpected, given the low capacity humans have for the conversion of α -linolenic acid to EPA (64). Nonetheless, findings from one study indicated an inverse association between concentrations of n-3 fatty acids in the phospholipid fraction (EPA and DHA combined) and the risk of fatal ischemic heart disease (65). Because of the small magnitude of the differences and lack of an effect on DHA, it is unlikely that these differences would contribute to risk modifications for ischemic heart disease as observed in this data set.

In the present study, both insulin concentration and the HOMA ratio, but not glucose concentrations, were higher after the participants consumed the diet with partially hydrogenated soybean oil than the diets enriched with soybean and canola oils. This pattern suggests a potential effect of this fat on insulin sensitivity. Although epidemiologic data suggested a relation between intake of *trans* fatty acid and risk of type 2 diabetes (66), in general, the clinical data have not supported this relation between *trans* fatty acids and indicators of glucose homeostasis (67-71). The differences resulting from substituting one type of fat for another were small, albeit significant, and this should be taken into consideration when interpreting the data.

Limitations of the present study include lack of generalizability because study participation was restricted to older moderately hypercholesterolemic subjects. However, dietary guidance to modify CVD risk factors is most clinically important for this group of persons. Differences in lipoprotein patterns could not be attributed to a specific fatty acid or pair of fatty acid substitutions resulting from the use of oils varying in a multiple as opposed to single fatty acids. The present study was designed to assess the effect of fat with distinct fatty acid profiles as actually consumed, not to distinguish the effects of individual fatty acids. The measures reported were restricted to intermediate markers of CVD risk. Only one type of partially hydrogenated fat was assessed; functional properties of this product may not be comparable with those of palm oil. Another limitation of the present study is that in some cases there were small shifts toward an increased risk, but of a rather modest magnitude. As noted, caution needs to be exercised in interpreting these data. Lacking at this time is an algorithm that can be applied to assess the cumulative effect of all indicators of CVD risk.

The present findings suggest that consumption of diets enriched with equivalent amounts of palm oil and partially hydrogenated soybean oil result in similar and less favorable concentrations of LDL cholesterol and apolipoprotein B than does

consumption of diets enriched with unsaturated fatty acids, either monounsaturated or polyunsaturated. In practice, it is unclear whether achieving similar levels of functional characteristics in foods would require identical amounts of these 2 fats. At the levels fed, the response to dietary fats relatively high in monounsaturated and polyunsaturated fatty acids was comparable. Differences in other CVD risk factors, HDL metabolism, and glucose homeostasis between the fats assessed were small. These results do not suggest that palm oil would be a good substitute by the food industry for partially hydrogenated fat if equivalent amounts need to be used and further suggest that reliance on oils relatively high in monounsaturated and polyunsaturated fatty acids would be a preferable alternative to both. 

We thank M Jauhiainen for the CETP, PLTP, and paraoxonase measures (National Public Health Institute, Helsinki, Finland) and J Frölich for the measurement of FER_{HDL} (Atherosclerosis Specialty Laboratory, Department of Pathology and Laboratory Medicine, UBC, Vancouver, Canada). The cooperation of the study participants is gratefully acknowledged.

SV-L was involved with data interpretation and manuscript preparation. LMA performed the statistical analysis and helped with interpretation of results. SMJ performed the lipid, lipoprotein, and apolipoprotein measurements. ATE performed the fatty acid analysis. AHL designed and conducted the intervention and supervised the project and manuscript preparation. None of the authors had any advisory board affiliations or financial interests in any organization sponsoring the research.

