

Effects of increasing dietary palmitoleic acid compared with palmitic and oleic acids on plasma lipids of hypercholesterolemic men

Paul Nestel,¹ Peter Clifton, and Manny Noakes

CSIRO Division of Human Nutrition, Adelaide 5000, Australia

Abstract Palmitoleic acid is a minor monounsaturated fatty acid in the human diet and in blood plasma. Because macadamia oil is at least one potentially large source of palmitoleic acid, we tested its effect on plasma lipid levels against two other dietary fatty acids, oleic acid and palmitic acid. The dietary adjustments, through the use of supplements, provided comparisons of the three test fatty acids in which palmitoleic could be judged as behaving either like a saturated or a monounsaturated acid. Thirty-four hypercholesterolemic men ate the three test diets in random order in 3-week periods. Plasma total cholesterol and low density lipoprotein (LDL) cholesterol concentrations were similar with palmitic and palmitoleic acids and significantly higher than with oleic acid. High density lipoprotein (HDL) cholesterol was significantly lower with palmitoleic than with palmitic acid. ■ The study confirms that, at least in hypercholesterolemic men, a modest increase in palmitic acid (+4% en) raises LDL cholesterol relative to oleic acid (+3% en), even when dietary cholesterol is low (< 165 mg/day). Palmitoleic acid (+4% en) behaves like a saturated and not a monounsaturated fatty acid in its effect on LDL cholesterol.—Nestel, P., P. Clifton, and M. Noakes. Effects of increasing dietary palmitoleic acid compared with palmitic and oleic acids on plasma lipids of hypercholesterolemic men. *J. Lipid Res.* 1994. 35: 656–662.

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To lower LDL cholesterol by dietary means is the initial step in the management of hypercholesterolemic subjects (1). While the overall objective is to reduce the consumption of saturated fatty acids and of cholesterol, the optimal dietary substitution remains controversial. A case can be made for a mix of starchy foods and of unsaturated fatty acids comprising oleic acid and lesser amounts of linoleic, α -linolenic, and longer chain n-3 fatty acids (2). The advantages of oleic acid have been recognized in recent years, yet virtually no attention has been paid to palmitoleic acid, the monounsaturated fatty acid with a 16 carbon chain (oleic is 18 carbons in length). Macadamia oil is a good source of palmitoleic acid.

Despite the general indictment of saturated fatty acids, it is clear that not all of the longer chain fatty acids have

equal cholesterol-raising effects. Stearic (18 carbons) has little, if any, effect (3), whereas myristic (14 carbons) is the most potent (4) although present importantly only in dairy fat, coconut oil, and palm kernel oil. Although dietary palmitic acid is generally regarded as cholesterol raising (4), some have claimed that it has minimal cholesterol-raising potential (5, 6), or is neutral when cholesterol intake is low or plasma cholesterol levels are normal (5). Others have consistently found that palmitic acid, usually tested as palm oil, raises LDL cholesterol significantly relative to oleic or linoleic acids (4, 7, 8). We have observed similar increases in LDL cholesterol with dietary enrichment by palm oil, butter fat, or elaidic acid, a *trans* fatty acid formed during hydrogenation of polyunsaturated oils, relative to oleic acid (8). A recent study comparing different fats and oils concluded that palmitic acid raises LDL cholesterol by about as much as does myristic acid (9).

The primary aim of the present clinical trial was to determine whether dietary palmitoleic acid is as effective as oleic acid in lowering LDL cholesterol. We included in the comparison a third diet rich in palmitic acid, so that the three diets were enriched almost equivalently by one of the three test fatty acids. We tested whether the effect of palmitoleic acid would resemble the effect of a monounsaturated fatty acid (oleic) or a saturated fatty acid (palmitic acid).

EXPERIMENTAL METHODS

Subjects

Thirty-four men with mild to moderately elevated plasma cholesterol were enrolled into the 11-week trial.

