

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

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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

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TABLE 1
Baseline 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 ± 10.3	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. 

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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.

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