

Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects¹⁻³

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ABSTRACT

Background: Elevations of postprandial triacylglycerol-rich plasma lipoproteins and suppressions of HDL-cholesterol concentrations are considered potentially atherogenic. Long-term studies have shown beneficial effects of monounsaturated fatty acids (eg, oleic acid) on fasting lipid and lipoprotein concentrations in humans. A direct stimulatory effect of oleic acid on the secretion of glucagon-like peptide 1 (GLP-1) was shown in animal studies.

Objective: We compared the postprandial responses of glucose, insulin, fatty acids, triacylglycerol, gastric inhibitory polypeptide (GIP), and GLP-1 to test meals rich in saturated and monounsaturated fatty acids.

Design: Ten young, lean, healthy persons ingested 3 meals: an energy-free soup consumed with 50 g carbohydrate (control meal), the control meal plus 100 g butter, and the control meal plus 80 g olive oil. Triacylglycerol and retinyl palmitate responses were measured in total plasma, in a chylomicron-rich fraction, and in a chylomicron-poor fraction.

Results: No significant differences in glucose, insulin, or fatty acid responses to the 2 fat-rich meals were seen. Plasma triacylglycerol responses were highest after the butter meal, with chylomicron triacylglycerol rising 2.5–5-fold. Retinyl palmitate responses were higher and more prolonged after the butter meal than after the control and olive oil meals, whereas both postprandial HDL-cholesterol concentrations and GLP-1 and GIP responses were higher after the olive oil meal than after the butter meal.

Conclusions: Olive oil induced lower triacylglycerol concentrations and higher HDL-cholesterol concentrations than butter, without eliciting differences in concentrations of glucose, insulin, or fatty acids. Furthermore, olive oil induced higher concentrations of GLP-1 and GIP than did butter, which may point to a relation between fatty acid composition, incretin responses, and triacylglycerol metabolism in the postprandial phase. *Am J Clin Nutr* 1999;69:1135–43.

KEY WORDS Saturated fat, monounsaturated fat, glucagon-like peptide 1, GLP-1, gastric inhibitory polypeptide, GIP, postprandial phase, triacylglycerol, olive oil, oleic acid, adults, HDL cholesterol, humans, incretins, lipemia

INTRODUCTION

Fat consumption is well above the generally recommended proportion in most Western countries, ie, dietary fat constitutes >30% of total energy. A high consumption of fat, especially saturated fat,

increases the risk of cardiovascular disease. Postprandial lipemia determines the plasma HDL-cholesterol concentration (1). The negative correlation between HDL cholesterol and coronary artery disease seems to originate in the highly positive correlation between postprandial triacylglycerol concentrations and coronary artery disease (2). Furthermore, cumulating evidence suggests that excessive postprandial triacylglycerol concentrations are an independent atherogenic factor (2, 3) and may be linked to the metabolic syndrome (4, 5). Beneficial effects of monounsaturated fatty acids on fasting concentrations of cholesterol and HDL cholesterol have been shown in healthy subjects in long-term studies (6–10). During fat absorption, an HDL-cholesterol-lowering effect of saturated fat (11) and an HDL-cholesterol-conserving effect of monounsaturated fat (12) were shown in healthy subjects. Higashi et al (13), however, found no significant differences in postprandial total or HDL-cholesterol concentrations but higher triacylglycerol responses to olive oil than to milk fat or safflower oil in healthy subjects.

Interestingly, we observed in subjects with type 2 diabetes that butter, compared with olive oil, augmented postprandial fatty acid and triacylglycerol responses when fat was consumed with carbohydrates (14). However, no direct comparisons have been carried out in healthy subjects of the effects of saturated and monounsaturated fats consumed with carbohydrates on postprandial lipid and lipoprotein concentrations.

