Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man

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Abstract Twenty patients consumed a liquid diet in which the predominant fatty acids were either saturated (Sat), monounsaturated (Mono), or polyunsaturated (Poly). The fats in these three diets comprised 40% of total calories and consisted of palm oil, high-oleic safflower oil, and high-linoleic safflower oil, respectively. During the third and fourth week of each dietary period, multiple samples of blood were taken and were analyzed for plasma total cholesterol (TC), triglycerides (TG), and cholesterol in lipoprotein fractions (VLDL-C, LDL-C, and HDL-C). Twelve of the patients had normal TG levels; in these patients, both Mono and Poly diets caused statistically significant and equal lowerings of plasma LDL-C, but the Poly diet lowered HDL-C levels more frequently than did the Mono diet. Neither diet changed the level of plasma TG. The proportions of total protein and the various lipid components in isolated fractions (VLDL, IDL, LDL, HDL) were not altered by the two diets. Eight patients had hypertriglyceridemia; these individuals showed considerable variability in response to Mono and Poly diets. Although there was a trend towards reductions in TC and LDL-C levels by both types of unsaturated fats, the changes were inconsistent; furthermore, HDL-C concentrations were low on the Sat diet and were unaffected by either the Mono or the Poly diet. ■ The results of this study show that oleic acid is as effective as linoleic acid in lowering LDL-C levels in normotriglyceridemic patients, and oleic acid seemingly reduces HDL-C levels less frequently than does linoleic acid. Neither type of unsaturated fat had striking effects on lipoprotein levels of hypertriglyceridemic patients.—**Mattson, F. H., and S. M. Grundy.** Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J. Lipid Res.* 1985. **26:** 194–202.

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Polyunsaturated fatty acids are known to reduce the plasma cholesterol when exchanged for saturated fatty acids. This has led to an emphasis on raising polyunsaturates in the diet; less attention has been given to decreasing saturates and, in fact, the consumption of saturated acids in the American diet has changed little (1). Recently, however, there is a growing concern that habitual intakes of large quantities of polyunsaturates may not be healthy. Their long-term safety has not been proven; they promote carcinogenesis in experimental animals (2), alter the composition of cell membranes (3), possibly raise risk for gallstones (4), and may reduce high density lipoproteins (HDL) (5–8).

These concerns about polyunsaturated fatty acids have led many investigators to favor carbohydrates as a replacement for saturated fatty acids. Rates of coronary heart disease (CHD) tend to be low in populations consuming high-carbohydrate, low-fat diets. These diets, however, are unpalatable to many people and alternative diets are needed. One possibility is to replace saturated fatty acids with monounsaturated fatty acids. The latter have been consumed in large quantities in the Mediterranean region where olive oil is used and where CHD rates are relatively low (9). If these fatty acids effectively lower cholesterol levels, they might be considered as an alternative to polyunsaturated fatty acids. Theoretical advantages of monounsaturates are that they are synthesized normally by the body and are less susceptible to chemical oxidation than polyunsaturates.

Of interest, little attention has been given to metabolic effects of monounsaturates. They are commonly thought to be "neutral" in their actions on plasma cholesterol levels. Unfortunately, no information is available about the relative influences of polyunsaturates and monounsaturates on the different lipoproteins of plasma. The purpose of the present study was to make this comparison.

Abbreviations: TC, total cholesterol; TG, triglycerides; C, cholesterol; VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

METHODS

Patients

Twenty patients were studied on the metabolic wards of the Veterans Administration Medical Centers in either Dallas, Texas or San Diego, California. Their clinical characteristics at the time of admission are shown in **Table 1.** All but two had plasma total cholesterol (TC) levels over 200 mg/dl at time of admission (mean = 263 ± 50(SD) mg/dl). Their admission levels of plasma triglycerides (TG) ranged from 111 to 496 mg/dl. Some patients had a history of atherosclerotic disease, but none had recent myocardial infarction, unstable angina pectoris, or congestive heart failure. Also, none had disease of the liver, gastrointestinal tract, kidneys, or endocrine system. The protocol used in this study was approved by the appropriate institutional review boards, and all patients gave informed consent for the studies.

Diets

Throughout the study, participants received a liquid formula diet (10), which supplied 40% of calories as fat, 44% as carbohydrate, and 16% as protein. To obtain a high intake of saturated, monounsaturated, or polyunsaturated fatty acids, the sole fats in these diets were palm oil, high-oleic safflower oil, or high-linoleic safflower oil, respectively. The distribution of fatty acids in these oils is given in **Table 2.** Assignment of the patients to the sequence of diets was in random order. Caloric intake was adjusted as needed to maintain the initial body weight. Each diet was consumed for 4 weeks. Fatty acids from random samples of diet were analyzed by gas-liquid chromatography to verify the correct diet.

