A High–Stearic Acid Diet Does Not Impair Glucose Tolerance and Insulin Sensitivity in Healthy Women

Anne M. Louheranta, Anu K. Turpeinen, Ursula S. Schwab, Helvi M. Vidgren, Markku T. Parviainen, and Matti I.J. Uusitupa

Results in epidemiological and experimental studies suggest that a diet rich in saturated fat may affect insulin sensitivity. However, no published data are available on the effect of stearic acid in this respect. Therefore, we examined the effects of a high–stearic acid diet and a high–oleic acid diet on glucose metabolism, serum lipids and lipoproteins, and blood coagulation factors in 15 healthy female subjects. 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 36% of energy (E%) as fat. In the experimental diets, 5 E% stearic or oleic acid was substituted for 5 E% of saturated fatty acids in the baseline diet. After the experimental diets, no differences were found in the insulin sensitivity index (mean ± SEM, 5.4 ± 1.9 *v* 5.2 ± 1.6 × 10^{-4} $min^{-1} \cdot \mu U^{-1} \cdot mL^{-1}$, nonsignificant [NS]), glucose effectiveness (0.026 ± 0.006 *v* 0.026 ± 0.003 min^{-1}, NS), or first-phase insulin reaction ([FPIR] 368 ± 57 *v* 374 ± 66 mU/L · min, NS). The concentration of serum lipids and lipoproteins and blood coagulation factors did not differ after the diet periods. In conclusion, a diet rich in stearic acid did not deteriorate glucose tolerance or insulin action in young healthy female subjects as compared with a diet rich in oleic acid.

Copyright © 1998 by W.B. Saunders Company

BOTH THE AMOUNT and quality of dietary fat have been suggested to affect glucose tolerance. In experimental animals, the fatty acid composition and amount of fat in the diet have been shown to affect insulin secretion[1-4] and insulin sensitivity.[5-7] In some epidemiological studies, a high intake of fat, especially saturated fat, has been associated with a deterioration of glucose tolerance. This association has been seen in healthy subjects,[8,9] subjects with impaired glucose tolerance[10,11] or non–insulin-dependent diabetes mellitus (NIDDM),[10] and also subjects with coronary artery disease.[12]

There are only a few studies concerning the effect of a change in the amount or quality of dietary fat on glucose and insulin metabolism in humans. In young healthy women[13] and middle-aged glucose-intolerant hyperlipidemic subjects,[14] replacement of a considerable proportion of saturated fat by unsaturated fat improved glucose tolerance. In NIDDM patients, a modest increase in insulin-mediated glucose disposal was seen after substitution of polyunsaturated fat for saturated fat.[15] Stearic acid is considered neutral with respect to its effect on serum lipids,[16,17] but almost nothing is known about its effects on glucose metabolism in humans. Previous studies where unsaturated fatty acids have been substituted for saturated fat have not focused on the effects of individual saturated fatty acids on glucose and insulin metabolism. The amount and quality of dietary fat may also affect thrombus formation, but the results concerning the effect of stearic acid in this respect are contradictory.[18-21]

As part of a series of studies evaluating the effects of single fatty acids on lipoprotein and glucose and insulin metabolism,[13,22,23] this study was planned to examine the effect of stearic acid on glucose tolerance and insulin secretion, serum lipids, and coagulation factors in young healthy women.

SUBJECTS AND METHODS

Subjects

Fifteen healthy women aged 22 ± 0.6 years (mean ± SEM; range, 19 to 32) participated in the study. The mean body mass index (BMI) was 22.6 ± 0.6 kg/m^2 (range, 19.2 to 26.4), and all subjects had normal liver, kidney, and thyroid function. Five of the subjects used low-estrogen oral contraceptives during the study, but no other medication was used. Two subjects were smokers, and they were advised to retain their regular smoking habits throughout the study. 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 high–stearic acid diet (stearic diet) and a high–oleic acid diet (oleic diet) for 4 weeks according to a randomized crossover design. Eight subjects started with the stearic diet and seven with the oleic diet. Both experimental diet periods were preceded by consumption of a baseline diet for 2 weeks. Weight and blood pressure were measured at 2-week intervals. Samples for laboratory analyses (serum lipid, lipoprotein, and apolipoprotein concentrations and coagulation factor values) were collected after a 12-hour fast at the beginning and end of each diet period. The height, routine hematological measures, and serum creatinine, thyroxine, and liver enzyme levels were determined at the beginning of the study. A frequently sampled intravenous glucose tolerance test (FSIGT) was performed after the first baseline period and after both experimental diet periods.

Diets

Both experimental diets and the baseline diet supplied 36% of energy (E%) as fat, 48 E% as carbohydrate, and 15 E% as protein. The cholesterol content in all three diets was about 30 mg/MJ, and the dietary fiber content was about 3 g/MJ. The calculated fatty acid composition of the baseline diet was 18 E% saturated, 12 E% monounsaturated, and 6 E% polyunsaturated fatty acids. During both the stearic and the oleic diet, 5 E% of saturated fatty acids in the baseline diet was substituted by stearic acid or oleic acid, respectively, but the experimental diets were otherwise kept identical.

