Different Effects of Palmitic and Stearic Acid–Enriched Diets on Serum Lipids and Lipoproteins and Plasma Cholesteryl Ester Transfer Protein Activity in Healthy Young Women

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The effects of palmitic and stearic acid–enriched diets on serum lipids, lipoproteins, apolipoproteins (apo) A-I and B, and plasma cholesteryl ester transfer protein (CETP) activity were examined in 12 healthy young women. Subjects followed the two experimental diets for 4 weeks according to a randomized crossover design. Both experimental diet periods were preceded by consumption of a baseline diet for 2 weeks. The diets provided 37% of total energy intake (E%) as fat, and differed only with respect to fatty acid composition. There was a substitution of 5E% of palmitic acid or stearic acid in the experimental diets for 5E% of monounsaturated fatty acids in the baseline diet. After the palmitic acid diet, serum total and high-density lipoprotein (HDL) cholesterol and apo A-I concentrations were higher (8%, $P = .015$, 9%, $P = .040$, and 11%, $P = .011$, respectively) and mean serum low-density lipoprotein (LDL) cholesterol concentration tended to be higher (8%, $P = .077$) as compared with values after the stearic acid diet. Plasma CETP activity increased in the palmitic acid diet as compared with the stearic acid diet (12%, $P = .006$). In conclusion, palmitic acid and stearic acid–enriched diets had different effects on serum lipids and lipoproteins and also on plasma CETP activity in young healthy women.

DIETARY SATURATED fatty acids have been shown to increase serum total cholesterol,[1,2] and dietary recommendations advise a reduction of intake of saturated fat.[3,4] The effects of saturated fatty acids on serum lipids and lipoproteins are related to their chain length[1,2]; fatty acids with 10 carbon atoms or less are considered neutral with respect to lipid metabolism, and fatty acids with 14 to 16 carbon atoms (myristic and palmitic acid) are generally considered to increase serum cholesterol concentrations,[5-7] although the cholesterol-increasing effect of palmitic acid has recently been questioned.[8,9] Stearic acid (18 carbon atoms) is considered neutral with respect to serum total cholesterol or low-density lipoprotein (LDL) cholesterol,[1,5,10-13] but the effect on high-density lipoprotein (HDL) cholesterol may be different, ie, stearic acid may have a HDL-decreasing effect.

Cholesteryl ester transfer protein (CETP) transfers cholesteryl esters from HDL to apolipoprotein (apo) B–containing particles and plays an important role in the regulation of HDL cholesterol concentration.[14] The relative rate of transfer has been found to be affected by the fatty acid composition of cholesteryl esters.[15,16] A monounsaturated fat–enriched diet and a fish oil–enriched diet have been shown to decrease plasma CETP activity as compared with a polyunsaturated fat–enriched diet,[17,18] but the effects of individual fatty acids on plasma CETP activity are unclear.

The aim of this study was to examine the effects of palmitic acid (C16:0) and stearic acid (C18:0), two common saturated fatty acids in the Western diet, on serum lipids, lipoproteins, apo A-I, apo B, and plasma CETP activity in young healthy women.

SUBJECTS AND METHODS

Subjects

Twelve healthy female volunteers aged 20 to 31 years participated in this study. All had normal body weight: body mass index ranged from 19 to 25 kg/m^2. None of the subjects were taking medication known to affect lipid metabolism, and all had normal liver, kidney, and thyroid function and were nonsmokers. Six subjects used low-estrogen oral contraceptives during the study. Initially, 13 women were recruited for the study, but one was excluded because of an elevated concentration of a liver enzyme. Baseline characteristics of the subjects are shown in Table 1.

Subjects provided informed consent for the study, and the study plan was approved by the Ethics Committee of the University of Kuopio.

Study Design

All subjects consumed both a palmitic acid–enriched diet (palmitic diet) and a stearic acid–enriched diet (stearic diet) for 4 weeks according to a randomized crossover study design. Six subjects were on the palmitic diet during the first dietary period and six were on the stearic diet. There were 2-week run-in and wash-out periods, with a baseline diet preceding the experimental diet periods. Routine hematological measurements, as well as liver enzymes and serum creatinine, were analyzed before beginning the study. Samples for determination of serum lipids, lipoproteins, apo A-I, apo B, and fatty acid composition of serum cholesteryl esters were taken after a 12-hour fast at the beginning and end of both experimental diet periods. Plasma CETP activity was analyzed from samples drawn at the end of the run-in period and at the end of both experimental diet periods. Body weight and blood pressure were measured at 2-week intervals.

Experimental Diets

Both experimental diets and the baseline diet supplied 37% of total energy intake (E%) as fat, 49E% as carbohydrate, and 14E%

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Table 1. Baseline Characteristics of the Subjects (N = 12)

Characteristic	Mean ± SEM
Age (yr)	23.5 ± 0.9
Body weight (kg)	61.5 ± 2.3
Body mass index (kg/m^2)	22.1 ± 0.7
Serum lipids (mmol/L)	
Total cholesterol	4.21 ± 0.17
HDL cholesterol	1.44 ± 0.06
LDL cholesterol	2.40 ± 0.13
VLDL cholesterol	0.38 ± 0.06
Total triglycerides	0.96 ± 0.14

as protein. Cholesterol content was approximately 25 mg/MJ, and dietary fiber content approximately 4 g/MJ. Fatty acid composition of the baseline diet was 15E% from saturated, 15E% from monounsaturated, and 5E% from polyunsaturated fatty acids. During both experimental diet periods, fatty acid composition was 15E% saturated fatty acids and 5E% additional palmitic acid or stearic acid, 10E% monounsaturated fatty acids, and 5E% polyunsaturated fatty acids.