TABLE 1. Clinical data

Patient	Age	Wt	Ideal Body Weight
	yr	*kg*	*%*
1	50	60	100
2	53	76	110
3	52	72	100
4	66	74	107
5	47	51	85
6	60	70	105
7	59	82	110
8	69	68	100
9	59	63	100
10	64	71	100
11	68	61	100
12	62	61	119
13	52	91	110
14	65	116	128
15	63	88	137
16	53	78	113
17	57	96	126
18	60	75	110
19	60	75	108
20	55	96	147

TABLE 2. Composition of dietary fats

Fatty Acid	Diet		
	Sat[a]	Mono[b]	Poly[c]
		wt %	
12:0	0.1	0.1	0.3
14:0	0.9	0.1	0.3
16:0	43.4	5.1	6.4
18:0	4.9	2.4	2.7
20:0	0.4	0.6	0.9
22:0		0.3	0.4
24:0			0.2
16:1	0.4	0.1	0.1
18:1	39.6	73.3	14.6
18:2	9.8	17.4	72.8
18:3	0.3	0.5	0.5
Sat, total	49.7	8.6	11.2
Mono, total	40.0	73.4	14.7
Poly, total	10.1	17.9	73.3
Sat, <18:0	44.4	5.8	9.7

[a]Palm oil.
[b]High oleic safflower oil.
[c]High linoleic safflower oil.

Blood samples

On days 17, 19, 20, 24, 26, and 27 of each period, fasting blood samples were drawn into tubes containing per ml of blood: 1.5 mg of EDTA, 1.0 mg of sodium azide, and 0.83 mg of *p*-chloromercuriphenol sulfonic acid. All samples were analyzed in the laboratory of the Lipid Research Clinic of the University of California, San Diego. For blood samples obtained in Dallas, the plasma was separated on site by centrifugation, packed in wet ice, and shipped to San Diego.

Each sample was analyzed by the Lipid Research Clinics procedures (11) for TC and TG on the Auto-Analyzer II and for cholesterol in very low density lipoproteins (VLDL-C), low density lipoproteins (LDL-C), and high density lipoproteins (HDL-C).

Equal portions of the six plasma samples for each dietary period were pooled. VLDL, intermediate density lipoproteins (IDL), LDL, and HDL were obtained for analysis by successive 24-hr preparative ultracentrifugations at densities 1.006, 1.019, 1.063, and 1.21 g/ml, respectively. The VLDL, LDL, and HDL fractions were suspended in saline of appropriate density and centrifuged again for 24 hr. The isolated LDL and HDL fractions were dialyzed to a density of 1.006 g/ml. All samples were stored at 4°C until compositional analyses were completed. Analyses were begun within 2 weeks. The procedures were the following: TC and TG with Auto-Analyzer II (11), free cholesterol and cholesteryl ester using the Boehringer Mannheim enzyme kit (12); total phospholipid by colorimetric determination of phospholipid (13); total protein on delipidated samples by a modification (14) of the method of Lowry et al. (15) using bovine serum albumin as a standard.

For each dietary period, two additional pools of plasma were prepared. One contained equal amounts of the plasma from the third week of each period (days 17, 19, and 20) and from the fourth week (days 24, 26, and 27). The HDL fraction was obtained by heparin-manganese precipitation; the method was identical to that of the Lipid Research Clinics procedure (11) except that 2 M manganese chloride was used for this isolation. HDL_2 was removed with dextran sulfate by the method of Gidez et al. (16); it was found that centrifugation at 10,000 rpm for 10 min was necessary to obtain complete precipitation of HDL_2 and a clear supernatant which contained HDL_3. The cholesterol content of the total HDL and HDL_3 was determined on the Auto-Analyzer II; that of HDL_2 was obtained by difference.

A comparison of lipoprotein levels for each subject of the three samples taken during week 3 with those taken during week 4 showed no differences. Therefore, the results for both weeks were pooled. Also, the plasma lipid and lipoprotein levels obtained on any diet could not be related to the sequence in which the fats were given.

RESULTS

The levels of TC, TG, VLDL-C, LDL-C, and HDL-C attained by all patients on each of the three diets are summarized in **Table 3.** Compared to the Sat diet, both unsaturated fatty acids caused significant reductions in TC and LDL-C, although there were no differences in degree of reductions between the two fats. No changes overall were produced by either unsaturated fat in levels of TG, VLDL-C, or HDL-C. However, considering the fact that the metabolism of each lipoprotein fraction (VLDL, LDL, and HDL), as well as the metabolism of cholesterol and bile acids, is markedly deranged in patients with hypertriglyceridemia (17-20), it would not be surprising if their responses to diet also were to differ from those of normotriglyceridemic subjects. For this reason, the patients were assigned to two groups on the basis of a cut-point for plasma TG of 210 mg/dl of the Sat diet; this level represents the 90th percentile cut-point in TG levels for the population of men of this age studied by the Lipid Research Clinics (21). By this criterion, patients 1-12 were classified as having normotriglyceridemia, and patients 13-20 had hypertriglyceridemia. The results to follow describe the findings in these two groups.