A link between incretin hormones [eg, gastric inhibitory polypeptide (GIP) and glucagon-like peptide 1 (GLP-1)] and fat homeostasis seems likely (15). In vitro studies have shown that oleic acid (18:1) stimulates GLP-1 secretion whereas saturated fatty acids do not (16). Monounsaturated fatty acids seem to have

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specific effects on the concentrations of incretin hormones. Furthermore, GIP and GLP-1 are important factors in postprandial insulin secretion and ventricular emptying. Thus, the 2 incretin hormones GIP and GLP-1 may be important in postprandial lipid metabolism. We therefore compared postprandial lipid and lipoprotein responses and investigated possible *in vivo* differences in GIP and GLP-1 responses in healthy subjects after ingestion of butter and olive oil.

SUBJECTS AND METHODS

Subjects

Ten healthy medical students, 5 women and 5 men, participated in the study. The students' mean (\pm SD) age was 23 ± 2 y. They were lean, with a mean body mass index (in kg/m^2) of 21.4 ± 1.7 , and had a mean fasting blood glucose concentration of 4.4 ± 0.4 mmol/L and a corresponding insulin concentration of 25.3 ± 8.8 pmol/L. Mean fasting concentrations of total cholesterol and triacylglycerol were 4.0 ± 0.6 and 1.0 ± 0.4 mmol/L, respectively. All participants were healthy and none had a family history of either type 2 diabetes or cardiovascular disease. None of the participants took any drug regularly and all were non-smokers. The study was approved by the local ethical committee of Aarhus County and all subjects gave their written, informed consent to participate.

Study design

Students participated in 3 studies with ≥ 1 wk between treatments. For the 24 h preceding each study, students ingested high-carbohydrate food delivered by the dietitian. Food amounts corresponded to individual energy requirements estimated by using the Harris-Benedict equation with adjustments for physical activity (17). Students were instructed to standardize and minimize their physical activity on the study mornings, ie, to get dressed without washing, travel to the experimental setting by bus, and be seated immediately on arrival at 0700. On arrival, an intracatheter was placed in an antecubital vein. The participants rested for 30 min (baseline period) and sat in a chair during the test. Basal blood samples were drawn at 0 min and the test meal was then ingested. From 0 to 480 min (or from 0 to 360 min after the control meal) blood samples were drawn every 30 min for the analysis of glucose, insulin, fatty acids, GLP-1, and GIP and every hour for the analysis of cholesterol, triacylglycerol, and retinyl palmitate (RP). Plasma was immediately separated by centrifugation at $2300 \times g$ for 10 min at 4°C and kept frozen at -20°C until analyzed, except for GIP and GLP-1 samples, which were stored at -80°C .

Test meals

In a randomized order, students received 1) an energy-free soup plus 50 g carbohydrate as white bread (control meal), 2) the control meal plus 100 g butter (butter meal), and 3) the control meal plus 80 g olive oil (olive oil meal). The apparent discrepancy in the amount of fat given was due to the 20% water content of butter. The manufacturers provided the nutrient contents of the unsalted butter and olive oil. The olive oil contained predominantly monounsaturated fatty acids (74%) and the butter contained mainly saturated fatty acids (72%). The soup was chilled briefly and then unmelted butter or olive oil was added. Sliced, raw leek was added to mask both the appearance and the

taste of the added fat. The students could not tell which fatty soup they were eating; thus, the study was single-blind. Test meals were ingested within 10 min and were served with 250 mL tap water. The students took a standard dose of vitamin A (30 mg, or 100 000 IU) in tablet form with the first spoonful of soup. Ingestion of vitamin A causes retinyl ester labeling of chylomicrons (18, 19). Test meals are therefore commonly supplemented with vitamin A as a means of quantifying lipoproteins of intestinal origin, ie, chylomicrons and chylomicron remnants (19–21).