During the baseline diet, butter was used as a main source of fat together with olive oil and a small amount of sunflower oil. Cocoa

From the Departments of Clinical Nutrition and Clinical Chemistry, University of Kuopio, Kuopio, Finland.

Submitted March 27, 1997; accepted November 9, 1997.

Supported by the Council for Health Research, Academy of Finland.

Address reprint requests to Anne M. Louheranta, MSc, Department of Clinical Nutrition, University of Kuopio, PO Box 1627, 70211 Kuopio, Finland.

Copyright © 1998 by W.B. Saunders Company

0026-0495/98/4705-0007$03.00/0

butter was used as a source of stearic acid and olive oil as a source of oleic acid. Both diets contained a small amount of butter and sunflower oil. Medium-fat dairy products were consumed during the diet periods, except for the low-fat milk consumed during the stearic diet and oleic diet. Because the baseline diet included milk fat and, as a result, more dietary cholesterol, 4 to 6 g egg yolk per day was added to the stearic diet and oleic diet to keep the intake of dietary cholesterol constant during the whole study. Except for cocoa butter, the diets were composed of common Finnish food stuffs. The subjects received fat products, vegetable oils, and dairy products free of charge. This, together with frequent dietary counseling, promoted good compliance.

The energy requirement of the subjects was estimated by 3-day food records kept before the study. The subjects received detailed oral and written instructions about the diets, specifying the amount of individual food stuffs 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 stable body weight and unchanged exercise habits during the study.

To control dietary compliance, the subjects kept 7-day food records (5 weekdays and 2 weekend days) during both experimental diets. During the baseline and washout periods, 4-day food records (3 weekdays and 1 weekend day) were kept. The subjects were asked to weigh everything they ate on a digital scale (provided by the study unit), where possible. For situations in which weighing was not possible, subjects were instructed to estimate portion sizes in household measures.

The diets were planned and nutrients in the food records were calculated using the Micro-Nutrica dietary analysis program (The Social Insurance Institution, Turku, Finland) based on the database of the Finnish Social Insurance Institution. The food composition tables are based on values obtained from Finnish food analyses and values taken from international food composition tables.[24]

Determination of the fatty acid composition of serum triglycerides and cholesteryl esters was used as an objective indicator of compliance to the experimental diets during the study.

Laboratory Analyses

Serum lipids and lipoproteins. To remove the very–low-density lipoprotein (VLDL) fraction, lipoproteins were separated by ultracentrifugation for 18 hours at a density of 1.006 kg/L. VLDL cholesterol was calculated as the difference between the mass of cholesterol in the serum and in the infranatant. High-density lipoprotein (HDL) in the infranatant was separated from low-density lipoprotein (LDL) by precipitation of LDL with dextran sulfate and magnesium chloride.[25] LDL cholesterol was calculated as the difference between the mass of cholesterol in the infranatant and HDL. Enzymatic colorimetric methods were used for the determination of cholesterol and triglycerides from whole serum and lipoprotein lipids with commercial kits (Monotest Cholesterol and Triglyceride GPO-PAP; Boehringer, Mannheim, Germany) using an automated instrument (Kone Specific Clinical Analyzer; Kone, Espoo, Finland). The coefficient of variation (CV) between measurements for serum total cholesterol was 0.9%, and for total triglycerides, 0.9% to 1.0% (two standards). The CV for HDL-cholesterol was 0.8% to 3.5% (two standards), and for HDL-triglycerides, 2.2% (one standard).

Serum samples for apolipoprotein A-I (apo A-I) and apo B were stored at −78°C until analyzed at the end of the study. Analyses were based on the measurement of immunoprecipitation enhanced by polyethylene glycol at 340 mm. An automated Kone Specific Clinical Analyzer and apo A-I and apo B reagents from Kone were used in the analyses. The CV for apo A-I within the measurement was 4.1% (one standard), and for apo B, 2.6% (one standard).

Lipoprotein(a). Apolipoprotein(a) [Apo(a)] in lipoprotein(a) [Lp(a)] was measured using the solid-phase two-site immunoradiometric assay from Mercodia (Uppsala, Sweden; the same assay was formerly supplied by Pharmacia Diagnostics, Uppsala, Sweden). This assay is based on a direct sandwich principle in which two monoclonal antibodies are directed against separate antigenic determinants on the Apo(a) molecule. The assay is calibrated against a highly purified Lp(a) preparation. The concentration of Apo(a) is expressed in units per liter. One unit of Apo(a) is approximately 0.7 mg Lp(a). The analytical parameters were validated to meet the criteria as defined by the manufacturer. The method sensitivity is 8.4 U/L (routine standardization at 16.8 to 840 U/L), and levels above 840 U/L were reanalyzed after further dilution (measuring range, ≤3,360 U/L). Reasonably low assay imprecision was found: between-assay CVs were 2.5%, 7.1%, 3.5%, and 6.0% at Lp(a) levels of 93.5, 123, 311, and 372 U/L, respectively. The assay is specific to Apo(a), and apo B has no measurable cross-reaction. Serum plasminogen up to 5 g/L yields no measurable cross-reaction in the assay.