Abbreviations: LDL, low density lipoprotein; HDL, high density lipoprotein; VLDL, very low density lipoprotein.

¹To whom correspondence and reprint should be addressed.

They had been screened from a healthy volunteer population. None were being treated for hyperlipidemia or suffered from any metabolic disorder, or were taking medication that might influence plasma lipids. Other exclusion criteria were ethanol intake > 40 g/day (actual intake averaged < 10 g/day) and heavy smoking (> 20 cigarettes/day). Informed consent was obtained and the study was approved by the Human Ethics Committee. The average age was 49 ± 9.8 (mean \pm SD) years; the average body mass index was 25.7 ± 2.96 kg/m². (Plasma lipids are presented in Results.)

Study design

The study design comprised four periods, an initial 7–10 day baseline period and three 3-week intervention periods with all subjects participating in all dietary segments.

After the baseline period, the subjects were randomized into three groups who ate the three test fatty acid-containing diets in differing order: Group 1: palmitoleic, oleic, palmitic; Group 2: palmitic, palmitoleic, oleic; Group 3: oleic, palmitic, palmitoleic. Subjects were not told of the nature of the fat source in the dietary supplements. Each test diet was thus tested either first, second, or third so that we could correct for any effects of time and of treatment order.

The oil formulations were designed to test whether palmitoleic acid would act like oleic acid or like palmitic acid (Tables 1, 2). If palmitoleic acid were to act as a monounsaturate, the combined palmitoleic and oleic acids in the palmitoleic diet equalled 17.3% energy, similar to the oleic acid in the oleic diet supplement. On the other hand, palmitic plus palmitoleic in the palmitoleic acid supplement (6.4%) roughly equalled palmitic (5.8%) in the palmitic diet supplement.

The theoretical differences in LDL cholesterol between the diets were computed from the equation recently proposed by Mensink and Katan (10) which includes monounsaturates. Although the potential effects are modest, they were sufficient to demonstrate a significant effect if one existed.

Test diets

During the baseline period, subjects were asked to consume their normal diets and to become familiar with keeping diet records and quantitating their fat intake with a view to lowering it toward that required during the intervention phases. Fat intake was ascertained using simplified food tables in the form of a fat counter. During the intervention phases, subjects were advised to maintain their background fat intake to less than 15% energy with an additional theoretical 25% fat energy coming from the test fats in the form of a 350-ml (42 g fat) aliquoted milk beverage and 25 g (20 g fat) margarine, both of which were taken on a daily basis.

Background diets

The background diet was obtained from a combination of self-selected foods such as meat and dairy products of known fat content and low-fat frozen meals (less than 10 g fat/meal) that were provided three times per week to facilitate meal planning. Subjects used their food tables to keep their background fat intake to a predetermined level and documented all foods contributing fat on a daily basis. A 3-day weighed food record was also kept during each test phase. Specific advice was given to avoid all margarines and oils other than those provided as the test fats, to avoid specific foods/nutritional supplements that may have had an independent effect on plasma lipids, and to maintain a similar pattern of eating throughout the study.

Test supplements

The test oils were prepared by Meadow Lea Foods (Sydney, Australia) and also incorporated into margarines. The oils were emulsified into vanilla-flavored drinks with skim milk and lecithin and subsequently homogenized and pasteurized. They were aliquoted into 350-ml (42 g fat) portions and provided to subjects in frozen form. The oils were formulated from macadamia oil, high oleic Trisun oil, and palm oil, and were partially hydrogenated in the margarines which were provided in tubs; 25 g (20 g fat) was used daily. The major fatty acids of the supplements are shown in Table 1, and Table 2 shows their final contribution to dietary fatty acids.

Dietary monitoring

Two subjects complained of gastrointestinal discomfort during the macadamia oil-rich diet, the only oil with which we were unfamiliar, but this effect was transient. In general, palatability of the test drinks was very high for the macadamia oil drink and lower for the palm oil drink, which differed a little in consistency compared to the other two. All subjects reported consuming the test drinks and margarines as directed.