Separation of chylomicron-rich and chylomicron-poor plasma fractions

To separate lipoproteins, the plasma samples were subjected to a single ultracentrifugation step to divide the samples into chylomicron-rich and chylomicron-poor fractions. A 4-mL plasma sample was overlaid with 2 mL of a solution with a density of 1006 g/L in a Quick-seal tube (no.344619) and was centrifuged in an Sw 50.3 Ti fixed-angle rotor (both from Beckman Instruments, Palo Alto, CA) at 4°C for 30 min at $26000 \times g$. Tubes were then sliced in a Beckman slicer 2 mL from the top and the chylomicron-rich supernates [with Svedberg flotation (S_p) unit values > 1000] were removed and brought to a final volume of 4 mL with saline. The infranatant layer, ie, the chylomicron-poor fraction, contains the plasma proteins and remaining lipoproteins, and thus the triacylglycerol concentration can be allocated to the chylomicrons in the chylomicron-rich fraction and to the VLDL, intermediate-density lipoprotein, and chylomicron remnants in the chylomicron-poor fraction. Triacylglycerol and cholesterol concentrations were measured in plasma and in both fractions, whereas HDL-cholesterol concentrations were measured only in the chylomicron-poor fraction. RP concentrations were measured in both the chylomicron-rich and the chylomicron-poor fractions. Measurement of RP gives an indirect measure of the intestinally produced lipoproteins (chylomicron) in the chylomicron-rich fraction and of the chylomicron-remnants in the chylomicron-poor fraction. High concentrations of chylomicron remnants are believed to be highly atherogenic. The samples for these analyses were kept shielded from light.

Analyses

Plasma glucose was measured by a glucose oxidase method (CV: 3.8%). Serum insulin concentrations were measured by an enzyme-linked immunosorbent assay method (CV: 1.7%) (22). Triacylglycerol, cholesterol (HDL cholesterol in the chylomicron-poor fraction only, after precipitation of apolipoprotein B-containing lipoproteins with phosphotungstic acid), and fatty acids were measured with standard enzymatic colorimetric assays by using commercial kits (Waco Chemicals, Neuss, Germany, and Boehringer Mannheim, Mannheim, Germany). GIP was measured by radioimmunoassay with the antiserum R65 moniodinated human GIP and human GIP as standards after extraction of the peptides from plasma according to a method described previously (23). The sensitivity and detection limit of the assay is ≈ 1 pmol/L. The assay is highly specific for GIP and does not cross-react with the 8-kDa immunoreactive component of unknown nature that cross-reacts in most GIP assays. Plasma concentrations of GLP-1 were measured as described previously (24) against standards of synthetic GLP-1 7-36 amide (proglucagon 78-106 amide) (25) by using an antiserum (code no. 89390) that can be used in a final dilution of 1:250 000, gives the assay a detection limit of 1 pmol/L, and has an intraassay CV $< 5\%$ at 20 pmol/L. This antiserum is

TABLE 1

Metabolic responses in healthy subjects to meals of soup plus 100 g white bread consumed alone (control meal) or plus olive oil (80 g) or butter (100 g)¹

	Control meal	Olive oil meal	Butter meal
Fasting blood glucose (mmol/L)	4.4 ± 0.3	4.5 ± 0.4	4.5 ± 0.4
Blood glucose area (mmol·360 min)	76.1 ± 82.6	28.1 ± 33.0	34.9 ± 52.5
Blood glucose area (mmol·480 min)	—	113.4 ± 36.7	127.4 ± 55.9
Fasting insulin (pmol/L)	25.3 ± 15.3	18.7 ± 6.2	26.7 ± 16.0
Insulin area (nmol·360 min)	10.3 ± 2.9	9.8 ± 5.3	10.4 ± 3.3
Insulin area (nmol·480 min)	—	9.9 ± 5.4	11.6 ± 5.4
Fasting fatty acids (mmol/L)	0.73 ± 0.29	0.87 ± 0.35	0.69 ± 0.40
Peak fatty acids (mmol/L)	0.92 ± 0.21	0.89 ± 0.40	0.88 ± 0.46
Nadir fatty acids (mmol/L)	0.11 ± 0.07	0.25 ± 0.08 ²	0.25 ± 0.10 ²

¹ $\bar{x} \pm SD$; $n = 10$.²Significantly different from the control meal, $P < 0.001$.

highly specific for the carboxy terminal of the proglucagon 78-107 amide and reacts neither with glycine-extended GLP-1 (proglucagon 78-108) nor with proglucagon 78-106. Thus, it mainly reacts with GLP-1 of intestinal origin (26). Before analysis, plasma was extracted with ethanol (70% by vol) (25). Retinyl esters were extracted and determined by isocratic adsorption HPLC as described previously (27, 28).