REFERENCES

1. Krauss RM, Eckel RH, Howard B, et al. AHA Scientific Statement: AHA Dietary Guidelines: Revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *J Nutr* 2001;131:132-46.
2. NCEP Expert Panel. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
3. McGandy RB, Hegsted DM, Myers ML. Use of semisynthetic fats in determining effects of specific dietary fatty acids on serum lipids in man. *Am J Clin Nutr* 1970;23:1288-98.
4. Keys A, Anderson JT, Grande F. Serum cholesterol response to change in the diet. *Metabolism* 1965;14:747-58.
5. USDA, Economic Research Service. Food Consumption (Per Capita) Data System. Food Availability. Updates 1 February 2004. Internet: <http://www.ers.usda.gov/data/foodconsumption/foodavailindex.htm> (accessed 14 December 2005).
6. Kromhout D, Menotti A, Bloemberg B, et al. Dietary saturated and *trans* fatty acids and cholesterol and 25-year mortality from coronary heart disease: the Seven Countries Study. *Prev Med* 1995;24:308-15.
7. Hu FB, Stampfer MJ, Manson JE, et al. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 1997;337:1491-9.
8. Clarke R, Frost C, Collins R, Appleby P, Peto R. Dietary lipids and blood cholesterol: quantitative meta-analysis of metabolic ward studies. *BMJ* 1997;314:112-7.
9. Mensink RP, Katan MB. Effect of dietary *trans* fatty acids on high density and low density lipoprotein cholesterol levels in healthy subjects. *N Engl J Med* 1990;323:439-45.
10. Lichtenstein AH, Ausman LM, Jalbert SM, Schaefer EJ. Effects of different forms of dietary hydrogenated fats on serum lipoprotein cholesterol levels. *N Engl J Med* 1999;340:1933-40.
11. Ash M, Dohlan E. Oil crops situation and outlook yearbook/OCS-2005/March 2005. Washington, DC: Market and Trade Economics Division, Economic Research Service, US Department of Agriculture, 2005:91.
12. Edem DO. Palm oil: biochemical, physiological, nutritional, hematological, and toxicological aspects: a review. *Plant Foods Hum Nutr* 2002;57:319-41.
13. USDA/Agricultural Research Service, Nutrient Data Laboratory. USDA National Nutrient Database for Standard Reference, Release 18. Updated 23 September 2005. Internet: <http://www.nal.usda.gov/food-comp> (accessed 30 November 2005).