Fatty acid composition of serum triglycerides and serum cholesteryl esters. In the analysis of fatty acid composition of serum triglycerides and serum cholesteryl esters, serum lipids were extracted with chloroform-methanol (2:1), and the lipid fractions were separated by solid-phase extraction with an aminopropyl column.[26] The fatty acids of triglycerides and cholesteryl esters were transmethylated with 14% borontrifluoride in methanol and analyzed with a gas chromatograph (HP 5890 Series II; Hewlett-Packard, Waldbronn, Germany) equipped with a HP-FFAP capillary column.

Hemostatic factors. The fibrinogen level was measured with an ACL 300 R coagulometer (Instrumentation Laboratory, Milan, Italy) from the light scattered by the clot during the prothrombin time assay (PT-fibrinogen; Instrumentation Laboratory). A single lot of IL Calibration plasma was used as a standard throughout the study. The intraassay precision of the method is 3.6%, and interassay precision is 2.3%. The samples were measured in duplicate; the difference of the duplicates should lie within 10% of the mean, or the analysis was repeated using a split sample.[27]

Factor VII (FVII) coagulant activity (FVII:C) was measured with the one-stage method using rabbit brain thromboplastin (Thromboplastin IS; Baxter Dade, Miami, FL) and human immunodepleted FVII-deficient plasma (Behring, Marburg, Germany). The assays were performed with the ACL 300 R coagulometer. A frozen plasma pool was used as a standard. The intraassay precision of this method is 2.4%, and the interassay precision is 3.9%.[27]

Blood samples for measurement of hemostatic factors were taken without compression. If the first puncture was not successful, the samples were taken from the contralateral arm. All deviations from the normal procedure, such as difficulty in blood collection or in preparation of the sample, nausea or fainting, and use of analgesics, were recorded.

FSIGT

A FSIGT was performed as previously described.[28] Due to technical difficulties, data are available for 14 of 15 subjects. First, two intravenous catheters were inserted in the antecubital veins on both arms, and fasting samples were drawn. A glucose dose of 300 mg/kg body weight was administered intravenously as a 50% solution over 1.5 minutes, followed by 10 mL 0.9% NaCl solution. Thereafter, a 0.9% NaCl solution was slowly infused until a bolus of insulin 0.03 U/kg was rapidly injected 20 minutes after the glucose dose. NaCl infusion was continued for 1.5 minutes after the insulin dose. To determine plasma glucose and insulin levels, venous blood samples were collected before the glucose dose (−5 and 0 minutes) and after the glucose dose (at 2, 4, 6, 8, 10, 12, 14, 16, 19, 22, 24, 27, 30, 40, 50, 60, 70, 90, 100, 120, 140, 160, and 180 minutes) via a catheter in the contralateral arm. To arterialize the venous blood, the arm was kept on a 50°C electric pad during the test. Plasma glucose was analyzed by a glucose oxidase method (Glucose Auto & Stat, Model GA-110; Daiichi, Kyoto, Japan) and plasma insulin by a radioimmunoassay (RIA) method (Phadaseph

Insulin RIA 100; Pharmacia Diagnostica, Uppsala, Sweden). The data were analyzed by calculating the glucose effectiveness (S_G) and insulin sensitivity index (S_I) with the Minmod program.[29] In addition, FPIR was determined by calculating the area under the insulin curve above the baseline level from 0 to 10 minutes.

Statistical Analyses

The data were analyzed using the SPSS/PC+ (version 4.0; SPSS, Chicago, IL) statistical program.[30] Before further analysis, normal distribution of the variables was checked with the Kolmogorov-Smirnov test. Paired *t* tests were used for two-tailed comparisons. The results of FSIGTs were analyzed by Friedman's test. To control the overall α level, Bonferroni adjustment was used. Data are expressed as the mean ± SEM, and a *P* value less than .05 was considered statistically significant.

RESULTS

Weight, Blood Pressure, and Diets

The mean value for measurements after the 2-week run-in and washout periods was taken as a baseline value in this study. Body weight (BMI after baseline diet, 22.1 ± 0.6 kg/m^2; after stearic diet, 22.0 ± 0.6 kg/m^2; after oleic diet, 22.0 ± 0.6 kg/m^2) and blood pressure (data not shown) remained stable during the study. The goals of the experimental diets were well achieved. The difference in the stearic acid content between experimental diets was 4.5 E%, and for monounsaturated fatty acids the difference was 6.5 E%. The amount of other energy nutrients, as well as dietary cholesterol and fiber, did not differ between the diets. The data for food records from the diet periods are shown in Table 1.