Statistical analysis

The number of participants needed to obtain sufficient statistical power (ie, >0.8) was calculated. Results are expressed as means \pm SDs of individually analyzed results for all 10 participants. The response data are given as peak and nadir concentrations and as incremental areas (area above baseline) (29). The data presented are all consistent with the hypothesis of normality. Paired data were compared by Student's t test. Multiple comparisons between mean values were made by analysis of variance (repeated measures) followed by Student's t test with Bonferroni's correction (RM-ANOVA; BMDP Statistical Software, Berkeley, CA). $P < 0.05$ was considered statistically significant.

RESULTS

All participants completed the study and ingested the test meals completely without problems. We found no significant differences in fasting concentrations of glucose, insulin, fatty acids, triacylglycerol, and cholesterol (in plasma and both fractions); RP (in both fractions); and HDL cholesterol, GLP-1, or GIP. Weight did not change significantly during the study period: the subjects' mean (\pm SD) weight at the start of the study was 68.9 ± 10.2 kg and that at the end was 69.2 ± 9.9 kg.

Blood glucose, insulin, and fatty acid responses

Metabolic responses to the 3 meals are shown in **Table 1** and postprandial concentrations of glucose, insulin, and fatty acids are shown in **Figure 1**. Fatty acid concentrations were lowest after the control meal (Table 1) and glucose (5.9 ± 0.9 compared with 4.9 ± 0.4 and 4.9 ± 0.8 mmol/L; $P = 0.01$) and insulin (211.6 ± 70.2 compared with 131.6 ± 59.7 and 153.2 ± 52.0 pmol/L; $P = 0.008$) concentrations were higher after the control meal than after either the olive oil or butter meal, respectively. Interestingly, lower individual nadir glucose values (3.0 ± 0.4 compared with 3.4 ± 0.4 mmol/L; $P = 0.04$) and lower average glucose concentrations (3.9 ± 0.2 compared with 4.3 ± 0.4 mmol/L; $P = 0.04$) were seen after the olive oil meal than after the control

meal. No significant differences, however, were found between the incremental areas of the glucose, insulin, and fatty acid responses (Table 1). Additionally, no significant differences in the time courses of the glucose, insulin, and fatty acid responses were found between the 2 fat-rich meals (Figure 1); insulin concentrations tended to peak earlier after ingestion of the control meal, but not significantly so.

Lipid responses

Postprandial triacylglycerol responses are shown in **Figure 2**. After the control meal, triacylglycerol concentrations in plasma, the chylomicron-rich fraction, and the chylomicron-poor fraction did not increase significantly. In contrast, the butter meal caused a significant increase in triacylglycerol concentrations, especially in the chylomicron-rich fraction during the initial 6 h; concentrations reached basal values after 8 h. Only small increases in plasma triacylglycerol concentrations were seen after the olive oil meal and practically no increases were found in the chylomicron-rich and chylomicron-poor fractions. As shown in the right panel of Figure 2, the incremental areas above baseline of plasma triacylglycerol after the fat-rich meals did not differ significantly, whereas the incremental areas after the butter meal were higher than after the olive oil meal in both the chylomicron-rich fraction (80.3 ± 57.2 compared with 43.8 ± 25.0 mmol·480 min/L; $P = 0.04$) and the chylomicron-poor fraction (42.5 ± 64.1 compared with 10.2 ± 12.1 mmol·480 min/L; $P = 0.04$).

HDL-cholesterol concentrations in the chylomicron-poor fraction are shown in **Figure 3**. HDL-cholesterol concentrations were practically unchanged after the olive oil meal but still significantly higher than after the butter meal during the 8-h study period. HDL-cholesterol concentrations were suppressed after both the butter and control meals. In contrast with after the control meal, after the butter meal HDL-cholesterol concentrations did not reach basal values over the 8 h.