14. Allison DB, Egan SK, Barraj LM, Caughman C, Infante M, Heimbach JT. Estimated intakes of *trans* fatty and other fatty acids in the US population. *J Am Diet Assoc* 1999;99:166–74.
15. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003;77:1146–55.
16. Judd JT, Clevidence BA, Muesing RA, Wittes J, Sunkin ME, Podczasy JJ. Dietary *trans* fatty acids: effects on plasma lipids and lipoproteins of healthy men and women. *Am J Clin Nutr* 1994;59:861–8.
17. Clevidence BA, Judd JT, Schaefer EJ, et al. Plasma (a) levels in men and women consuming diets enriched in saturated, *cis*-, or *trans*-monounsaturated fatty acids. *Arterioscler Thromb Vasc Biol* 1997;17:1657–61.
18. Judd JT, Baer DJ, Clevidence BA, et al. Effects of margarine compared with those of butter on blood lipid profiles related to cardiovascular disease risk factors in normolipemic adults fed controlled diets. *Am J Clin Nutr* 1998;68:768–77.
19. Lichtenstein AH, Ausman LM, Carrasco WV, et al. Rice bran oil consumption and plasma lipid levels in moderately hypercholesterolemic humans. *Arterioscler Thromb* 1994;14:549–56.
20. Lichtenstein AH, Ausman LM, Jalbert SM, et al. Efficacy of a Therapeutic Lifestyle Change/Step 2 diet in moderately hypercholesterolemic middle-aged and elderly female and male subjects. *J Lipid Res* 2002;43:264–73.
21. Havel RJ, Eder HA, Bragdon JH. Distribution and chemical composition of ultracentrifugally separated lipoproteins in human serum. *J Clin Invest* 1955;34:1345–53.
22. McNamara JR, Schaefer EJ. Automated enzymatic conventionalized lipid analyses for plasma and lipoprotein fractions. *Clin Chim Acta* 1987;166:1–8.
23. Warnick GR, Bederson J, Alberts JJ. Dextran sulfate-Mg²⁺ precipitation procedure for quantitation of high density lipoprotein cholesterol. *Clin Chem* 1982;28:1379–88.
24. Nguyen T, Warnick GR. Improved methods for separation of total HDL and subclasses. *Clin Chem* 1989;35:1086–94.
25. Contois JH, McNamara JR, Lammi-Keefe CJ, Wilson PWF, Massov T, Schaefer EJ. Reference intervals for plasma apolipoprotein B determined with a conventionalized reformulated immunoturbidimetric assay: results from the Framingham Offspring Study. *Clin Chem* 1996;42:515–23.
26. Contois JH, McNamara JR, Lammi-Keefe CJ, Wilson PWF, Massov T, Schaefer EJ. Reference intervals for plasma apolipoprotein A-I determined with a standardized commercial immunoturbidimetric assay: results from the Framingham Offspring Study. *Clin Chem* 1996;42:507–14.
27. Parra HJ, Mezdoor H, Ghalim N, Bard J-M, Fruchart J-C. Differential electroimmunoassay of human Lp A-I lipoprotein particles on ready-to-use plates. *Clin Chem* 1990;36:1431–5.
28. Jenner JL, Ordovas JM, Lamon-Fava S, et al. Effects of age, sex, and menopausal status on plasma lipoprotein (a) levels. The Framingham Offspring Study. *Circulation* 1993;87:1135–41.
29. Vidgren HM, Louheranta AM, Agren JJ, Schwab US, Uusitupa MI. Divergent incorporation of dietary *trans* fatty acids in different serum lipid fractions. *Lipids* 1998;33:955–62.
30. Morgan CR, Lazarow A. Immunoassay of insulin: two antibody system. Plasma insulin levels in normal, subdiabetic, and diabetic rats. *Diabetes* 1963;12:115–26.
31. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β -cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–9.
32. Wallace TM, Matthews DR. The assessment of insulin resistance in man. *Diabet Med* 2002;19:527–34.
33. Dobiášová M, Frohlich JJ. Assays of lecithin cholesteryl acyltransferase (LCAT). In: Ordovas JM, ed. *Lipoprotein protocols*. Totowa, NJ: Humana Press, 1998:217–30.
34. Dobiášová M, Frohlich JJ. Understanding the mechanism of LCAT reaction may help to explain the high predictive value of LDL/HDL cholesterol. *Physiol Res* 1998;47:387–97.
35. Groener JEM, Pelton RW, Kostner GM. Improved estimation of cholesteryl ester transfer/exchange activity in serum or plasma. *Clin Chem* 1986;32:283–6.
36. Damen J, Regts J, Scherphof G. Transfer of (¹⁴C) phosphatidylcholine between liposomes and human plasma high density lipoprotein. Partial purification of a transfer-stimulating plasma factor using a rapid transfer assay. *Biochim Biophys Acta* 1982;712:444–52.
37. Jauhiainen M, Metso J, Pahlman R, Blomqvist S, Van Tol A, Ehnholm C. Human plasma phospholipid transfer protein causes high density lipoprotein conversion. *J Biol Chem* 1993;268:4032–6.
38. Pussinen P, Jauhiainen M, Metso J, Tyynelä J, Ehnholm C. Pig plasma phospholipid transfer protein facilitates HDL interconversion. *J Lipid Res* 1995;36:975–85.
39. Gan KN, Smolen A, Eckerson HW, La Du BN. Purification of human serum paraoxonase/arylesterase. Evidence for one esterase catalyzing both activities. *Drug Metab Dispos* 1991;19:100–6.
40. Hu FB, Manson JE, Willett WC. Types of dietary fat and risk of coronary heart disease: a critical review. *J Am Coll Nutr* 2001;20:5–19.
41. Lichtenstein AH. Dietary fat and cardiovascular disease risk: quantity or quality? *J Womens Health* 2003;12:109–14.
42. Mattson F, Grundy S. Comparison of effects of dietary saturated, mono-unsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J Lipid Res* 1985;26:194–202.
43. Denke MA, Grundy SM. Comparison of effects of lauric acid and palmitic acid on plasma lipids and lipoproteins. *Am J Clin Nutr* 1992;56:895–8.
44. Müller H, Jordal O, Kierulf P, Kirkhus B, Pedersen JJ. Replacement of partially hydrogenated soybean oil by palm oil in margarine without unfavorable effects on serum lipoproteins. *Lipids* 1998;33:879–87.
45. Bautista LE, Herrán OF, Serrano C. Effects of palm oil and dietary cholesterol on plasma lipoproteins: results from a dietary crossover trial in free-living subjects. *Eur J Clin Nutr* 2001;55:748–54.
46. Cater NB, Heller HJ, Denke MA. Comparison of the effects of medium-chain triacylglycerols, palm oil, and high oleic acid sunflower oil on plasma triacylglycerol fatty acids and lipid and lipoprotein concentrations in humans. *Am J Clin Nutr* 1997;65:41–5.
47. Marzuki A, Arshad F, Razak TA, Jaarin K. Influence of dietary fat on plasma lipid profiles of Malaysian adolescents. *Am J Clin Nutr* 1991;53(suppl):1010S–4S.
48. Choudhury N, Tan L, Truswell AS. Comparison of palmolein and olive oil: effects on plasma lipids and vitamin E in young adults. *Am J Clin Nutr* 1995;61:1043–51.
49. Zhang J, Ping W, Chunrong W, Shou CX, Keyou G. Nonhypercholesterolemic effects of a palm oil diet in Chinese adults. *J Nutr* 1997;127:509S–13S.
50. Zhang J, Wang CR, Xue AN, Ge KY. Effects of red palm oil on serum lipids and plasma carotenoid levels in Chinese male adults. *Biomed Environm Sci* 2003;16:348–54.
51. Hayes KC, Pronczuk A, Lindsey S, Diersen-Schade D. Dietary saturated fatty acids (12:0, 14:0, 16:0) differ in their impact on plasma cholesterol and lipoproteins in nonhuman primates. *Am J Clin Nutr* 1991;53:491–8.
52. Khosla P, Hajri T, Pronczuk A, Hayes KC. Decreasing dietary lauric and myristic acids improves plasma lipids more favorably than decreasing dietary palmitic acid in rhesus monkeys fed AHA step I type diets. *J Nutr* 1997;127:525S–30S.
53. Sundram K, Hayes KC, Siru OH. Dietary palmitic acid results in lower serum cholesterol than does a lauric-myristic acid combination in normolipemic humans. *Am J Clin Nutr* 1994;59:841–6.
54. Tholstrup T, Marckmann P, Jespersen J, Sandstrom B. Fat high in stearic acid favorably affects blood lipids and factor VII coagulant activity in comparison with fats high in palmitic acid or high in myristic and lauric acids. *Am J Clin Nutr* 1994;59:371–7.
55. de Roos NM, Schouten EG, Katan MB. Consumption of a solid fat rich in lauric acid results in a more favorable serum lipid profile in healthy men and women than consumption of a solid fat rich in *trans*-fatty acids. *J Nutr* 2001;131:242–5.
56. Lichtenstein AH, Jauhiainen M, McGladdery S, et al. Impact of hydrogenated fat on high density lipoprotein subfractions and metabolism. *J Lipid Res* 2001;42:597–604.
57. Yu S, Yarnell JWG, Sweetnam P, Bolton CH. High density lipoprotein subfractions and the risk of coronary heart disease: 9-years follow-up in the Caerphilly Study. *Atherosclerosis* 2003;166:331–8.
58. Gardner CD, Tribble DL, Young DR, Ahn D, Fortmann SP. Associations of HDL, HDL2, and HDL3 cholesterol and apolipoproteins A-I and B with lifestyle factors in healthy women and men: the Stanford Five City Project. *Prev Med* 2000;31:346–56.
59. Morgan JM, Carey C, Lincoff A, Capuzzi DM. High-density lipoprotein