TABLE 3. Mean levels of lipids and lipoprotein-cholesterol attained by all patients in each of three dietary periods

Diet	Lipid or Lipoprotein Fraction				
	TC	TG	LDL-C	VLDL-C	HDL-C
	mg/dl ± SEM				
Sat	224 ± 10	259 ± 39	143 ± 11	42 ± 7	39 ± 2
Mono	197 ± 6[a]	249 ± 38	119 ± 8[a]	40 ± 6	38 ± 2
Poly	191 ± 8[ab]	231 ± 36[b]	120 ± 9[ab]	36 ± 6[b]	35 ± 2[b]

[a]Values significantly lower than on Sat diet ($P < 0.05$, paired t-test).
[b]Values on Poly diet not significantly different than on Mono diet.

Normotriglyceridemic patients

The lipid and lipoprotein levels for individual patients of this group are given in **Table 4** and **Table 5.** The group means for changes in each plasma component, both in concentrations and percentages, are given in Table 5.

Total lipids. Relative to the Sat period, both unsaturated fats caused significant reductions in plasma TC in eleven of the twelve patients (Table 4). TC levels fell by 31.1 mg/dl (12.5%) on the Mono diet and 36.9 mg/dl (15.6%) on the Poly diet (**Table 6**). The percentage decrease appeared to be a function of initial levels. Four patients (Nos. 1, 2, 3, and 5), who had the highest TC levels on palm oil, had average reductions of 21 and 22% on high-oleic and high-linoleic diets, respectively. In contrast, the four patients whose levels were below 200 mg/dl on the Sat diet had decreases of only 8 and 12% on the Mono and Poly diets, respectively. With few exceptions, TG levels remained unchanged throughout the three dietary periods (Tables 3 and 5).

Lipoprotein cholesterol. In eleven of twelve subjects, both Mono and Poly diets significantly lowered plasma LDL-C levels (Table 4). Compared to the Sat period, the Mono diet lowered LDL-C by a mean of 31.3 mg/dl (17.7%), and the Poly diet reduced LDL-C by 29.5 mg/dl (17.1%) (Table 5). The two unsaturated fat diets had a less uniform effect on HDL-C levels (Table 5). Whereas the Poly diet significantly reduced HDL-C levels in nine of twelve individuals, only four had a significant reduction during the Mono period. In two patients, HDL-C was significantly higher on the Mono diet than on the Sat diet; this response occurred only in one individual on the Poly diet. This divergence of responses in HDL-C levels between the two diets was also noted for the means of the changes (Table 6). On the Mono diet, the change in HDL-C, either as concentration or percentage, was small and not statistically significant. The Poly diet caused a significant decrease in concentrations of HDL-C (-5.0 ± 1.7 mg/dl, $P < 0.02$), although the percentage reduction ($9.8 \pm 4.7\%$) was not statistically significant. Levels of HDL_3-C, which were approximately 70% of total HDL-C, showed no differences among the three dietary periods. Only one patient on the Mono diet and three on the Poly diet had a lower level of VLDL-C than that on the Sat diet (Table 5).

TABLE 4. Plasma lipid levels attained by normotriglyceridemic patients in each of three dietary periods[a]

Patient	Plasma Cholesterol			Plasma Triglycerides		
	Diet			Diet		
	Sat	Mono	Poly	Sat	Mono	Poly
			mg/dl ± SD			
1	278 ± 4	218 ± 10^b	194 ± 8^b	199 ± 27	190 ± 26	136 ± 20^b
2	241 ± 8	200 ± 9^b	171 ± 8^b	95 ± 18	85 ± 11	73 ± 17
3	320 ± 13	241 ± 9^b	242 ± 6^b	209 ± 33	160 ± 16^b	204 ± 20
4	206 ± 11	177 ± 9^b	180 ± 8^b	147 ± 17	162 ± 18	174 ± 18^c
5	327 ± 10	263 ± 15^b	303 ± 11^b	156 ± 11	163 ± 18	144 ± 22
6	198 ± 9	181 ± 7^b	180 ± 10^b	112 ± 13	73 ± 10^b	70 ± 5^b
7	183 ± 7	175 ± 5^b	180 ± 8	189 ± 11	190 ± 16	221 ± 13^c
8	219 ± 4	213 ± 14	188 ± 8^b	127 ± 7	129 ± 8	120 ± 8
9	203 ± 10	185 ± 6^b	172 ± 7^b	119 ± 10	124 ± 4	108 ± 5
10	184 ± 7	157 ± 5^b	147 ± 5^b	174 ± 25	156 ± 8	160 ± 10
11	203 ± 2	190 ± 7^b	193 ± 6^b	67 ± 7	79 ± 21	93 ± 13^c
12	171 ± 6	160 ± 7^b	139 ± 6^b	122 ± 13	101 ± 7^b	93 ± 7^b

[a]Each value is the mean of six blood samples taken during the third and fourth week of each dietary period.
[b,c]Statistically significant change from Sat period (Student's *t*-test, $P < 0.05$); [b], lower; [c], higher.