Fatty Acid Composition of Serum Lipids

After the stearic diet, the proportion of stearic acid was significantly higher in both serum triglycerides (Table 2) and cholesteryl esters (Table 3) as compared with the oleic diet. The proportions of both stearic acid and oleic acid were increased as compared with the baseline diet. After the oleic diet, the proportion of oleic acid increased and was significantly higher

Table 1. Energy Intake, Proportion of Energy Nutrients, and Intake of Dietary Cholesterol and Fiber During the Diet Periods

Parameter	Baseline Diet (n = 15)	Stearic Diet (n = 15)	Oleic Diet (n = 15)
Energy			
kJ	7,918 ± 355	7,584 ± 238	7,602 ± 303
kcal	1,885 ± 85	1,806 ± 57	1,810 ± 72
Fat (E%)	40.0 ± 0.5	38.9 ± 0.6	40.5 ± 0.7
Fatty acids (E%)			
Saturated	18.1 ± 0.3	18.5 ± 0.4	12.8 ± 0.4
Lauric acid	0.8 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
Myristic acid	2.5 ± 0.1	1.3 ± 0.0	1.4 ± 0.1
Palmitic acid	8.4 ± 0.1	8.3 ± 0.2	6.9 ± 0.2
Stearic acid	3.0 ± 0.0	6.8 ± 0.2	2.3 ± 0.1
Monounsaturated	12.7 ± 0.3	12.1 ± 0.2	18.6 ± 0.3
Polyunsaturated	6.5 ± 0.3	6.4 ± 0.4	6.4 ± 0.2
Linoleic acid	5.7 ± 0.3	5.7 ± 0.4	5.7 ± 0.2
α-Linolenic acid	0.5 ± 0.1	0.4 ± 0.0	0.5 ± 0.0
Carbohydrate (E%)	43.3 ± 0.3	44.8 ± 0.5	41.6 ± 1.0
Protein (E%)	14.1 ± 0.3	13.6 ± 0.4	14.2 ± 0.4
Cholesterol (mg/MJ)	32.0 ± 1.8	30.4 ± 2.7	28.2 ± 1.9
Fiber (g/MJ)	3.0 ± 0.2	2.9 ± 0.2	2.8 ± 0.2

Table 2. Fatty Acid Composition of Serum Triglycerides (mol% of total) After Consumption of the Baseline Diet and Experimental Diets

Fatty Acid	Baseline Diet (n = 15)	Stearic Diet (n = 15)	Oleic Diet (n = 15)	P§
Myristic (C14:0)	3.11 ± 0.14	2.52 ± 0.27	2.43 ± 0.14†	NS
Palmitic (C16:0)	28.19 ± 0.56	27.63 ± 0.87	26.42 ± 0.62*	NS
Palmitoleic (C16:1)	4.75 ± 0.23	3.79 ± 0.27†	4.21 ± 0.29*	NS
Stearic (C18:0)	3.08 ± 0.08	4.87 ± 0.29‡	2.77 ± 0.11*	<.001
Oleic (C18:1, n-9)‖	38.15 ± 0.40	39.78 ± 0.30†	43.75 ± 0.66‡	<.001
Linoleic (C18:2, n-6)	19.10 ± 0.55	17.94 ± 1.02	17.01 ± 0.56†	NS
γ-linolenic (C18:3, n-6)	0.40 ± 0.03	0.47 ± 0.06	0.45 ± 0.06	NS
α-linolenic (C18:3, n-3)	1.30 ± 0.06	1.19 ± 0.13	1.18 ± 0.07	NS
Dihomo-γ-linolenic (C20:3, n-6)	0.29 ± 0.02	0.30 ± 0.05	0.29 ± 0.03	NS
Arachidonic (C20:4, n-6)	0.98 ± 0.04	0.93 ± 0.05	0.91 ± 0.08	NS
Eicosapentaenoic (C20:5, n-3)	0.36 ± 0.04	0.34 ± 0.02	0.32 ± 0.03	NS
Docosapentaenoic (C22:5, n-3)	0.30 ± 0.03	0.24 ± 0.03*	0.26 ± 0.04	NS

*P < .05, †P < .01, ‡P < .001: *v* baseline diet.
§P for the difference between the experimental diet periods.
‖Includes C18:1, n-7.