TABLE 1. Fatty acid composition of the three sets of supplements

Fatty Acid %	Palmitoleic		Oleic		Palmitic	
	Oil	Margarine	Oil	Margarine	Oil	Margarine
C12:0 Lauric		0.3				0.2
C14:0 Myristic	0.8	0.8	0.2	0.4	0.6	0.6
C16:0 Palmitic	9.0	12.4	8.9	13.0	25.2	23.3
C18:0 Stearic	3.2	4.1	3.0	4.5	3.7	5.2
C20:0 Arachidic			0.4	0.3		0.4
C22:0 Behenic	0.7		0.8	0.6		0.5
C16:1 Palmitoleic	18.4	13.9				
C18:1 Oleic	59.6	49.1	77.8	58.9	62.9	49.0
C18:1 Elaidic		13.1		15.1		14.7
C20:1 Gadoleic	2.6	2.0	0.4			
C18:2 Linoleic	3.2	2.3	6.7	5.6	6.5	5.1
C18:3 Linolenic	2.5	2.0	1.8	1.5	1.1	1.0

TABLE 2. Contribution of supplement fatty acids to dietary energy (%)

Fatty Acids	Supplement		
	Palmitoleic	Oleic	Palmitic
C16:0 Palmitic	2.4	2.4	5.8
C18:0 Stearic	0.8	0.8	1.0
C16:1 Palmitoleic	4.0	0	0
C18:1 Oleic	13.3	17.0	13.8
C18:1 Elaidic	1.0	1.2	1.1
C18:2 Linoleic	0.7	1.5	1.4
C18:3 Linolenic	0.6	0.4	0.3

Subjects were interviewed on four occasions during each 3-week period for changes in body weight, and diet records were reviewed extensively by the research dietitian (MN) on two of these occasions.

At the commencement of the study the subjects were provided with digital electronic scales and instructed to record all food and beverage intake on 3 consecutive days (Sunday, Monday, Tuesday) during each study period as well as recording fat sources and intake on a daily basis. Food records were checked with the subject for completeness and compared to daily fat intakes (excluding the test supplements) to ensure that they were representative of that individual's average fat intake. One subject did not maintain an adequately low fat intake and his dietary records were excluded from the analysis. A total of 9 days (excluding the baseline phase) of detailed food records were kept for each subject and subsequently coded and analyzed. Nutrient intakes were calculated by a computer database of foods in which nutrient composition was based on McCance and Widdowson's *The Composition of Foods* (11) modified to include Australian foods from published sources, commercial sources, and, in the case of the dietary supplements and frozen meals, from direct food analysis.

Measurements

Blood was drawn from fasting subjects on 2 consecutive days at the end of the baseline period and three times at the end of each of the three other periods. The values in each test period were averaged.

Plasma total cholesterol and triglyceride concentrations were determined by enzymatic methods (12, 13) on an automated analyzer (Cobas Bio, Hoffmann-La Roche, Basel, Switzerland). High density lipoprotein (HDL) cholesterol was determined after precipitating low density lipoprotein (LDL) and very low density lipoprotein (VLDL) with PEG 6000 (14). LDL cholesterol was calculated using the equation of Friedewald, Levy, and Fredrickson (15).

Plasma fatty acids were analyzed by gas chromatography in each subject during each of the four dietary periods

(16). The capillary column [100 m × 0.22 mm i.d. BP × 70 (SGE) had the capacity to resolve *trans* fatty acids. The *trans* fatty acids in the test fats were quantified by gas chromatography.

Statistical analysis

Repeated measures analyses of variance with and without covariates were performed using Genstat 5, release 1.3, 1988 (Lawes Agricultural Trust, Rothamsted Experimental Station) on a Sun Workstation. Covariates included in the equation were linear and quadratic functions of time and treatment order.