The responses of intestinally derived lipoproteins, ie, RP concentrations, are shown in **Figure 4**. In the chylomicron-rich fraction, RP concentrations were significantly higher after the butter meal than after either the olive oil or control meal from 240 min throughout the observation period. The incremental response area after the butter meal also tended to be higher than that after either the olive oil or control meal (17660 ± 15854 compared with 12770 ± 7370 and 7372 ± 5731 $\mu\text{g/L}$, respectively; $P = 0.07$). The timing of peak values after the olive oil and control meals was not significantly different, whereas RP concentrations peaked later after the butter meal than after either the olive oil or control meal. In the chylomicron-

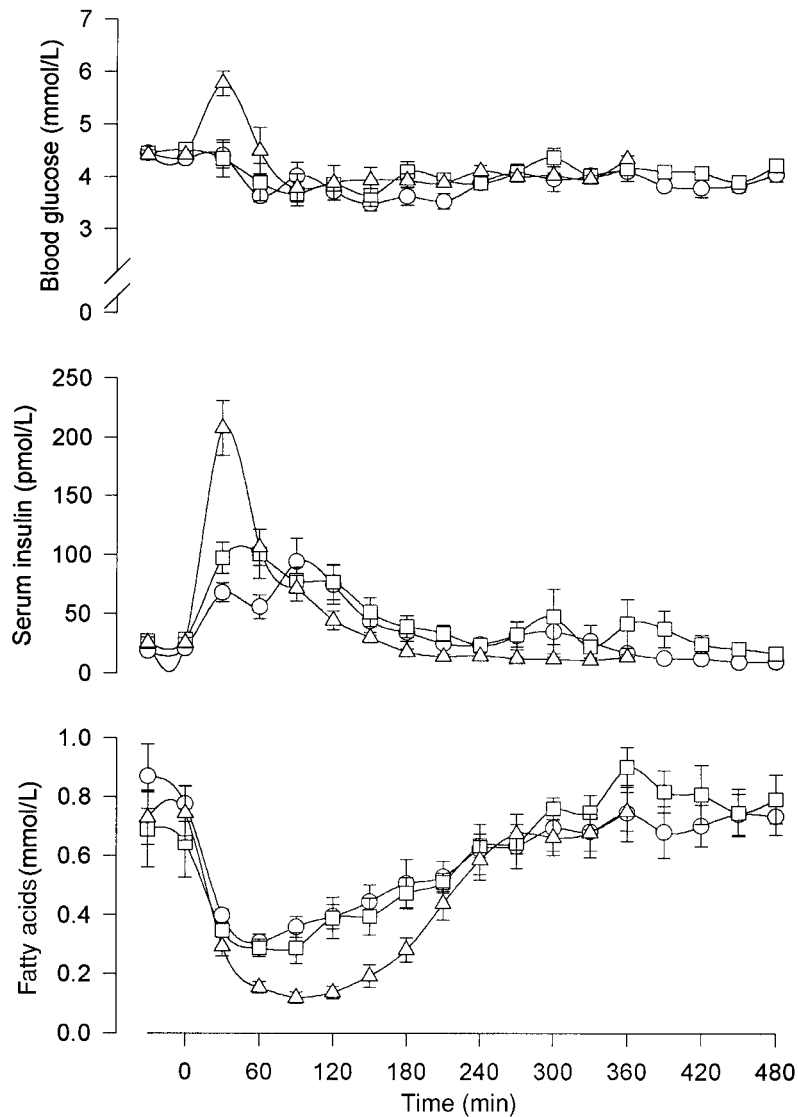


FIGURE 1. Mean (\pm SE) postprandial glucose, insulin, and fatty acid responses in 10 healthy subjects to a control meal of soup plus 50 g carbohydrates (Δ), the control meal plus 80 g olive oil (\circ), and the control meal plus 100 g butter (\square).

poor fraction the timing of peak values was not significantly different between the 3 meals. During the initial 3 h, RP values were highest after the control meal and were intermediate after the butter meal. The incremental response areas in the chylomicron-poor fraction for the 480-min observation period tended to be higher after the butter meal than after the olive oil meal (28630 ± 11468 compared with $22860 \pm 4492 \mu\text{g} \cdot 480 \text{ min/L}$; $P = 0.06$).