Table 3. Fatty Acid Composition of Serum Cholesteryl Esters (mol% of total) After Consumption of the Baseline Diet and Experimental Diets

Fatty Acid	Baseline Diet (n = 15)	Stearic Diet (n = 15)	Oleic Diet (n = 15)	P§
Myristic (C14:0)	1.24 ± 0.03	0.89 ± 0.06‡	1.00 ± 0.05‡	NS
Palmitic (C16:0)	12.25 ± 0.20	11.73 ± 0.26*	12.36 ± 0.19	<.05
Palmitoleic (C16:1)	3.24 ± 0.26	2.82 ± 0.26	3.38 ± 0.53	NS
Stearic (C18:0)	1.08 ± 0.12	1.27 ± 0.09	0.96 ± 0.06	<.01
Oleic (C18:1, n-9)‖	17.80 ± 0.26	18.57 ± 0.38*	21.05 ± 0.27‡	<.001
Linoleic (C18:2, n-6)	56.12 ± 0.60	57.07 ± 0.78	53.56 ± 0.92†	<.05
γ-linolenic (C18:3, n-6)	0.55 ± 0.03	0.53 ± 0.05	0.58 ± 0.05	NS
α-linolenic (C18:3, n-3)	0.66 ± 0.02	0.62 ± 0.05	0.64 ± 0.04	NS
Dihomo-γ-linolenic (C20:3, n-6)	0.57 ± 0.04	0.55 ± 0.05	0.51 ± 0.05	NS
Arachidonic (C20:4, n-6)	4.86 ± 0.21	4.55 ± 0.22	4.50 ± 0.19	NS
Eicosapentaenoic (C20:5, n-3)	0.82 ± 0.11	0.77 ± 0.10	0.87 ± 0.12	NS
Docosahexaenoic (C22:6, n-3)	0.59 ± 0.07	0.62 ± 0.07	0.59 ± 0.05	NS

*P < .05, †P < .01, ‡P < .001: *v* baseline diet.
§P for the difference between the experimental diet periods.
‖Includes C18:1, n-7.

Table 4. S_I, S_G, and FPIR at the End of the Run-in Period and After Consumption of the Experimental Diets

Parameter	Run-in Period (n = 14)	Stearic Diet (n = 14)	Oleic Diet (n = 14)	P*
S_I (10^{-4} min^{-1} · μU · mL^{-1})	5.28 ± 1.44	5.42 ± 1.87	5.20 ± 1.61	NS
S_G (min^{-1})	0.028 ± 0.005	0.026 ± 0.006	0.026 ± 0.003	NS
FPIR (mU/L · min)	386 ± 72	368 ± 57	374 ± 66	NS

*P for the difference between the experimental diet periods.

in both lipid fractions as compared with the stearic diet and baseline diet.

Glucose and Insulin Metabolism

At baseline, S_I was 3.3 to 9.9 × 10^{-4} min^{-1} · μU^{-1} · mL^{-1}. No differences were found in S_I, S_G, or FPIR at the end of the experimental diet periods (Table 4). Insulin and glucose curves during the FSIGT are shown in Fig 1.

Serum Lipids, Lipoproteins, and Clotting Factors

There were no differences in serum lipid, lipoprotein, apo A-I and B, or Lp(a) concentrations after the experimental diet periods (Table 5). In addition, coagulation factor levels were similar after the experimental diet periods (Table 6).

As a secondary analysis the results for serum lipids and lipoproteins at the end of the stearic and oleic diets were compared with results at the end of the baseline diet. The serum total cholesterol level was 7.7% lower after the stearic diet and 5.9% lower after the oleic diet compared with the baseline diet. Similarly, the LDL-cholesterol concentration was reduced by 9.9% versus 6.4% after the stearic and oleic diets, respectively. HDL-cholesterol was significantly lower after the stearic diet (5.3%) and also tended to be lower after the oleic diet (4.7%) in comparison to the baseline diet. Serum triglyceride concentrations remained stable during the study. The serum apo A-I concentration was 6.6% lower after the stearic diet and 5.0% lower after the oleic diet compared with the baseline diet. For apo B, the reduction was 10.6% versus 7.0% after the stearic and oleic diets, respectively.

Table 5. Concentrations of Serum Total and Lipoprotein Cholesterol, Total and Lipoprotein Triglycerides (mmol/L), Apo A-I and B (g/L), and Lp(a) (U/L) After Consumption of the Baseline Diet and the Experimental Diets

Parameter	Baseline Diet (n = 15)	Stearic Diet (n = 15)	Oleic Diet (n = 15)	P§
Cholesterol				
Total	4.84 ± 0.15	4.46 ± 0.14†	4.54 ± 0.14*	NS
HDL	1.52 ± 0.05	1.43 ± 0.05*	1.44 ± 0.06	NS
LDL	2.95 ± 0.13	2.64 ± 0.10†	2.73 ± 0.09*	NS
VLDL	0.37 ± 0.03	0.39 ± 0.05	0.36 ± 0.03	NS
Triglycerides				
Total	0.84 ± 0.06	0.81 ± 0.07	0.87 ± 0.08	NS
HDL	0.18 ± 0.01	0.18 ± 0.01	0.18 ± 0.02	NS
LDL	0.23 ± 0.01	0.23 ± 0.01	0.23 ± 0.02	NS
VLDL	0.43 ± 0.05	0.40 ± 0.06	0.47 ± 0.06	NS
Apolipoproteins and Lp(a)				
Apo A-I	1.29 ± 0.04	1.20 ± 0.03†	1.22 ± 0.04*	NS
Apo B	0.62 ± 0.03	0.55 ± 0.02†	0.57 ± 0.02*	NS
Lp(a)	206.8 ± 70.4	200.6 ± 60.1	184.3 ± 60.2	NS

*$P < .05$, †$P < .01$, ‡$P < .001$: *v* baseline diet.
§*P* for the difference between the experimental diet periods.