Lipoprotein composition. The percentage composition of the isolated lipoprotein fractions is given in **Table 7.** None of the values were changed significantly by any of the three dietary fats. Since the chemical compositions of the various lipoprotein fractions were the same regardless of the dietary regimen, the plasma concentration of the cholesterol component of a lipoprotein was a direct reflection of the plasma concentration of the entire lipoprotein. Thus, on the Sat diet, the mean level of LDL-total mass averaged 516 mg/dl and it decreased to 425 mg/dl on the Poly diet and to 417 mg/dl on the Mono diet.

Hypertriglyceridemic patients

For this group, plasma lipid concentrations for individual patients are presented in **Table 8,** and corresponding levels of LDL-C, VLDL-C, and HDL-C are given in **Table 9.** The means of the changes for all eight patients expressed as concentration and percentage are presented in **Table 10.**

Total lipids. The levels of plasma TC attained on the unsaturated diets relative to that on the saturated diet varied considerably among the hypertriglyceridemic patients (Table 8). On the Mono diet, three patients had significantly lower TG levels, but overall, the reduction was not statistically significant. On the Poly diet, six individuals and the group as a whole showed significant reductions in TC levels (Table 10). The plasma TG responses on the Mono and Poly diets varied widely; some patients exhibited a decrease, others an increase (Table 7). For the group means, alterations were not significant for either

TABLE 5. Plasma lipoprotein cholesterol levels attained by normotriglyceridemic patients in each of three dietary periods[a]

Patient	LDL-C Diet			VLDL-C Diet			HDL-C Diet		
	Sat	Mono	Poly	Sat	Mono	Poly	Sat	Mono	Poly
					mg/dl ± SD				
1	201 ± 8	133 ± 7^b	134 ± 10^b	37 ± 7	35 ± 7	21 ± 5^b	39 ± 4	51 ± 4^c	39 ± 2
2	160 ± 6	130 ± 6^b	108 ± 8^b	14 ± 2	12 ± 1	10 ± 2^b	67 ± 6	57 ± 3^b	54 ± 3^b
3	227 ± 7	159 ± 12^b	162 ± 8^b	39 ± 8	27 ± 4^b	37 ± 9	55 ± 7	55 ± 3	43 ± 4^b
4	152 ± 9	125 ± 7^b	130 ± 6^b	16 ± 4	19 ± 3	20 ± 3	38 ± 2	34 ± 2^b	30 ± 2^b
5	289 ± 9	229 ± 11^b	254 ± 8^b	15 ± 3	15 ± 5	19 ± 9	23 ± 1	19 ± 1^b	31 ± 1^c
6	147 ± 7	124 ± 4^b	126 ± 11^b	7 ± 5	12 ± 4	9 ± 6	45 ± 2	46 ± 4	46 ± 2
7	122 ± 9	117 ± 6	124 ± 3	29 ± 9	31 ± 8	27 ± 6	32 ± 1	27 ± 3^b	29 ± 3^b
8	158 ± 5	147 ± 1^b	143 ± 6^b	25 ± 4	29 ± 4	16 ± 3^b	37 ± 2	37 ± 3	29 ± 3^b
9	136 ± 4	114 ± 7^b	117 ± 5^b	17 ± 3	22 ± 6	15 ± 3	50 ± 3	49 ± 2	40 ± 2^b
10	130 ± 6	103 ± 6^b	100 ± 6^b	23 ± 5	23 ± 5	21 ± 4	31 ± 2	32 ± 3	26 ± 1^b
11	142 ± 9	127 ± 10^b	136 ± 9	9 ± 4	13 ± 7	11 ± 2	53 ± 6	50 ± 1	45 ± 4^b
12	122 ± 5	100 ± 5^b	95 ± 5^b	16 ± 6	24 ± 3^c	15 ± 2	33 ± 2	36 ± 1^c	29 ± 1^b

[a]Each value is the mean of six blood samples taken during the third and fourth week of each dietary period.
[b,c]Statistically significant change from Sat period (Student's *t*-test, $P < 0.05$); [b], lower; [c], higher.

TABLE 6. Mean changes in plasma lipid levels from Sat period in normotriglyceridemic patients[a]

	Diet		Diet	
	Mono	Poly	Mono	Poly
	mg/dl		%	
Total cholesterol				
Mean ± SEM	−31.1 ± 7.1	−36.9 ± 7.6	−12.5 ± 2.1	−15.6 ± 2.6
P	0.01[b]	0.001[b]	0.001[b]	0.001[b]
Total triglyceride				
Mean ± SEM	−8.7 ± 5.8	−8.8 ± 8.3	−5.2 ± 4.3	−11.1 ± 8.8
P	NS	NS	NS	NS
LDL-cholesterol				
Mean ± SEM	−31.3 ± 6.3	−29.5 ± 6.4	−17.7 ± 2.6	−17.1 ± 3.2
P	0.001[b]	0.001[b]	0.001[b]	0.001[b]
VLDL-cholesterol				
Mean ± SEM	1.4 ± 2.3	−0.7 ± 1.8	16.4 ± 8.3	1.4 ± 7.0
P	NS	NS	NS	NS
HDL-cholesterol				
Mean ± SEM	−0.7 ± 1.5	−5.0 ± 1.7	−1.2 ± 3.8	−9.8 ± 4.7
P	NS	0.02[b]	NS	NS

[a]Mean of the changes shown by each of 12 subjects.
[b]Mono (or Poly) diet significantly different from Sat diet at *P* value shown by paired *t*-test.

unsaturated fat (Table 10).