RESULTS

Dietary compliance

Mean body weights did not differ significantly between dietary periods, nor were individual changes in body weight significant (mean weights at the end of the four periods were: 78.5, 78.3, 78.4, and 78.5 kg). The food diaries and records of daily fat intake showed that all subjects complied well to both the low fat background diet and the daily consumption of the foods containing the test fats. The patterns of food consumption are shown in **Table 3**. In terms of macronutrient intake, the values did not differ among the treatment periods and the calculated consumption data achieved their targets in terms of total fat (37% en) and the proportions of classes of fatty acids. The low consumption of cholesterol should be noted (< 200 mg daily).

Plasma lipids and lipoproteins (Table 4)

There were significant time effects for total cholesterol ($P < 0.001$), for LDL cholesterol ($P < 0.003$), and for HDL cholesterol ($P < 0.001$). Time and order of treatments were therefore included as covariates in the statistical analyses of the effects of treatments. Treatment order had no significant effect when time was included as a covariate.

For both total cholesterol and LDL cholesterol the oleic acid diet resulted in highly significantly lower values than either the palmitic or palmitoleic diets and the degree of significance increased slightly when the time-effect was taken into account in the comparison of palmitoleic and oleic effects. The differences between the palmitoleic and palmitic acid diets were small and insignificant for both total and LDL cholesterol. There were no significant differences between diets for triglyceride, but HDL cholesterol was significantly higher with the palmitic acid than with the palmitoleic acid supplement.

Interestingly, the differences between the mean values for LDL cholesterol were close to, but somewhat higher, than those predicted: -0.15 mmol/l and -0.17 mmol/l for predicted and observed differences between oleic and palmitoleic (assuming the latter as a saturate) and -0.13

TABLE 3. Nutritional profile of diets consumed during the three treatment periods as assessed from 3-day weighed food records. Data for the three groups have been pooled

Nutrient	Palmitoleic	Oleic	Palmitic
Protein % en	15.9 ± 0.5	15.6 ± 0.5	15.2 ± 0.5
Fat % en	37.6 ± 1.0	36.5 ± 0.9	37.6 ± 0.9
Carbohydrate % en	47.1 ± 1.2	48.0 ± 1.1	47.7 ± 1.1
Energy, kcal	2329 ± 68	2308 ± 70	2348 ± 64
Fibre, g	27.3 ± 1.9	30.2 ± 2.4	28.5 ± 2.0
Cholesterol, mg	162 ± 13	147 ± 10	156 ± 11
Alcohol, g	7.9 ± 1.7	9.1 ± 1.6	7.7 ± 1.8
Polyunsaturates % en	3.0 ± 0.2	3.4 ± 0.1	3.3 ± 0.1
Monounsaturates % en	21.9 ± 0.6	20.9 ± 0.5	18.3 ± 0.5
Saturates % en	8.0 ± 0.3	7.7 ± 0.3	11.4 ± 0.3
% Capric C10:0	0.08 ± 0.01	0.08 ± 0.01	0.08 ± 0.01
% Lauric C12:0	0.17 ± 0.02	0.15 ± 0.02	0.16 ± 0.01
% Myristic C14:0	0.71 ± 0.05	0.56 ± 0.04	0.66 ± 0.03
% Palmitic C16:0	4.77 ± 0.16	4.62 ± 0.13	8.03 ± 0.21
% Stearic C18:0	1.87 ± 0.08	1.77 ± 0.07	2.03 ± 0.09
% Palmitoleic C16:1	4.13 ± 0.11	0.31 ± 0.02	0.32 ± 0.02
% Oleic C18:1	16.9 ± 0.45	20.3 ± 0.52	17.6 ± 0.45
% Elaidic C18:1 <i>trans</i>	2.01 ± 0.03	2.22 ± 0.04	2.14 ± 0.05
% Linoleic C18:2	2.09 ± 0.15	2.72 ± 0.07	2.67 ± 0.08
% Linolenic C18:3	0.71 ± 0.02	0.55 ± 0.9	0.42 ± 0.01
% Eicosenoic C20:1	0.65 ± 0.02	0.16 ± 0.02	0.13 ± 0.02

Values given as mean ± SEM.

mmol/l and -0.16 mmol/l for predicted and observed differences between oleic and palmitic.