DISCUSSION

In the present study, the effect of stearic acid on glucose and insulin metabolism, serum lipids and lipoproteins, and clotting factors was evaluated in young healthy women. The experimental diets differed only with respect to fatty acid composition, and the dietary goals were well achieved. Between the stearic diet and oleic diet, the difference in stearic acid content was 4.5 E%, and for monounsaturated fatty acids the difference was 6.5 E%. The changes in the fatty acid composition of serum cholesteryl

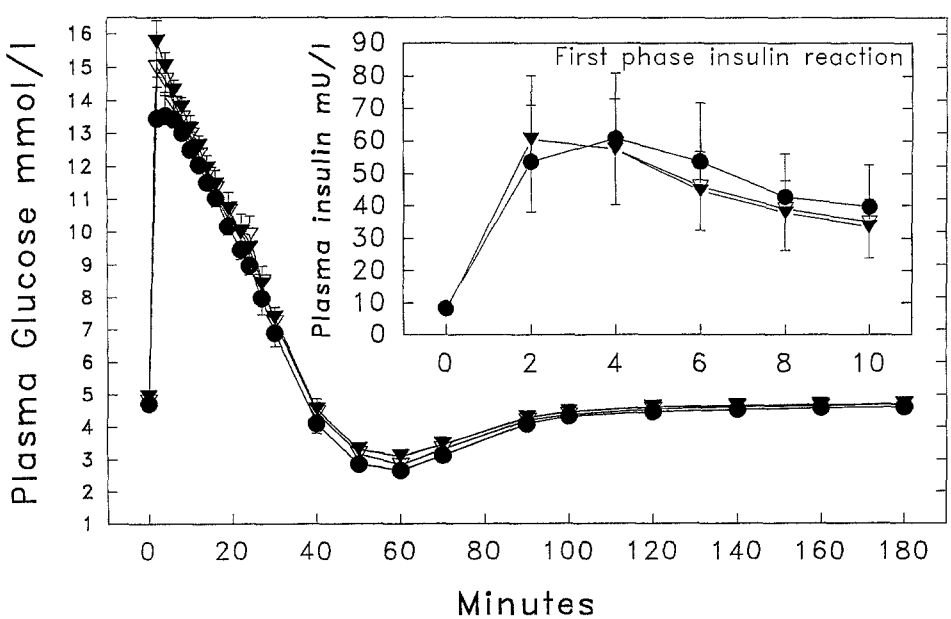

Fig 1. Plasma glucose (0 to 180 minutes) and insulin (0 to 10 minutes) concentrations during the FSIGTs. Glucose 0.3 g/kg was given at 0 minutes and insulin 0.03 mU at 20 minutes. ●, Baseline diet; ▽, stearic diet; ▼, oleic diet.

Table 6. Serum FVII:C Activity and Fibrinogen Concentration After Consumption of the Baseline Diet and Experimental Diets

	Baseline Diet (n = 14)	Stearic Diet (n = 14)	Oleic Diet (n = 14)	P*
FVII:C (%)	92.8 ± 2.7	97.6 ± 3.9	96.4 ± 3.9	NS
Fibrinogen (g/L)	3.1 ± 0.1	3.4 ± 0.2	3.3 ± 0.2	NS

*P for the difference between the experimental diet periods.

esters and triglycerides support data from the food records indicating that dietary compliance in this study was good.

There are only a few studies in which the effect of single saturated fatty acids on glucose and insulin metabolism has been examined. Schwab et al[22] reported recently the effects of lauric acid– and palmitic acid–enriched diets on glucose and insulin metabolism in young healthy females. No differences in S_G, S_I, or insulin secretion measured by the FSIGT were found when 4 E% monounsaturated fatty acids in the baseline diet was replaced with either lauric or palmitic acid. In murine islets, prior incubation with stearic acid resulted in diminished insulin secretion in response to glucose stimulation.[1] On the other hand, in rat adipocytes, stearic acid was shown to stimulate glucose transport in a study by Hunnicutt et al.[31] In the present study, the FSIGT was used to evaluate the effect of stearic acid on glucose and insulin metabolism. The FSIGT is considered a practical and reproducible method with acceptable intraindividual variation in young healthy subjects.[32] Based on epidemiological data, saturated fat has been associated with the deterioration[8-12] and unsaturated fat with the improvement[33] of glucose tolerance, but in this study, the effect of stearic acid on glucose and insulin metabolism was similar to that of oleic acid. These results describe the effect of short-term changes in stearic acid intake in young healthy women. Although the results may be more pronounced had the duration of the dietary intervention been longer or the characteristics of the study subjects differed, it is highly unlikely that the study outcome would have been altered.