Refined palm oil and butter were used as a source of palmitic acid (22 to 33 g/d palm oil and 10 to 15 g/d butter, lowest to highest level of energy intake). Cocoa butter was used as a source of stearic acid (28 to 40 g/d cocoa butter). Both diets contained a small amount of soybean oil (2 to 5 g/d in the palmitic diet and 6 to 9 g/d in the stearic diet). During the baseline diet, a spread of butter and low–erucic acid rapeseed oil (80% of total fat as butter and 20% as rapeseed oil) was used as a main source of fat (25 to 40 g/d) together with olive oil (12 to 16 g/d) and a small amount of sunflower oil (2 to 3 g/d). These vegetable oils were used in addition to the main fat sources to obtain a constant content of linoleic and α-linolenic acids in the diets. Medium-fat dairy products were consumed during all diet periods. Because the baseline diet included some milk fat, and as a result more dietary cholesterol than other diets in this study, egg yolk (4 to 5 g/d) was added to the experimental diets to keep the intake of dietary cholesterol constant during the whole study. Except for palm oil and cocoa butter, the diets were composed of common Finnish foodstuffs. The subjects received fat products, vegetable oils, and dairy products free of charge. This together with frequent dietary counseling promoted good compliance.

The diets were calculated for four levels of energy intake: 5.9, 6.7, 7.5, and 8.4 MJ (1,400, 1,600, 1,800 and 2,000 kcal, respectively). The energy requirement of the subjects was estimated by 3-day food records kept before the study. Subjects received detailed written instructions about the diets, specifying the amounts of individual foodstuffs by main food groups (fat, dairy products, cereals, vegetables and roots, fruit and berries, meat and meat products, as well as sugar and sweets). It was stressed that the subjects should maintain a stable body weight and unchanged exercise habits during the study.

To assess dietary compliance, subjects kept 7-day food records (5 weekdays and 2 weekend days) during both experimental diets. During the baseline diet periods (run-in and wash-out periods), 3-day food records (2 weekdays and 1 weekend day) were kept. Subjects were asked to weigh food items on a digital scale before consumption whenever possible. For situations in which weighing would not have been possible, subjects received both oral and written instructions with pictures to help estimate portion sizes. Determination of fatty acid composition of serum cholesteryl esters was used as an objective indicator of compliance with the experimental diets during the study.

Diets were planned and nutrients in food records were calculated using the Micro-Nutrica dietary analysis program based on the database of the Finnish Social Insurance Institute. Food composition tables were based on values obtained from Finnish food analyses and values taken from international food composition tables.[19]

Laboratory Methods

To remove the very–low-density lipoprotein (VLDL) fraction, serum samples were centrifuged for 18 hours at 105,000× *g* and 4°C. HDL in the infranatant was separated from LDL by precipitation of LDL with dextran sulfate and magnesium chloride.[20] LDL cholesterol was calculated as the difference between the mass of cholesterol in the infranatant and HDL. Enzymatic colorimetric methods were used for determination of cholesterol and triglycerides from whole serum and lipoprotein lipids using commercial kits (Monotest Cholesterol and Triglyceride GPO-PAP; Boehringer, Mannheim, Germany) with an automated instrument (Kone Specific Clinical Analyzer; Kone, Espoo, Finland). In analysis of total cholesterol the coefficient of variation between measurements using two different standards was 1.16% to 1.57%, and in analysis of total triglycerides it was 0.02% to 1.75%. In HDL cholesterol analysis the coefficient of variation was 1.43% to 1.87% (three different standards), and in analysis of HDL triglycerides it was 2.13% (one standard).

Serum samples for determination of apo A-I and apo B were stored at −70°C until analyzed at the end of the study. Analyses were based on the measurement of immunoprecipitation enhanced by polyethylene glycol at 340 nm.[21] The Kone Specific Clinical Analyzer and ApoA-I and ApoB reagents from Orion Diagnostica (Espoo, Finland) were used in the analyses. In apo A-I analysis the coefficient of variation within the measurement was 3.28% to 4.83%, and in apo B analysis it was 1.73% to 2.82% (two standards).