Nevertheless, the confidence limits around the mean differences for LDL cholesterol were large: palmitoleic-oleic = 0.17 (0.01-0.35) mmol/l; palmitic-oleic = 0.16 (0.02-0.31) mmol/l; palmitoleic-palmitic = 0.01 (-0.18-0.17) mmol/l.

Thus palmitoleic resembled the saturated fatty acid, palmitic, rather than the monounsaturated fatty acid, oleic. However, the differences, though highly significant, need to be viewed with some caution given the variability in responses.

Plasma fatty acids

The percentage values for the major fatty acids are shown in Table 5. Eating more palmitoleic acid increased plasma palmitoleic acid by about 60% and also led to a small increase in stearic acid (compared to the palmitic

diet) and a small reduction in α -linolenic acid (compared with the oleic diet, despite increased consumption). Eating more palmitic acid increased the percentage of that fatty acid in comparison with the other two diets. Plasma oleic acid was not raised significantly during the oleic diet.

DISCUSSION

The results show that the study had the power to differentiate between the effects of oleic acid and palmitic acid on LDL cholesterol. An increase in dietary palmitic acid equal to about 4% energy, in comparison with a similar increase in dietary oleic acid, led to a highly significant difference in LDL cholesterol. This is consistent with the majority of similar studies, although the differences in fatty acid intake have generally been greater

TABLE 4. Plasma lipids at baseline and after the dietary interventions and differences achieving statistical significance

Diet	Total Cholesterol	LDL Cholesterol	HDL Cholesterol	Triglyceride
<i>mean ± SD, mmol/l</i>				
Baseline	5.83 ± 0.62	4.22 ± 0.61	1.08 ± 0.25	1.18 ± 0.42
Palmitoleic	5.73 ± 0.61	4.06 ± 0.63	1.10 ± 0.23	1.28 ± 0.50
Oleic	5.58 ± 0.63	3.89 ± 0.60	1.12 ± 0.24	1.27 ± 0.53
Palmitic	5.78 ± 0.73	4.05 ± 0.64	1.14 ± 0.24	1.30 ± 0.58

Differences in total cholesterol: palmitoleic vs. oleic: 0.15 mmol/l ($P < 0.05$); adjusted for time $P < 0.05$; palmitic vs. oleic: 0.20 mmol/l ($P < 0.01$); adjusted for time $P < 0.01$. Differences in LDL cholesterol: palmitoleic vs. oleic: 0.17 mmol/l ($P < 0.02$); adjusted for time $P < 0.01$; palmitic vs. oleic: 0.16 mmol/l ($P < 0.02$); adjusted for time $P < 0.02$. Difference in HDL cholesterol: palmitoleic vs. palmitic: 0.04 mmol/l ($P < 0.02$); adjusted for time $P < 0.005$.

TABLE 5. Plasma fatty acid composition

Diet	Plasma Fatty Acid %											
	14:0	16:0	16:1	18:0	18:1	18:2	18:3	20:3	20:4	20:5	22:5	22:6
Baseline	0.8	20.9	3.3	6.4	24.5	30.6	0.6	1.5	7.1	1.0	0.7	2.7
Palmitoleic	0.8	20.7	5.4	6.7	31.0	24.5	0.4	1.5	6.0	1.0	0.5	1.5
Oleic	0.8	20.9	3.1	6.3	32.3	25.6	0.6	1.4	5.9	1.1	0.5	1.5
Palmitic	0.8	22.5	3.2	6.4	30.9	25.6	0.6	1.5	5.4	1.0	0.5	1.6

Palmitoleic diet: increase 16:1 $P < 0.001$ vs. both; increase 18:0 $P < 0.01$ vs. palmitic; decrease 18:3 $P < 0.001$ vs. oleic, $P < 0.01$ vs. palmitic. Palmitic diet: increase 16:0 $P < 0.0001$ vs. both.