Compatible with many previous studies,[16,17,34,35] the effect on serum lipids and lipoproteins was similar to that of oleic acid. However, it should be noted that an increase in the proportion of both oleic acid and stearic acid in serum triglycerides was seen after consumption of the stearic diet. This probably reflects the endogenous conversion of stearic acid to oleic acid, which has been suggested as one of the potential mechanisms for the neutral effects of stearic acid on lipid metabolism. This hypothesis was supported by animal experiments wherein a high conversion rate of stearic acid to oleic acid was demonstrated in rodent liver triglycerides[36] and mouse macrophage phospholipids.[37] In two recent human studies[38,39] that have addressed this issue, the estimate for the conversion rate of stearic acid to oleic acid varied from 9% to 14%. Thus, the conversion of stearic acid to oleic acid may contribute to the neutral effect of stearate on glucose and lipid metabolism observed in the present study, but it is unlikely that this pathway is the major mechanism.

It has been proposed that stearic acid is not absorbed as well as the other fatty acids, and this could be one explanation for the unique effects of stearic acid. In fact, in some studies stearic acid has been found to be absorbed less well than other fatty acids,[40-42] but in other studies no difference in absorbability compared with other fatty acids was seen.[43,44] There was no significant difference in body weight after the experimental diet periods in the present study. Furthermore, consumption of both the stearic diet and oleic diet resulted in significant increases in the proportion of stearic acid and oleic acid in serum triglycerides and cholesteryl esters, respectively. Thus, it seems unlikely that the effect of stearic acid in the present study could be explained by a lower absorption of this fatty acid.

There are only a few in vivo studies on the effect of stearic acid on coagulation factors. With in vitro studies, stearic acid seems to promote coagulation.[18,19] So far, the results of in vivo studies are contradictory. In the metabolic feeding study by Tholstrup et al,[20] stearic acid resulted in lower FVII:C activity compared with fats high in saturated fatty acids with 12 to 16 carbon atoms. The duration of the diet periods was 3 weeks. In the intervention study by Mitropoulos et al,[21] plasma FVII:C was 6.5% and 13.1% higher after unsaturated- and saturated-fat diet periods, respectively, than after a low-fat diet. The diet periods lasted 4 weeks each. In addition, the plasma concentration of stearic acid had a strong positive association with FVII:C. In the present study, the high–stearic acid diet did not affect the level of coagulation factors compared with the high–oleic acid diet.

In conclusion, a high–stearic acid diet had a similar effect on serum lipids, lipoproteins, and coagulation factors as a high–oleic acid diet. Furthermore, stearic acid did not deteriorate glucose tolerance and insulin sensitivity.

ACKNOWLEDGMENT

We thank Tom Krusius and Elina Vahtera from the Blood Service, Finnish Red Cross, Helsinki, Finland, for analyzing the coagulation factors. We also thank Fazer Chocolate, Van den Bergh Foods, and Valio, Helsinki, Finland, for supplying the special fats and dairy products for the study participants.

REFERENCES

1. Opara EC, Garfinkel M, Hubbard VS, et al: Effect of fatty acids on insulin release: Role of chain length and degree of unsaturation. Am J Physiol 266:E635-E639, 1994

2. Miteo H, Hashizume Y, Hanaki Y, et al: Chemical specificity of short-chain fatty acids in stimulating insulin and glucagon secretion in sheep. Am J Physiol 267:E234-E241, 1994

3. Warnotte C, Gilon P, Nenquin M, et al: Mechanisms of the stimulation of insulin release by saturated fatty acids. A study of palmitate effects in mouse β-cells. Diabetes 43:703-711, 1994

4. Zhou YP, Grill VE: Long-term exposure of rat pancreatic islets to fatty acids inhibits glucose-induced insulin secretion and biosynthesis through a glucose fatty acid cycle. J Clin Invest 93:870-876, 1994

5. Storlien LH, Jenkins AB, Chisholm DJ, et al: Influence of dietary fat composition on development of insulin resistance in rats. Relationship to muscle triglyceride and ω-3 fatty acids in muscle phospholipid. Diabetes 40:280-289, 1991

6. Pedersen O, Kahn RC, Flier JS, et al: High-fat feeding causes insulin resistance and a marked decrease in the expression of glucose transporters (Glut 4) in fat cells of rats. Endocrinology 129:771-777, 1991

7. Buchanan T, Fisler JS, Underberger S, et al: Whole body insulin sensitivity in Osborne-Mendel and S 5B/Pl rats eating a low- or high-fat diet. Am J Physiol 263:R785-R789, 1992

8. Lovejoy J, DiGirolamo M: Habitual dietary intake and insulin sensitivity in lean and obese adults. Am J Clin Nutr 55:1174-1179, 1992

9. Parker DR, Weiss ST, Troisi R, et al: Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: The Normative Aging Study. Am J Clin Nutr 58:129-136, 1993