CETP activity in plasma samples was determined as previously described.[22,23] LDL and HDL, used for measurement of CETP activity, were isolated from plasma of healthy controls by sequential ultracentrifugation. Plasma was adjusted to density 1.019 g/mL with a NaCl-NaBr solution and centrifuged in a Beckman Ti60 rotor (Beckman Instruments, Palo Alto, CA) at 160,000 × *g* and 15°C for 18 hours. VLDL and intermediate-density lipoprotein in the supernatant were removed by tube-slicing, and the infranatant was adjusted to 1.063 g/mL to isolate the LDL fraction (d = 1.019 to 1.063 g/mL). The density of the infranatant was increased to 1.090 g/mL, and it was centrifuged as above for 24 hours. The surface layer, a mixture of light HDL particles and apo B–containing particles such as lipoprotein(a), was discarded. The infranatant was then adjusted to 1.210 g/mL, and the HDL fraction (d = 1.090 to 1.210 g/mL) was isolated after centrifugation for 48 hours. Finally, LDL and HDL fractions were reisolated at densities 1.070 and 1.210 g/mL, respectively, and dialyzed against 0.15 mol/L NaCl–1 nmol/L EDTA, pH 7.4.

The LDL fraction isolated from the plasma of healthy volunteers was labeled with [1,2(*n*)-^{3}H]-cholesteryl oleate[24] and reisolated by ultracentrifugation. ApoB–containing lipoproteins in the subjects' plasma samples were precipitated with polyethylene glycol. Aliquots of the supernatant were incubated in triplicate at 37°C with labeled LDL and unlabeled HDL (also isolated from the plasma of volunteers). After incubation for 12 hours, the tubes were cooled on crushed ice and bovine serum albumin and carrier LDL were added. LDL was precipitated with $MgCl_2$–dextran sulfate, and an aliquot of the supernatant was counted for radioactivity in a scintillation counter.

The CETP assay measures the exchange of cholesteryl esters between LDL and HDL. The same activity was observed when labeled HDL was used as the substrate.[24] In the assay, the maximal capacity of cholesteryl ester exchange is measured. This accurately

reflects the concentration of CETP protein in plasma.[22] Intraassay and day-to-day variations of the method are 4.0% and 6.6%, respectively.[24]

In the analysis of fatty acid composition of serum cholesteryl esters, serum samples were extracted with chloroform methanol (2:1) and lipid classes were separated by solid-phase extraction with an aminopropyl column.[25] Fatty acids were analyzed by the Carlo Erba Vega 6130 gas chromatograph (Carlo Erba Instruments, Milan, Italy) equipped with an NB-351 silica capillary column (HNU-Nordion, Helsinki, Finland).

Statistical Analysis

The data were analyzed with the SPSS/PC+ statistical program.[26] Before further analyses, normal distribution of the variables was checked with the Kolmogorov-Smirnov test. An ANOVA for repeated measurements[27] was performed to assess whether there was any carryover effect and to test if there were changes in variables with time. When the analysis indicated that the overall change in a variable with time was significant ($P < .05$), paired t tests were used for two-tailed comparisons. Comparisons within the diet periods were performed by comparing the results at 4 weeks with the results at 0 weeks (ie, at the end of the preceding baseline diet period). Comparisons between the palmitic diet and the stearic diet were made by comparing results at the 4-week time point. Bonferroni adjustment was used to control the overall α level. All data are expressed as the mean ± SEM.

RESULTS

Dietary Compliance

There were no changes in body weight during the palmitic diet (61.2 ± 2.3 *v* 61.2 ± 2.4 kg, beginning *v* end of diet). During the stearic diet, body weight marginally decreased by a mean of 0.4 kg (61.1 ± 2.3 *v* 60.7 ± 2.3 kg, $P = .021$).

The goals of the experimental diets were well achieved. The difference in palmitic acid content between experimental diets was 3.2E%, and for stearic acid content the difference was 4.8E%. The smaller difference in stearic acid content was due to the use of cocoa butter as a source of stearic acid; cocoa butter is also moderately rich in palmitic acid. The content of myristic acid was lowest in the stearic diet, and in the palmitic diet it was also lower than in the baseline diet. The difference between experimental diets was 0.6E%. The experimental diets provided approximately 4E% more saturated fatty acids than the baseline diet because of substitution of palmitic and stearic acids in the experimental diets for monoenes in the baseline diet. Results of food records from the diet periods are shown in Table 2.

During the stearic diet, the proportion of stearic acid in serum cholesteryl esters increased and that of α-linolenic acid decreased significantly. The proportions of myristic and palmitic acids were higher and the proportions of stearic and oleic acids were lower at the end of the palmitic acid diet as compared with the end of the stearic diet. Fatty acid compositions of serum cholesteryl esters are presented in Table 3.

Serum Lipids and Lipoproteins

The results of the statistical analysis indicated that the order of the diet periods did not affect the results of this study. The mean concentration of total cholesterol was significantly higher ($P = .015$) and those of LDL cholesterol and total triglycerides tended to be higher after the palmitic diet versus the stearic diet ($P = .077$ and $P = .066$, respectively). HDL cholesterol concentration was significantly lower after the stearic diet than after the palmitic diet ($P = .040$) (Table 4).