(4, 7, 8). We were constrained to a more modest difference in order to test palmitoleic acid which is not sufficiently abundant in naturally occurring oils. In view of the strength of the result in the case of palmitic acid, it seems highly probable that the outcome for palmitoleic acid can be accepted with equal confidence. The average LDL cholesterol values with the palmitoleic acid and the palmitic acid diets were similar and each differed significantly from the oleic acid diet. Nevertheless, as pointed out earlier, the variances around the mean differences were relatively large, giving rise to a degree of caution.

Palmitoleic acid, therefore, resembled the saturated fatty acid and not the monounsaturated fatty acid in its effect on the LDL cholesterol concentration. The same conclusion can be drawn from the plasma total cholesterol levels, but because of differences in HDL cholesterol (in themselves significant for the palmitic vs. palmitoleic comparison), the influence of palmitoleic acid reached greater statistical significance for LDL than for total cholesterol.

There was also an effect of time on both LDL and HDL cholesterol with a tendency for the concentration to rise during the third and final dietary period, by an average of 0.21 mmol/l for LDL, irrespective of the nature of the fatty acid supplement. This is not explained on the basis of food intake records, which at face value, showed full compliance, with similar intakes of energy and macronutrients during the three periods. Rather it suggests partial regression to the pre-intervention values which is not unusual in interventions of any kind (17). However, the design of the experiment, which ensured that each of the three supplements was tested once during the first or second or third period, allowed order of treatment and the effect of time to be excluded. When these factors were accounted for, palmitoleic acid still behaved as a saturated fatty acid; in fact, in the comparison with oleic acid the statistical significance firmed.

This raises the question of the metabolic fate of palmitoleic acid. It was clearly absorbed as its concentration in plasma rose by an average of about 60%. Palmitoleic acid would normally be elongated to oleic acid and, although this did not lead to a significant increase in plasma oleate, it is not surprising given the much larger

dietary intake of oleic acid. It is noteworthy that the plasma oleic acid concentration did not increase even during the oleic acid-enriched diet which is not unusual with moderate increases in dietary oleate (18).

If, as seems theoretically probable, palmitoleic acid was destined to be converted to oleic acid, why did its effect on LDL cholesterol differ? This would depend on the fractional rate of conversion to oleic acid and the absolute amount of such conversion. This rate may be slow or conversion only partial. Then again, the different positions of the double bond in oleic and palmitoleic acids may be important. Clearly, as moderate amounts of palmitoleic acid are always found in plasma, either of these possibilities exists. Retroconversion to palmitic acid is most unlikely and there was no such indication from the plasma palmitate level. A dietary intervention that leads to increased plasma palmitoleic acid is a low-fat high-carbohydrate diet which stimulates lipogenesis (19). However, the LDL cholesterol level falls with carbohydrate-rich diets despite increased endogenous fluxes of palmitic and palmitoleic acids. Why then should the source of these two fatty acids (exogenous versus endogenous) result in diverse effects on LDL cholesterol? After all, conversion to the "cholesterol-neutral" stearate and oleate occurs under both circumstances. The one obvious difference is in the amount of fat and in the divergent metabolic effects of dietary carbohydrate and of dietary fat on LDL metabolism. The removal of LDL from plasma, measured as its fractional catabolic rate, is stimulated by dietary carbohydrate (20) and its production from VLDL is decreased (21). This effect has been ascribed to a change in the conformation of apolipoprotein B and altered exposure of epitopes that interact with the LDL receptor (22).