Lipoprotein cholesterol. Responses in LDL-C levels to both unsaturated fats also varied among the individuals with high plasma TG (Table 8); in most instances, the level of LDL-C was lower when the diets contained the unsaturated fats, but the changes relative to the Sat period were statistically significant only for the Mono period (Table 9). There were no consistent differences in the levels of VLDL-C or HDL-C during any of the dietary periods. The percent of total HDL as HDL_3, approximately 80%, was similarly unchanged during the three periods.

Lipoprotein composition. The percentage composition of the lipoproteins for the hypertriglyceridemic patients is given in **Table 11.** The proportions of the different components of the lipoproteins remained essentially constant regardless of the composition of the dietary fat.

DISCUSSION

The purpose of this study was to compare monounsaturated (oleic) and polyunsaturated (linoleic) acids when substituted for saturated (palmitic) acids for their effects on the plasma lipoproteins. For this purpose, edible fats were selected which, although at the extremes of percentages of fatty acids under investigation, nevertheless

TABLE 7. Percentage composition of lipoprotein fractions isolated from normotriglyceridemic patients consuming diets of different fatty acid composition[a,b]

Fraction	Diet	CE	FC	TG	PL	Pro	Total Chol	Pro/C
					% of total lipoprotein			
VLDL	Sat	8.9 ± 1.8	5.9 ± 1.1	51.4 ± 4.9	23.7 ± 5.1	9.9 ± 0.7	11.1 ± 1.5	0.9 ± 0.1
	Mono	9.1 ± 2.1	6.4 ± 1.3	50.4 ± 5.2	23.9 ± 6.4	10.0 ± 0.8	11.6 ± 2.0	0.9 ± 0.2
	Poly	10.0 ± 2.3	6.6 ± 1.5	49.4 ± 8.0	23.1 ± 3.6	10.8 ± 1.3	12.4 ± 2.6	0.9 ± 0.1
IDL	Sat	18.6 ± 4.1	5.9 ± 1.0	19.0 ± 4.1	40.0 ± 4.4	16.1 ± 1.7	16.7 ± 3.3	0.9 ± 0.2
	Mono	18.9 ± 3.8	5.8 ± 0.8	17.5 ± 3.4	40.1 ± 4.4	17.6 ± 2.3	16.7 ± 2.9	1.0 ± 0.3
	Poly	18.1 ± 12.9	5.6 ± 0.8	18.6 ± 4.4	39.8 ± 2.8	17.8 ± 2.5	15.9 ± 2.4	1.1 ± 0.2
LDL	Sat	40.1 ± 1.6	9.3 ± 0.6	5.5 ± 1.0	23.0 ± 1.6	21.7 ± 1.3	32.6 ± 1.1	0.7 ± 0.1
	Mono	39.6 ± 1.9	9.3 ± 0.8	6.2 ± 1.6	22.1 ± 1.2	22.6 ± 1.6	32.2 ± 1.0	0.7 ± 0.1
	Poly	40.2 ± 1.4	9.1 ± 0.6	5.9 ± 1.0	22.0 ± 0.8	22.7 ± 1.7	32.0 ± 0.4	0.7 ± 0.04
HDL	Sat	20.6 ± 1.4	3.0 ± 9.5	5.7 ± 3.7	24.2 ± 2.0	46.3 ± 2.7	14.9 ± 1.3	3.1 ± 0.4
	Mono	20.7 ± 4.5	3.1 ± 0.3	5.9 ± 2.4	23.5 ± 1.4	46.6 ± 2.9	15.1 ± 1.03	3.1 ± 0.3
	Poly	20.9 ± 1.8	2.9 ± 0.5	7.5 ± 3.7	23.3 ± 0.7	45.3 ± 2.3	14.9 ± 1.6	3.1 ± 0.3

[a]Mean ± SD; n = 12.
[b]CE, cholesteryl ester; FC, free cholesterol; TG, triglyceride; PL, phospholipid; Pro, protein, C, total cholesterol.