As compared with concentrations measured after the baseline diet, serum total and LDL cholesterol concentrations were significantly higher after the palmitic diet (12% and 15%, $P = .001$, respectively; Table 4), as was the LDL/HDL cholesterol ratio (1.63 *v* 1.84, $P = .043$). After the stearic diet, there were no significant differences in serum total or lipoprotein cholesterol or lipoprotein triglyceride concentrations as compared with values after the baseline diet. However, mean HDL cholesterol concentration tended to be lower (10%, $P = .061$), and due to this the LDL/HDL cholesterol ratio tended to be higher (1.71 *v* 1.87, $P = .129$) after the stearic acid diet than after the baseline diet.

Table 2. Energy Intake, Proportion of Energy Nutrients, and Cholesterol and Fiber Intake During the Diet Periods

Parameter	Baseline PA	Palmitic Diet	Baseline SA	Stearic Diet
Energy (kJ)	7,073 ± 226	7,367 ± 219	6,985 ± 276	7,240 ± 209
Fat (E%)	37.8 ± 0.8	37.7 ± 0.5	37.1 ± 0.7	37.8 ± 0.6
Fatty acids (E%)				
Saturated	15.4 ± 0.4	18.7 ± 0.2	15.4 ± 0.2	19.0 ± 0.4
Myristic acid	2.1 ± 0.1	1.8 ± 0.0	2.1 ± 0.1	1.2 ± 0.1
Palmitic acid	7.3 ± 0.2	11.8 ± 0.1	7.2 ± 0.1	8.5 ± 0.2
Stearic acid	2.7 ± 0.1	2.4 ± 0.0	2.7 ± 0.1	7.3 ± 0.1
Monounsaturated	14.4 ± 0.4	12.2 ± 0.2	13.7 ± 0.5	11.9 ± 0.3
Polyunsaturated	5.2 ± 0.2	4.7 ± 0.2	5.3 ± 0.3	5.0 ± 0.2
Linoleic acid	4.2 ± 0.2	4.0 ± 0.1	4.3 ± 0.3	4.1 ± 0.2
α-Linolenic acid	0.8 ± 0.0	0.5 ± 0.0	0.8 ± 0.0	0.6 ± 0.0
Carbohydrate (E%)	45.8 ± 0.8	46.5 ± 0.5	47.2 ± 0.6	46.6 ± 0.6
Protein (E%)	14.7 ± 0.3	14.3 ± 0.2	14.4 ± 0.4	14.0 ± 0.1
Cholesterol (mg/MJ)	25.6 ± 1.5	27.3 ± 0.9	25.9 ± 1.7	23.8 ± 0.7
Fiber (g/MJ)	3.9 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	3.5 ± 0.2

NOTE. Values are the mean ± SEM; N = 12.

Abbreviations: baseline PA, baseline diet period preceding the palmitic diet; baseline SA, baseline diet period preceding the stearic diet.

Table 3. Fatty Acid Composition of Serum Cholesteryl Esters (mol% of total) at the Beginning and End of the Experimental Diet Periods

Fatty Acid	Palmitic Diet 0 Weeks	Palmitic Diet 4 Weeks	P*	Stearic Diet 0 Weeks	Stearic Diet 4 Weeks
Myristic (C14:0)	1.26 ± 0.08	1.31 ± 0.09	<.05	1.38 ± 0.06	1.14 ± 0.11
Palmitic (C16:0)	11.66 ± 0.14	12.05 ± 0.23	<.05	11.72 ± 0.26	11.21 ± 0.17
Stearic (C18:0)	0.59 ± 0.04	0.60 ± 0.05	<.001	0.63 ± 0.06	0.98 ± 0.08†
Oleic (C18:1,(1)-9)	19.20 ± 0.46	19.04 ± 0.37	<.01	19.72 ± 0.55	20.09 ± 0.50
Linoleic (C18:2,(1)-6)	53.60 ± 0.81	53.58 ± 0.76		52.97 ± 1.02	53.56 ± 0.62
α-Linolenic (C18:3,(1)-3)	0.78 ± 0.04	0.74 ± 0.05		0.87 ± 0.05	0.68 ± 0.04‡

NOTE. Values are the mean ± SEM; N = 12.
*Difference between diet periods.
†$P < .001$
‡$P < .01$: difference within the diet period.

In the palmitic diet, apo A-I concentration was significantly higher as compared with the stearic diet ($P = .011$; Table 5). As compared with values obtained after the baseline diet, apo A-I and apo B concentrations were higher after the palmitic diet (8%, $P = .009$, and 12%, $P = .025$, respectively). In the stearic diet, there was a significant difference in apo A-I concentration only; the concentration was 7% lower ($P = .014$) after the stearic diet as compared with the baseline diet.

Plasma CETP Activity

In the palmitic diet, CETP activity was significantly higher than in the stearic diet ($P = .006$), and the mean change in CETP activity was also significantly greater in the palmitic diet as compared with the stearic diet ($P = .006$; Table 5). Plasma CETP activity was significantly higher after the palmitic diet as compared with the baseline diet (17%, $P = .001$). Individual responses during both the palmitic and stearic diets are presented in Fig 1.

Neither plasma CETP activity nor the change in activity correlated significantly with the concentration or changes in the concentration of serum total or lipoprotein lipids during consumption of the palmitic diet. During consumption of the stearic diet, the change in plasma CETP activity correlated significantly negatively with the change in HDL cholesterol concentration ($r = -.65$, $P = .022$), as well as with the change in non-HDL cholesterol concentration ($r = -.82$, $P = .001$).