10. Marshall JA, Hamman RF, Baxter J: High-fat, low-carbohydrate diet and the etiology of non–insulin-dependent diabetes mellitus: The San Luis Valley Diabetes Study. Am J Epidemiol 134:590-603, 1991

11. Marshall JA, Shetterly S, Hoag S, et al: Dietary fat predicts conversion from impaired glucose tolerance to NIDDM. The San Luis Valley Diabetes Study. Diabetes Care 17:50-56, 1994

12. Maron DJ, Fair JM, Haskell WL, et al: Saturated fat intake and insulin resistance in men with coronary artery disease. Circulation 84:2020-2027, 1991

13. Uusitupa M, Schwab U, Mäkimattila S, et al: Effects of two high-fat diets with different fatty acid composition on glucose and lipid metabolism in healthy young women. Am J Clin Nutr 59:1310-1316, 1994

14. Vessby B, Gustafsson I-B, Boberg J, et al: Substituting polyunsaturated for saturated fat as a single change in a Swedish diet: Effects on serum lipoprotein metabolism and glucose tolerance in patients with hyperlipoproteinaemia. Eur J Clin Invest 10:193-202, 1980

15. Heine RJ, Mulder C, Popp-Snijders C, et al: Linoleic-acid–enriched diet: Long-term effects on serum lipoprotein and apolipoprotein concentrations and insulin sensitivity in noninsulin-dependent diabetic patients. Am J Clin Nutr 49:448-456, 1989

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

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

18. Connor W: The acceleration of thrombus formation by certain fatty acids. J Clin Invest 41:1199-1205, 1962

19. Botti RE, Ratnoff OD: The clot-promoting effect of soaps of long-chain saturated fatty acids. J Clin Invest 42:1569-1577, 1963

20. Tholstrup T, Marckmann P, Jespersen J, et al: 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 59:371-377, 1994

21. Mitropoulos KA, Miller GJ, Martin JC, et al: Dietary fat induces changes in factor VII coagulant activity through effects on plasma free stearic acid concentration. Arterioscler Thromb 14:214-222, 1994

22. Schwab US, Niskanen LK, Maliranta HM, et al: Lauric and palmitic acid enriched diets have minimal impact on serum lipid and lipoprotein concentrations and glucose metabolism in healthy women. J Nutr 125:466-473, 1995

23. Schwab US, Maliranta HM, Sarkkinen ES, et al: 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. Metabolism 45:143-149, 1996

24. Rastas M, Seppänen R, Knuts L-R, et al: Nutrient Composition of Foods. Helsinki, Finland, Social Insurance Institution, 1992

25. 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

26. 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

27. Salomaa V, Rasi V, Pekkanen J, et al: Haemostatic factors and prevalent coronary heart disease; the FINRISK Haemostasis Study. Eur Heart J 15:1293-1299, 1994

28. Bergman RN: Toward physiological understanding of glucose tolerance. Minimal model approach. Diabetes 38:1512-1527, 1989

29. Pacini G, Bergman RN: A computer program to calculate insulin sensitivity and pancreatic responsivity from the frequently sampled intravenous glucose tolerance test. Comput Methods Programs Biomed 23:112-122, 1986

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

31. Hunnicutt JW, Hardy RW, Williford J, et al: Saturated fatty acid–induced insulin resistance in rat adipocytes. Diabetes 43:540-545, 1994

32. Ferrari P, Alleman Y, Shaw S, et al: Reproducibility of insulin sensitivity measured by the minimal model method. Diabetologia 34:327-330, 1991

33. Colditz GA, Manson JE, Stampfer MJ, et al: Diet and risk of clinical diabetes in women. Am J Clin Nutr 55:1018-1023, 1992

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

35. 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

36. Bonanome A, Bennet M, Grundy SM: Metabolic effects of dietary stearic acid in mice: Changes in the fatty acid composition of triglycerides and phospholipids in various tissues. Atherosclerosis 94:119-127, 1992

37. Garg ML: Stearic acid desaturation and incorporation into murine peritoneal macrophage lipids. J Clin Biochem Nutr 13:169-178, 1992

38. Emken EA, Adlof RO, Rohwedder WK, et al: Influence of linoleic acid on desaturation and uptake of deuterium-labeled palmitic and stearic acids in humans. Biochim Biophys Acta 1170:173-181, 1993

39. Rhee SK, Kayani AJ, Ciszek A, et al: Desaturation and interconversion of dietary stearic and palmitic acids in human plasma and lipoproteins. Am J Clin Nutr 65:451-458, 1997

40. 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

41. 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

42. Dougherty RM, Allman MA, Iacono JM: Effects of diets containing high or low amounts of stearic acid on plasma lipoprotein factors and fecal fatty acid excretion of men. Am J Clin Nutr 61:1120-1128, 1995

43. Mattson FH: The absorbability of stearic acid when fed as a simple or mixed triglyceride. J Nutr 119:338-342, 1959

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