TABLE 8. Plasma lipid levels attained by hypertriglyceridemic patients in each of three dietary periods[a]

Patients	Plasma Cholesterol Diet			Plasma Triglycerides Diet		
	Sat	Mono	Poly	Sat	Mono	Poly
			mg/dl ± SD			
13	300 ± 6	219 ± 6[b]	205 ± 18[b]	381 ± 23	238 ± 16[b]	224 ± 48[b]
14	183 ± 19	176 ± 9	157 ± 4[b]	268 ± 33	348 ± 32[c]	247 ± 19
15	209 ± 6	173 ± 7[b]	180 ± 8[b]	628 ± 45	498 ± 28[b]	346 ± 15[b]
16	196 ± 13	201 ± 8	205 ± 8	462 ± 65	678 ± 103[c]	630 ± 53[c]
17	171 ± 4	173 ± 6	179 ± 5[c]	472 ± 40	456 ± 44	430 ± 24
18	238 ± 13	191 ± 10[b]	199 ± 9[b]	321 ± 31	304 ± 52	273 ± 26[b]
19	201 ± 8	193 ± 6	175 ± 6[b]	243 ± 15	292 ± 11[c]	229 ± 12
20	255 ± 13	248 ± 7	232 ± 8[b]	695 ± 122	552 ± 54[b]	649 ± 27

[a]Each value is the mean of six blood samples taken during the third and fourth week of each dietary period.
[b,c]Statistically significant change from Sat period (Student's *t*-test, $P < 0.05$); [b], lower; [c], higher.

were typical in chain length to those in the American diet. Two types of patients were studied: twelve with normal TG levels and eight with high plasma TG. When their data were pooled, both monounsaturates and polyunsaturates appeared to induce equivalent reductions in TC and LDL-C levels as compared to saturates (Table 3). No changes were noted in HDL-C concentrations for the group as a whole. However, because of the multiple defects in cholesterol and lipoprotein metabolism associated with hypertriglyceridemia (17–20), the decision was made to examine and discuss the responses of the two types of patients separately.

Normotriglyceridemic patients

Both types of unsaturated fats significantly reduced plasma TC levels in eleven of the twelve normotriglyceridemic patients. The mean decrease was slightly greater for the Poly diet than for the Mono diet, although this difference was not statistically significant. Keys, Anderson, and Grande (22, 23) proposed that for every 1% increase in caloric intake in the form of saturated fatty acids, the plasma TC will rise by about 2.7 mg/dl; and for every 1% increase in polyunsaturated fatty acids, the TC level will fall by about 1.4 mg/dl. The Keys equation assumes that monounsaturates have no effect on the cholesterol level. If these predictions are applied to our experimental design, the exchange of high-linoleic safflower oil for palm oil should have reduced plasma TC by about 78 mg/dl. Assuming that monounsaturates are "neutral," the diet containing high-oleic safflower oil, because of its reduced intake of saturated fatty acids, should have lowered plasma TC by 45 mg/dl. Our mean results for polyunsaturates in particular were not consistent with the Keys equation; furthermore, both unsaturated fats reduced TC levels by equal amounts—approximately 35 mg/dl.

Our failure to achieve the change predicted for polyunsaturates may have several explanations. Plasma TC levels fell by an average of 41 mg/dl from admission values to the mean on the Sat diet; this reduction upon starting

TABLE 9. Plasma lipoprotein cholesterol levels attained by hypertriglyceridemic patients in each of three dietary periods[a]

Patient	LDL-C Diet			VLDL-C Diet			HDL-C Diet		
	Sat	Mono	Poly	Sat	Mono	Poly	Sat	Mono	Poly
					mg/dl ± SD				
13	185 ± 6	146 ± 13[b]	127 ± 15[b]	76 ± 8	37 ± 8[b]	39 ± 6[b]	40 ± 4	36 ± 4	39 ± 5
14	97 ± 11	82 ± 8[b]	84 ± 4[b]	58 ± 8	69 ± 8[c]	45 ± 4[b]	29 ± 3	26 ± 2	28 ± 3
15	86 ± 5	74 ± 7[b]	93 ± 3[c]	92 ± 8	68 ± 5[c]	50 ± 4[b]	31 ± 1	31 ± 1	37 ± 4[c]
16	84 ± 13	55 ± 7[b]	57 ± 6[b]	77 ± 17	113 ± 14[c]	115 ± 5[c]	36 ± 3	34 ± 6	33 ± 2
17	76 ± 4	76 ± 5	81 ± 7	65 ± 2	67 ± 10	70 ± 8	30 ± 2	31 ± 2	28 ± 1
18	146 ± 8	110 ± 5[b]	127 ± 9[b]	51 ± 6	42 ± 6[b]	38 ± 8[b]	41 ± 3	40 ± 4	35 ± 4[b]
19	119 ± 4	110 ± 6[b]	105 ± 2[b]	48 ± 6	47 ± 1	39 ± 6[b]	34 ± 1	36 ± 2	32 ± 1
20	106 ± 7	116 ± 9	93 ± 3[b]	117 ± 14	97 ± 11[b]	108 ± 9	32 ± 1	34 ± 1	31 ± 1

[a]Each value is the mean of six blood samples taken during the third and fourth week of each dietary period.
[b,c]Statistically significant change from Sat period (Student's *t*-test, $P < 0.05$); [b], lower; [c], higher.