DISCUSSION

In the present study, the effects of diets enriched in palmitic and stearic acids on serum lipids, lipoproteins, and apolipoproteins, and plasma CETP activity were examined in young healthy women. Experimental diets were composed of natural foodstuffs and differed from the baseline diet only with respect to fatty acid composition. According to the food records, there were no major differences in the proportions of energy nutrients, dietary fiber, and polyunsaturated fatty acids between diet periods, and the proportion of saturated and monounsaturated fatty acids also corresponded to the diet plans. To avoid changes in the proportion of carbohydrate and protein, palmitic and stearic acids were supplemented in the experimental diets within the fat component by replacing 5E% of monounsaturated fatty acids with palmitic acid or stearic acid.

Palmitic acid is the most abundant saturated fatty acid in the Western diet. In recent literature, the cholesterol-increasing effect of palmitic acid has been questioned.[8,9,28] However, in the present study, the diet rich in palmitic acid increased serum total cholesterol concentrations as compared with the diet rich in stearic acid and the baseline diet. This is in accordance with the results of most previously

Table 4. Serum Lipids (mmol/L), Lipoproteins (mmol/L), and Apos A-I and B (g/L) at the Beginning and End of Experimental Diet Periods

Parameter	Palmitic Diet 0 Weeks	Palmitic Diet 4 Weeks	P†	Stearic Diet 0 Weeks	Stearic Diet 4 Weeks
Cholesterol					
Total	4.16 ± 0.18	4.71 ± 0.14*	<.05	4.52 ± 0.22	4.32 ± 0.21
HDL	1.44 ± 0.06	1.51 ± 0.07	<.05	1.50 ± 0.06	1.37 ± 0.06
LDL	2.35 ± 0.13	2.78 ± 0.12*		2.56 ± 0.18	2.56 ± 0.15
VLDL	0.39 ± 0.06	0.42 ± 0.07		0.36 ± 0.06	0.39 ± 0.06
Triglycerides					
Total	0.89 ± 0.12	1.00 ± 0.15		1.01 ± 0.16	0.84 ± 0.12
HDL	0.19 ± 0.02	0.18 ± 0.02		0.21 ± 0.02	0.17 ± 0.06
LDL	0.25 ± 0.03	0.22 ± 0.03		0.25 ± 0.03	0.22 ± 0.03
VLDL	0.45 ± 0.09	0.59 ± 0.13		0.55 ± 0.13	0.45 ± 0.09*
Apo A-I	1.45 ± 0.05	1.57 ± 0.05‡	<.05	1.51 ± 0.04	1.40 ± 0.06§
Apo B	0.57 ± 0.04	0.65 ± 0.05§		0.65 ± 0.05	0.61 ± 0.05

NOTE. Values are the mean ± SEM; N = 12.
*$P < .001$, ‡$P < .01$, §$P < .05$: difference within the diet period.
†Difference between diet periods.

Table 5. Plasma CETP Activity (nmol/h/mL) at the End of the Baseline and Both Diet Periods and Mean Changes in CETP Activity During the Diet Periods

Parameter	Baseline	Palmitic Diet	Stearic Diet	P†
CETP activity	88 ± 5	106 ± 6*	93 ± 6	<.01
Mean change in activity		18 ± 3	4 ± 3	<.01

NOTE. Values are the mean ± SEM; N = 12.
*$P < .001$ *v* baseline.
†Difference between diet periods.

published studies.[1,5-7,10,29] The amount of myristic acid was lower (0.3 E%) in this diet period as compared with the baseline diet, so myristic acid cannot be responsible for the increase in LDL cholesterol concentration during this diet period. HDL cholesterol concentration did not increase significantly in the palmitic diet, but there was a significant increase in apo A-I concentration. As a result of the increase in LDL cholesterol concentration, the LDL/HDL cholesterol ratio increased during this diet period. Unlike in some human and animal studies,[9,30] no effects of palmitic acid on serum total or lipoprotein triglyceride concentrations were found in this study. The serum cholesterol-increasing effect of saturated fatty acids occurs largely in the LDL fraction. This may be due to the decrease in the activity of LDL receptors, and as a result, conversion of VLDL remnants to LDL increases and the fractional catabolic rate for LDL decreases.[31]

The effect of stearic acid on serum total and LDL cholesterol concentrations is well documented, and it is generally considered to have neutral or even hypocholesterolemic effects on lipid metabolism.[1,5,7,10-13,32-34] However, the effect on HDL cholesterol concentration and apo A-I, the main apolipoprotein of HDL, is not clear. In the present study, serum total cholesterol concentration was lower after the stearic diet as compared with the palmitic diet, but there was no difference in LDL cholesterol concentration, and the lower total cholesterol concentration was due to the lower concentration of HDL cholesterol. As compared with the baseline diet, serum total cholesterol tended to decrease during the stearic diet due to a decrease in HDL cholesterol concentration. The amount of myristic acid in the stearic diet was 0.9E% lower than in the baseline diet. According to the equation of the effects of individual saturated fatty acids,[1] a 0.9E% decrease in the amount of myristic acid would result in a decrease of 0.27 mmol/L in serum total cholesterol concentration. The observed decrease in the present study was 0.20 mmol/L. However, according to previously published studies, a change in the amount of myristic and palmitic acids in the diet causes mostly a change in total cholesterol concentration due to a change in LDL cholesterol concentration, whereas HDL cholesterol concentration changes only slightly or not at all.[11,35] In some recently published studies, stearic acid also has been found to have a tendency to decrease HDL cholesterol concentration as compared with diets high in palmitic or oleic acids[5] or a diet high in linoleic acid.[12] It is unclear whether this is due to decreased synthesis or increased catabolism of this particle.