Palmitic acid fed to animals within a cholesterol-rich diet will further raise the LDL cholesterol concentration (23). Experiments with other saturated fats have shown that the rise in LDL reflected down-regulation of LDL receptor activity (24, 25). The overall response is influenced by the presence of dietary linoleic acid and of cholesterol (5, 23); given the appropriate circumstances, dietary palmitic acid will raise the LDL cholesterol concentration. This is not a general characteristic of saturated fatty acids and is shared only with myristic acid (14

carbons) and probably with lauric acid (12 carbons) (4). Stearic acid (18 carbons) no longer exhibits this characteristic (3). There are other metabolic effects exerted by fatty acids that show hierarchical change with elongation and polyunsaturation. The inhibition of triglyceride secretion from the liver increases in this manner: secretion is stimulated by oleic acid and then declines to outright inhibition with eicosapentaenoic acid (26).

There is, therefore, no a priori reason why palmitoleic and oleic acids should influence LDL metabolism similarly. Oleic acid (within olive oil) is itself not as effective at stimulating LDL clearance as is linoleic acid (within corn oil) in guinea pigs (27). Linoleic acid stimulates LDL receptor-mediated LDL removal, at least in animal experiments (28); nevertheless as dietary oleic acid and linoleic acid lead to similar LDL cholesterol-lowering when substituted for saturated fatty acids in humans (29), it is likely that both substitutions improve LDL removal capacity.

Our results, therefore, imply that palmitoleic acid, at least in the amount eaten, is less potent than oleic acid in derepressing LDL receptor activity. This may be related to the lengths of the fatty acids or the positions of the double bond (n-7 for palmitoleic and n-9 for oleic). A differential effect on LDL production from VLDL is also possible but less likely in view of the high capacity of oleic acid to stimulate hepatic triglyceride production and lipoprotein secretion (30). The influence of palmitoleic acid on LDL receptor activity has not been tested directly. Further, palmitoleic acid also lowered HDL cholesterol when compared with palmitic acid and in this respect resembled findings with elaidic acid (7). We have observed increased cholesteryl ester transfer protein activity in similar subjects eating a diet rich in elaidic acid (M. Abbey and P. Nestel, unpublished observation); one outcome of such a change is to lower HDL cholesterol.

The LDL-raising effect of palmitic acid remains controversial. Most (4, 7, 8) but by no means all (5, 6) reports of test subjects eating palmitic acid-rich palm oil have shown higher LDL cholesterol in comparison with unsaturated oils such as safflower oil or canola oil. Hayes and Khosla (5), in particular, have argued that palmitic acid raises LDL significantly only in the presence of dietary cholesterol and/or in the absence of counterbalancing amounts of linoleic acid. They have furthermore shown that myristic acid is more potent than palmitic acid in raising LDL in monkeys (5); in hamsters, myristic acid markedly inhibits LDL receptor-mediated removal of LDL (31).

Our present study shows that a quite modest substitution of palmitic acid (from palm oil) for oleic acid (from Trisun) results in a significantly increased LDL cholesterol concentration. This occurred in the context of a low cholesterol intake. It should, however, be noted that this occurred in middle-aged men whose average plasma

cholesterol level was moderately higher than the mean for Australian men of this age. This is important because we have shown that age, gender, and the LDL cholesterol concentration all influence the response to dietary saturated fat (32). Excess plasma cholesterol generated by eating saturated fat is transported in plasma lipoproteins; its distribution between LDL and HDL depends on the preceding factors. Proportionately less is carried in HDL₂ and more in LDL, in men than in women, in older than in younger men, and in men with higher pre-existing LDL cholesterol levels (32). Our present findings reinforce the validity of earlier conclusions that dietary palmitic acid is likely to raise the plasma cholesterol concentration in hypercholesterolemic men. Although palmitoleic acid appears to have a similar effect, it is conceivable that higher intakes that may substantially increase oleic acid formation may lead to different results. However, there is little support for this in the present study. ■

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