TABLE 10. Mean changes in plasma lipid levels from Sat period in hypertriglyceridemic patients[a]

	Diet		Diet	
	Mono	Poly	Mono	Poly
	mg/dl		%	
Total cholesterol				
Mean ± SEM	−22.4 ± 10.6	−27.6 ± 11.4	−8.8 ± 3.9	−11.2 ± 4.2
P	NS	0.05[b]	NS	0.05[b]
Total triglyceride				
Mean ± SEM	−13.0 ± 44.8	−55.4 ± 45.3	1.1 ± 10.2	−9.8 ± 9.2
P	NS	NS	NS	NS
LDL-cholesterol				
Mean ± SEM	−16.0 ± 6.2	−16.4 ± 7.2	−13.5 ± 5.1	−12.2 ± 5.3
P	0.05[b]	NS	0.05[b]	NS
VLDL-cholesterol				
Mean ± SEM	−5.5 ± 8.2	−10.0 ± 8.8	−5.6 ± 10.5	−14.0 ± 11.1
P	NS	NS	NS	NS
HDL-cholesterol				
Mean ± SEM	−0.6 ± 0.8	−1.4 ± 1.3	−1.6 ± 2.4	−3.5 ± 3.7
P	NS	NS	NS	NS

[a]Mean of the changes shown by each of 12 subjects.
[b]Mono (or Poly) diet significantly different from Sat diet at *P* value shown by paired *t*-test.

metabolic-ward studies is a well recognized phenomenon, and it may have blunted the response to unsaturated fats. As a result of this initial fall, several of the patients had relatively low TC levels on the Sat diet, and their further reductions on unsaturates were especially small. Those with higher cholesterol levels on the Sat diet had greater falls on polyunsaturates. Indeed, in those four who had the highest TC levels on Sat diet, the Poly diet caused an average reduction of 64 mg/dl, which is more in line with the prediction of Keys et al. (22, 23). The use of palm oil as a source of saturates may have contributed to the deviation from prediction because Keys et al. (22, 23) employed fats containing a variety of saturated fatty acids. Hegsted et al. (24) subsequently showed that lauric and myristic acids are more hypercholesterolemic than palmitic acid, and since palm oil contains only 1% of these shorter fatty acids, it may have caused a lesser rise in TC levels than the fats used by Keys et al. (22).

Other variables may have contributed to differences in response to polyunsaturated fatty acids. Previous investigators (22, 24–28) have employed different kinds of subjects (e.g., students, prison inmates, patients in mental institutions, and hyperlipidemic patients) who were of variable ages and consumed different kinds of diets (i.e., chewing-type vs. liquid diets). All of the factors may have affected the degree of response to polyunsaturates, although not its direction.

The most important finding of the present study is that

TABLE 11. Percentage composition of lipoprotein fractions isolated from hypertriglyceridemic patients consuming diets of different fatty acid composition[a,b]

Fraction	Diet	CE	FC	TG	PL	Pro	Total Chol	Pro/C
					% of total lipoprotein			
VLDL	Sat	10.8 ± 2.1	6.1 ± 0.4	56.9 ± 4.7	17.5 ± 1.2	8.7 ± 1.3	12.3 ± 1.5	0.7 ± 0.04
	Mono	10.3 ± 1.8	5.6 ± 0.3	57.9 ± 3.02	17.2 ± 1.05	8.8 ± 0.7	11.6 ± 1.4	0.8 ± 0.1
	Poly	10.2 ± 1.8	5.9 ± 0.5	56.2 ± 3.7	17.7 ± 1.3	9.9 ± 0.9	10.5 ± 4.2	0.8 ± 0.1
IDL	Sat	21.9 ± 4.8	6.3 ± 1.1	23.8 ± 4.3	32.7 ± 3.1	15.1 ± 1.3	19.1 ± 3.7	0.8 ± 0.1
	Mono	19.5 ± 4.0	6.1 ± 1.2	28.1 ± 7.3	31.3 ± 3.9	14.9 ± 2.1	1.47 ± 3.3	0.9 ± 0.2
	Poly	20.1 ± 4.3	6.1 ± 1.0	26.2 ± 6.9	31.3 ± 2.7	16.3 ± 1.4	17.8 ± 3.4	0.9 ± 0.1
LDL	Sat	40.4 ± 3.3	7.7 ± 0.7	7.9 ± 2.9	20.9 ± 0.6	23.1 ± 1.4	31.1 ± 0.1	0.7 ± 1.8
	Mono	37.6 ± 4.2	7.4 ± 0.7	10.5 ± 4.3	20.9 ± 0.9	23.4 ± 0.6	29.2 ± 2.6	0.8 ± 0.1
	Poly	38.8 ± 3.9	7.5 ± 0.6	9.2 ± 3.4	20.6 ± 0.4	23.8 ± 1.01	29.9 ± 2.3	0.8 ± 0.1
HDL	Sat	18.4 ± 1.4	2.4 ± 0.2	6.3 ± 1.5	23.8 ± 1.5	48.9 ± 2.2	13.1 ± 0.8	3.8 ± 0.3
	Mono	16.2 ± 2.5	2.4 ± 0.2	8.4 ± 1.9	23.1 ± 1.3	49.9 ± 1.7	11.7 ± 1.6	4.3 ± 0.8
	Poly	17.1 ± 2.5	2.3 ± 0.3	7.2 ± 1.9	22.4 ± 2.3	51.0 ± 1.7	12.1 ± 1.6	4.3 ± 0.7