- subfractions and risk of coronary artery disease. *Curr Atheroscler Rep* 2004;6:359–65.
60. Sharrett AR, Ballantyne CM, Coady SA, et al. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: the Atherosclerosis Risk in Communities (ARIC) Study. *Circulation* 2001;104:1108–13.
 61. Mensink RP, Hornstra G. The proportion of *trans* monounsaturated fatty acids in serum triacylglycerols or platelet phospholipids as an objective indicator of their short-term intake in healthy men. *Br J Nutr* 1995;73:605–12.
 62. Raatz SK, Bibus D, Thomas W, Kris-Etherton PM. Total fat intake modifies plasma fatty acid composition in humans. *J Nutr* 2001;131:231–4.
 63. Lichtenstein AH, Erkkilä AT, Lamarche B, Schwab US, Jalbert SM, Ausman LM. Influence of hydrogenated fat and butter on CVD risk factors: remnant-like particles, glucose and insulin, blood pressure and C-reactive protein. *Atherosclerosis* 2003;171:97–107.
 64. Goyens PLL, Spilker ME, Zock PL, Katan MB, Mensink RP. Compartmental modeling to quantify α -linolenic acid conversion after longer term intake of multiple tracer boluses. *J Lipid Res* 2005;46:1474–83.
 65. Lemaitre RN, King IB, Mozaffarian D, Kuller LH, Tracy RP, Siscovick DS. n-3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. *Am J Clin Nutr* 2003;77:319–25.
 66. Salmerón J, Hu FB, Manson JE, et al. Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr* 2001;73:1019–26.
 67. Lovejoy J, Champagne C, Smith S, et al. Relationship of dietary fat and serum cholesterol ester and phospholipid fatty acids to markers of insulin resistance in men and women with a range of glucose tolerance. *Metabolism* 2001;50:86–92.
 68. Lovejoy JC, Smith SR, Champagne CM, et al. Effects of diets enriched in saturated (palmitic), monounsaturated (oleic), or *trans* (elaidic) fatty acids on insulin sensitivity and substrate oxidation in healthy adults. *Diabetes Care* 2002;25:1283–8.
 69. Jensen J, Bysted A, Dawids S, Hermansen K, Hølmer G. The effect of palm oil, lard, and puff-pastry margarine on postprandial lipid and hormone responses in normal-weight and obese young women. *Br J Nutr* 1999;82:469–79.
 70. Vessby B, Uusitupa MI, Hermansen K, et al. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: the KANWU study. *Diabetologia* 2001;44:312–9.
 71. Louheranta AM, Turpeinen AK, Vidgren HM, Schwab US, Uusitupa MI. A high-*trans* fatty acid diet and insulin sensitivity in young healthy women. *Metabolism* 1999;48:870–5.