GIP and GLP-1 responses

During the initial 3 h, GLP-1 responses (**Figure 5**) to the olive oil meal ($1512 \pm 1182 \text{ pmol} \cdot 180 \text{ min/L}$) were higher than responses to the control meal ($467 \pm 446 \text{ pmol} \cdot 180 \text{ min/L}$) ($P < 0.001$). Responses to the butter meal ($1077 \pm 568 \text{ pmol} \cdot 180 \text{ min/L}$) were not significantly different from those to either the olive oil or control meal. From 180 min to the end of the study period, no significant differences were found between the fat-rich meals, both of which induced higher responses than did the control meal.

The GIP responses displayed another pattern (**Figure 5**). The butter and olive oil meals induced similar increases in activity during the first 3 h, which were higher than the responses to the control meal (16400 ± 5977 and 13700 ± 5733 compared with $8609 \pm 3556 \text{ pmol} \cdot 180 \text{ min/L}$, respectively; $P < 0.001$). Subsequently, the incremental responses to the olive oil meal were higher than those to either the control or butter meal, even after 480 min (36800 ± 1312 for the olive oil meal compared with $28400 \pm 1073 \text{ pmol} \cdot 480 \text{ min/L}$ for the butter meal; $P = 0.003$).

DISCUSSION

Our results indicate that saturated and monounsaturated fats consumed with carbohydrates may exert differential effects on postprandial triacylglycerol and lipoprotein metabolism as well as on postprandial HDL-cholesterol concentrations. A possible link between postprandial lipemia and GLP-1 activity was found