[a]Mean ± SD; n = 12.
[b]CE, cholesteryl ester; FC, free cholesterol; TG, triglyceride; PL, phospholipid; Pro, protein, C, total cholesterol.

the two unsaturated fats induced almost identical reductions in plasma LDL-C, i.e., 17% for both. In earlier studies, e.g., those forming the bases of the Keys equation (22, 23), measurements of the responses in the individual lipoprotein fractions were not made. Thus, the possibility cannot be excluded that the seemingly greater reduction in total TC by polyunsaturated compared to monounsaturated fatty acids may have been due to a greater decrement in a lipoprotein fraction other than LDL, for example, in HDL.

Recently, Becker et al. (29) compared effects of saturated, monounsaturated, and polyunsaturated fatty acids on levels of lipid and lipoproteins in young men. They too found that both types of unsaturated acids lowered TC and LDL-C compared to saturated fatty acids. The magnitude of lowering of TC likewise was considerably less than that predicted by the Keys equation (22, 23). In contrast to our results, however, they reported that polyunsaturated fatty acids lowered TC and LDL-C levels somewhat more than did monounsaturated fats.

The effects of fatty acids on HDL concentrations have been a subject of dispute. Several investigators, however, have reported that polyunsaturates lower plasma levels of HDL-C (5-8). In the current normotriglyceridemic patients, the Poly diet lowered HDL-C concentrations by an average of 5 mg/dl, a change that was statistically significant. The Mono diet did not cause a statistical decrease in the average HDL-C concentration. Furthermore, nine of twelve individuals in this group showed a significant decrease in HDL-C on the high-linoleic oil; but, by contrast, only four individuals had a significant fall during ingestion of the high oleic oil, and two of the patients had a significant rise in HDL-C on the Mono diet. The current data thus highly suggest that even if oleic acid causes a decrease in HDL-C levels in some patients, it does so less frequently than linoleic acid; obviously, larger numbers of patients must be studied before this difference can be accepted with certainty.

In the recent report of Becker et al. (29), a decrease in plasma HDL-C was not noted when polyunsaturated fatty acids were substituted for saturates. This apparent lack of change, which is contrary to the findings of several others (5-8), might reflect the way in which their data were presented; only means from multiple subjects were reported. We, too, found no differences among the means, but when the means were examined for individual changes (by the paired *t*-test), the Poly diet showed a significant decrease in HDL-C levels. More generally, we avoided a comparison of group means because the between-individual variation often was so large that between-diet effects were obscured. By using each patient as his own control, the normal between-individual variation was minimized.

Hypertriglyceridemic patients

Compared to a high-fat diet, a diet rich in carbohydrate raises TG levels in patients with endogenous hypertriglyceridemia (30); conversely, dietary fats lower the plasma TG relative to carbohydrates. The specific effects of different kinds of fatty acids have not been studied adequately. However, it has been reported that polyunsaturates lower TG levels relative to saturates (31). This response was not observed consistently in our study, although it was noted in a few patients. A similar inconsistency was observed for monounsaturates.

In patients with high TG levels, polyunsaturates caused a small but statistically significant reduction in plasma TC levels, but for monounsaturates the decrease was not significant. Still, the fall in LDL-C on the Mono diet was significant, although not on the Poly diet. This reduction of LDL-C by monounsaturates might be beneficial. Several modes of therapy for hypertriglyceridemia raise LDL-C levels (32), and this paradoxical response might be mitigated by the simultaneous use of a diet rich in monounsaturated fatty acids.

Patients with hypertriglyceridemia generally have lower concentrations of HDL-C than do normotriglyceridemic subjects (19). This difference again was noted in our patients. Neither of the unsaturated oils elevated HDL-C levels in this group of patients nor did they cause a decrease. The proportion of HDL as HDL_3 was similarly unaffected. Thus the three fats had no effect on the level or composition of HDL in hypertriglyceridemic patients.

Conclusion

This work was carried out to compare the relative actions of oleic acid and linoleic acid on concentrations of plasma lipids and lipoproteins and on composition of lipoproteins. The major finding of the study was that the two unsaturated fatty acids had almost identical effectiveness in reducing plasma TC and LDL-C. The current results, furthermore, are in accord with previous studies (5-8) showing that high intakes of linoleic acid frequently lower HDL-C levels; this response appeared to occur less often when the patients were taking large quantities of oleic acid. ■

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