There has been speculation as to why stearic acid has no serum cholesterol-increasing effect even though it is a saturated fatty acid. A possible mechanism for the neutral or decreasing effect of stearic acid on serum total cholesterol concentration could be that stearic acid is rapidly converted to oleic acid,[36-38] which does not increase serum total cholesterol concentration.[31] In some studies, stearic acid has been found to be absorbed less well than, for example, palmitic acid,[11,39,40] but in other studies no differences have been found in the absorbability as compared with other fatty acids.[5,41,42] In this study, subjects lost 0.4 kg in the stearic diet, but the energy intake was also marginally less than in the palmitic diet. It is thus unlikely that the effect of stearic acid in the present study could be explained by lower absorption of this fatty acid.

Non-HDL particles (VLDL, IDL, and LDL) are the acceptor particles of cholesteryl esters transferred by CETP,[43] and the lipid composition of these particles has been shown to affect the rate of cholesteryl ester transfer.[15,16] Since LDL particles are removed from the circulation by specific hepatic receptors,[44] the increased CETP activity may lead to stimulation of reverse cholesterol transport from peripheral tissues to the liver. On the other hand, the finding that patients with established coronary artery disease have increased transfer of cholesteryl esters from HDL to VLDL and LDL[45] and that atherosclerotic lesions

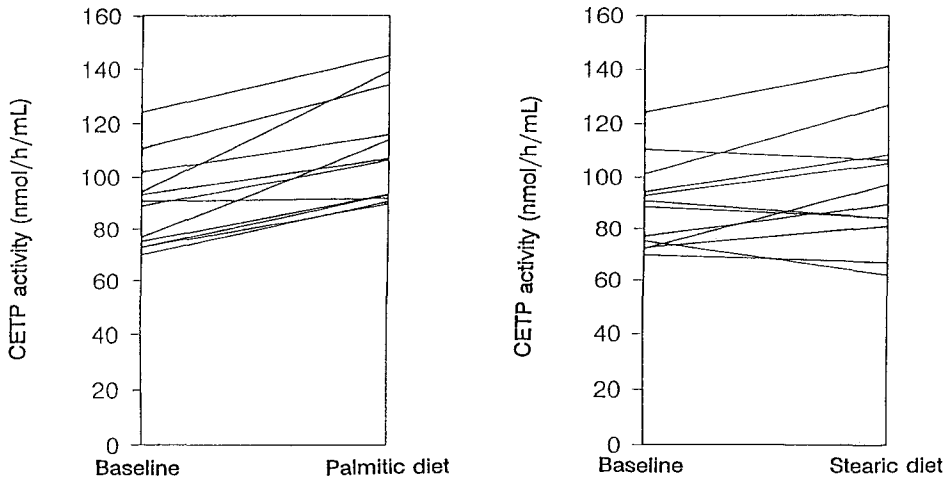

Fig 1. Individual responses of plasma CETP activity during palmitic and stearic diets versus the baseline diet.

develop in arteries of mice expressing the transgenic CETP gene[46] suggest that high CETP activity may be atherogenic.

In addition to its central role in reverse cholesterol transport from the periphery to the liver, CETP is also involved in the regulation of serum lipoprotein levels. There is an inverse correlation between plasma CETP activity and HDL cholesterol concentration.[24] A high plasma CETP activity is also associated with high concentrations of serum total or non-HDL cholesterol in hypercholesterolemic patients.[47,48] Because previously published studies suggest that the effects of palmitic acid and stearic acid on serum HDL cholesterol concentration may differ, it was of interest to find out whether this could be related to simultaneous changes in plasma CETP activity. CETP activity was significantly higher in the palmitic diet than in the stearic diet. Furthermore, as compared with the baseline diet, plasma CETP activity increased in all subjects in the palmitic diet.

A diet rich in cholesterol and fat has been found to increase hepatic mRNA concentrations of CETP in nonhuman primates and rabbits, suggesting an increase in the synthetic rate of CETP.[49,50] Diet-induced alterations in plasma CETP activity in the present study may be due to direct effects of dietary fatty acids on CETP synthesis, but changes in serum lipoprotein concentrations may also play a role in the alteration of plasma CETP activity; increased plasma CETP activity coincided with an increase in serum LDL cholesterol and apo B concentrations in the palmitic diet. However, correlations between plasma CETP activity and these two variables were not statistically significant in the palmitic diet, likely because of the small variation among subjects in plasma CETP response in this diet.