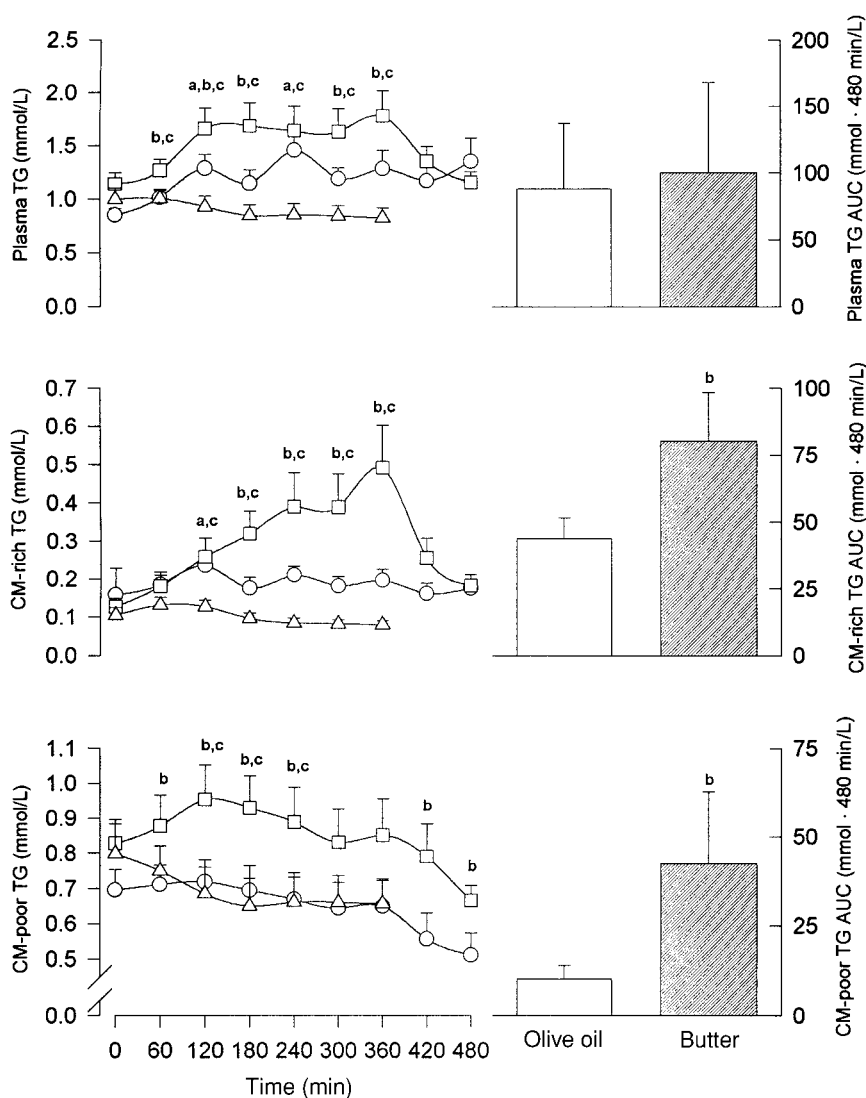


FIGURE 2. Mean (\pm SE) postprandial triacylglycerol (TG) responses in plasma, the chylomicron (CM)-rich fraction, and the CM-poor fraction in 10 healthy subjects to a control meal of soup plus 50 g carbohydrates (Δ), the control meal plus 80 g olive oil (\circ), and the control meal plus 100 g butter (\square). In the right panel are the corresponding areas under the curves (AUCs) after the olive oil and butter meals. b: butter > olive oil (repeated-measures ANOVA).

with olive oil, which induced higher responses in both GLP-1 and GIP than did butter. No significant differences in the responses of glucose, insulin, or fatty acids to olive oil or butter were found. Gatti et al (30) found large reductions in postprandial glucose responses to monounsaturated but not saturated fat in healthy subjects. On the other hand, they found no significant differences in insulin responses, which agrees with our results. The uniformity of the insulin responses to the olive oil and butter meals in our study may appear surprising because the responses of the incretin hormones were highest after the olive oil meal. Thus, as compared with the butter meal, one might have expected higher insulin responses especially to the carbohydrate control meal and to the olive oil meal as a result of higher postprandial concentrations of GIP (31) and GLP-1 (32).

The difference in incretin hormone responses is puzzling. Both GIP and GLP-1 secretion increase after ingestion of glucose and a mixed meal in humans (31, 32), and a mixture of glucose and fat

was a strong stimulator of both incretin hormones in pigs (33). Rocca and Brubaker (16) reported that monounsaturated fatty acids with a chain length >14 carbons, eg, oleic acid, were stronger stimulators of GLP-1 secretion in enterocyte cultures from rats than were fatty acids with a chain length of 14–18 carbons and a degree of unsaturation of from 0 to 2. About 90% of the fatty acids in olive oil have ≥ 18 carbon atoms and 74% are monounsaturated, whereas 72% of butter is saturated fatty acids. Our findings suggest that monounsaturated fat is a potent stimulator of postprandial GIP and GLP-1 secretion in healthy subjects, which to our knowledge has not been reported previously. In our study, similar amounts of carbohydrate and fat were ingested in the 2 fat-rich meals.

A difference in gastric emptying after the ingestion of fat may influence postprandial responses (34). As judged by the glucose responses in Figure 1, however, gastric emptying was delayed equally after the 2 fat-rich meals and the control meal. The average glucose response to the olive oil but not to the butter meal was lower