In conclusion, in young healthy women, palmitic acid and stearic acid had different effects on serum lipids and lipoproteins: serum total and HDL cholesterol, as well as apo A-I, concentrations were higher after the palmitic acid–enriched diet as compared with the stearic acid–enriched diet. Furthermore, the diet rich in palmitic acid resulted in higher plasma CETP activity than the diet rich in stearic acid.

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REFERENCES

1. Hegsted DM, McGandy RB, Myers ML, et al: Quantitative effects of dietary fat on serum cholesterol in man. Am J Clin Nutr 17:281-295, 1965

2. Keys A, Anderson JT, Grande F: Serum cholesterol response to changes in the diet. I. Iodine value of dietary fat versus 2S-P. Metabolism 14:747-758, 1965

3. Grundy SM, Bilheimer D, Chait A, et al: Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult-Treatment-Panel-II). JAMA 269:3015-3023, 1993

4. Recommendations of the European Atherosclerosis Society prepared by the International Task Force for Prevention of Coronary Heart Disease: Prevention of coronary heart disease: Scientific background and new clinical guidelines. Nutr Metab Cardiovasc Dis 2:113-156, 1992

5. Bonanome A, Grundy SM: Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. N Engl J Med 318:1244-1248, 1988

6. Mattson FH, Grundy SM: Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. J Lipid Res 26:194-202, 1985

7. Grande F, Anderson JT, Keys A: Comparison of effects of palmitic and stearic acids in the diet on serum cholesterol in man. Am J Clin Nutr 23:1184-1193, 1970

8. Marzuki A, Arshad F, Razak TA, et al: Influence of dietary fat on plasma lipid profiles of Malaysian adolescents. Am J Clin Nutr 53:1010S-1014S, 1991

9. Ng TKW, Hayes KC, DeWitt GF, et al: Dietary palmitic and oleic acids exert similar effects on serum cholesterol and lipoprotein profiles in normocholesterolemic men and women. J Am Coll Nutr 11:383-390, 1992

10. Keys A, Anderson JT, Grande F: Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. Metabolism 14:776-787, 1965

11. Denke MA, Grundy SM: Effects of fats high in stearic acid on lipid and lipoprotein concentrations in men. Am J Clin Nutr 54:1036-1040, 1991

12. Zock PL, Katan MB: Hydrogenation alternatives: Effects of *trans* fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. J Lipid Res 33:399-410, 1992

13. Kris-Etherton PM, Derr J, Mitchell DC, et al: The role of fatty acid saturation on plasma lipids, lipoproteins, and apolipoproteins. I. Effects of whole food diets high in cocoa butter, olive oil, soybean oil, dairy butter, and milk chocolate on the plasma lipids of young men. Metabolism 42:121-129, 1993

14. Tall A, Granot E, Brocia R, et al: Accelerated transfer of cholesteryl esters in dyslipidemic plasma. Role of cholesteryl ester transfer protein. J Clin Invest 79:1217-1225, 1987

15. Morton RE: Specificity of lipid transfer protein for molecular species of cholesteryl ester. J Lipid Res 27:523-529, 1986

16. Mann CJ, Yen FT, Grant AM, et al: Mechanism of plasma cholesteryl ester transfer in hypertriglyceridemia. J Clin Invest 88:2059-2066, 1991

17. Abbey M, Clifton P, Kestin M, et al: Effect of fish oil on lipoproteins, lecithin:cholesterol acyltransferase, and lipid transfer protein activity in humans. Arteriosclerosis 10:85-94, 1990

18. Groener JEM, van Ramshorst EM, Katan MB, et al: Diet-induced alteration in the activity of plasma lipid transfer protein in normolipidemic human subjects. Atherosclerosis 87:221-226, 1991

19. Rastas M, Seppänen R, Knuts L-R, et al: Nutrient Composition of Foods. Helsinki, Finland, Social Insurance Institution, 1989

20. Penttilä IM, Voutilainen E, Laitinen O, et al: Comparison of different analytical and precipitation methods for the direct estimation of high-density lipoprotein cholesterol. Scand J Clin Lab Invest 41:353-360, 1981

21. Fruchart JC, Kora I, Cachera C, et al: Simultaneous measurement of plasma apolipoproteins A-I and B by electroimmunoassay. Clin Chem 28:59-61, 1982

22. Hannuksela M, Marcel YL, Kesäniemi YA, et al: Reduction in the concentration and activity of plasma cholesteryl ester transfer protein by alcohol. J Lipid Res 33:737-744, 1992

23. Groener JEM, Pelton RW, Kostner GM: Improved estimation of cholesteryl ester transfer/exchange activity in serum or plasma. Clin Chem 32:283-286, 1986

24. Savolainen MJ, Hannuksela M, Seppänen S, et al: Increased high-density lipoprotein cholesterol concentration in alcoholics is related to low cholesteryl ester transfer protein activity. Eur J Clin Invest 20:593-599, 1990

25. Ågren JJ, Julkunen A, Penttilä I: Rapid separation of serum lipids for fatty acid analysis by a single aminopropyl column. J Lipid Res 33:1871-1876, 1992

26. Norusis MJ (ed): SPSS/PC+ 4.0 Base Manual for the IBM PC/XT/AT and PS/2. Chicago, IL, SPSS, 1990

27. Norusis MJ (ed): SPSS/PC+ Advanced Statistics 4.0 for the IBM/XT/AT and PS/2. Chicago, IL, SPSS, 1990

28. Ng TKW, Hassan K, Lim JB, et al: Nonhypercholesterolemic effects of a palm-oil diet in Malaysian volunteers. Am J Clin Nutr 53:1015S-1020S, 1991

29. Grundy SM, Vega GL: Plasma cholesterol responsiveness to saturated fatty acids. Am J Clin Nutr 47:822-824, 1988

30. Khosla P, Hayes KC: Comparison between the effects of dietary saturated (16:0), monounsaturated (18:1), and polyunsaturated (18:2) fatty acids on plasma lipoprotein metabolism in cebus and rhesus monkeys fed cholesterol-free diets. Am J Clin Nutr 55:51-62, 1992

31. Grundy SM, Denke MA: Dietary influences on serum lipids and lipoproteins. J Lipid Res 31:1149-1172, 1990

32. Ahrens EH Jr, Hirsch J, Insull W Jr, et al: The influence of dietary fats on serum lipid levels in man. Lancet 1:943-953, 1957

33. Erickson BA, Coots RH, Mattson FH, et al: The effect of partial hydrogenation of dietary fats, of the ratio of polyunsaturated to saturated fatty acids, and of dietary cholesterol upon plasma lipids in man. J Clin Invest 43:2017-2025, 1964

34. Reiser R, Probstfield JL, Silvers A, et al: Plasma lipid and lipoprotein response of humans to beef fat, coconut oil and safflower oil. Am J Clin Nutr 42:190-197, 1985

35. Zock PL, de Vries JHM, Katan MB: Impact of myristic acid versus palmitic acid on serum lipid and lipoprotein levels in healthy women and men. Arterioscler Thromb 14:567-575, 1994

36. Elovson J: Immediate fate of albumin-bound [I-^{14}C]stearic acid following its intraportal injection into carbohydrate refed fats: Early course of desaturation and esterification in the liver. Biochim Biophys Acta 106:480-494, 1965

37. Nichaman MZ, Sweeley CC, Olson RE: Plasma fatty acids in normolipemic and hyperlipemic subjects during fasting and after linoleate feeding. Am J Clin Nutr 20:1057-1069, 1967

38. Myher JJ, Kuksis A, Breckenridge WC, et al: Comparative studies of triacylglycerol structure of very low density lipoproteins and chylomicrons of normolipemic subjects and patients with type II hyperlipoproteinemia. Lipids 20:90-101, 1985

39. Chen IS, Subramaniam S, Vahouny GV, et al: A comparison of the digestion and absorption of cocoa butter and palm kernel oil and their effects on cholesterol absorption in rats. J Nutr 119:1569-1573, 1989

40. Mitchell DC, McMahon KE, Shively CA, et al: Digestibility of cocoa butter and corn oil in human subjects: A preliminary study. Am J Clin Nutr 50:983-986, 1989

41. Mattson FH: The absorbability of stearic acid when fed as a simple or mixed triglyceride. J Nutr 69:338-342, 1959

42. Bonanome A, Grundy SM: Intestinal absorption of stearic acid after consumption of high fat meals in humans. J Nutr 119:1556-1560, 1989

43. Tall AR: Plasma cholesteryl ester transfer protein. J Lipid Res 34:1255-1274, 1993

44. Brown MS, Goldstein JL: A receptor-mediated pathway for cholesterol homeostasis. Science 232:34-47, 1986

45. Bhatnagar D, Durrington PN, Channon KM, et al: Increased transfer of cholesteryl esters from high density lipoproteins to low density and very low density lipoproteins in patients with angiographic evidence of coronary artery disease. Atherosclerosis 98:25-32, 1993

46. Marotti KR, Castle CK, Boyle TP, et al: Severe atherosclerosis in transgenic mice expressing simian cholesteryl ester transfer protein. Nature 364:73-75, 1993

47. Groener JEM, Van Rozen AJ, Erkelens DW: Cholesteryl ester transfer activity. Localization and role in the distribution of cholesteryl ester among lipoproteins in man. Atherosclerosis 50:261-271, 1984

48. Groener JEM, Jacobs DMLHA, Van Rozen AJ, et al: Diet, lipoproteins, and cholesteryl ester transfer activity in hyperlipidemic subjects. Clin Nutr 4:35-38, 1985

49. Quinet EM, Agellon LB, Kroon PA, et al: Atherogenic diet increases cholesteryl ester transfer protein messenger RNA levels in rabbit liver. J Clin Invest 85:357-363, 1990

50. Pape ME, Rehberg EF, Marotti KR, et al: Molecular cloning, sequence, and expression of cynomolgus monkey cholesteryl ester transfer protein. Inverse correlation between hepatic cholesteryl ester transfer protein mRNA levels and plasma high density lipoprotein levels. Arterioscler Thromb 11:1759-1771, 1991