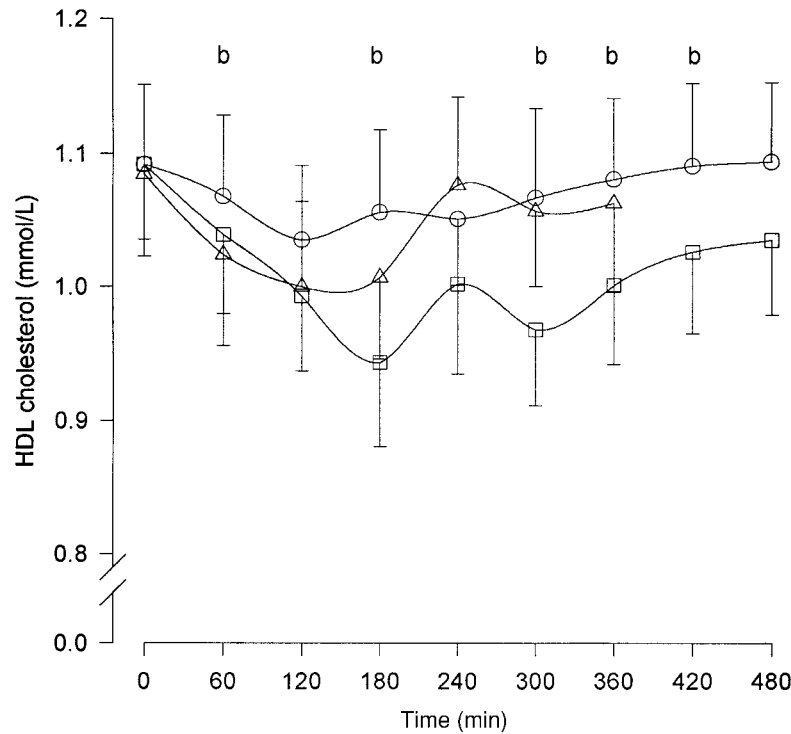


FIGURE 3. Mean (\pm SE) postprandial HDL-cholesterol responses in 10 healthy subjects to a control meal of soup plus 50 g carbohydrates (Δ), the control meal plus 80 g olive oil (\circ), and the control meal plus 100 g butter (\square). b: butter > olive oil (repeated-measures ANOVA).

than the response to the control meal, suggesting slightly more retarded gastric emptying after the olive oil meal, and to a lesser degree after the butter meal, than after the control meal. Postprandial fatty acid responses to the 2 fat-rich meals did not differ significantly, but were higher after the fat-rich meals than after the control meal as expected.

Triacylglycerol concentrations after the butter meal were higher than after the olive oil and control meals at several time points in plasma, the chylomicron-rich fraction, and the chylomicron-poor fraction (Figure 2). Because of relatively large variations in individual response areas in plasma, however, no significant differences in triacylglycerol response areas after the olive oil and butter meals were found.

RP responses indicated higher total production of chylomicrons after the butter meal than after the olive oil or control meal (Figure 4). In the chylomicron-poor fraction, the highest RP responses were seen after the control meal, which corroborates the findings of Chait et al (35), who showed that the smaller the fat load, the greater the number of particles in the VLDL fraction and the fewer the number in the chylomicron fraction. Furthermore, Hazzard and Bierman (21) showed that without a fat load, most of the labeled retinyl palmitate was associated with lipoprotein particles of S_f 20–400 (VLDL).

The use of RP responses as markers of chylomicron and chylomicron remnant metabolism has been questioned (36, 37). However, Krasinski et al (36) found that transfer of triacylglycerol from triacylglycerol-rich lipoproteins to intermediate-density lipoproteins did not occur during the initial 6 h after a fat load. Furthermore, Karpe et al (37) reported that RP is a valid tracer substance of intestinal lipoproteins and found in addition that the RP response is a reliable marker of chylomicron responses

during the first hours after a fat load. In our study in fact, the largest differences in RP responses were seen within the first 4–6 postprandial hours.

HDL-cholesterol responses to the olive oil meal were not inhibited as they were to the butter meal (Figure 3). Postprandial suppression of HDL cholesterol was shown previously in healthy subjects after the ingestion of cream (11), but in this study the cream was not compared with other fat types. Later, de Bruin et al (12) showed a postprandial HDL-cholesterol conserving effect after the ingestion of olive oil but not soybean oil; however, no significant differences in triacylglycerol responses were found. Our results may seem puzzling because responses of glucose, fatty acids, and insulin were not significantly different after ingestion of the butter and olive oil meals, whereas triacylglycerol responses were clearly higher in plasma, the chylomicron-rich fraction, and the chylomicron-poor fraction after the butter meal. Our results suggest that the incretins, ie, GLP-1 and GIP, may serve as a link between the type of fat ingested and postprandial triacylglycerol and HDL-cholesterol metabolism. A stimulating effect of GIP on lipoprotein lipase independent of insulin was suggested in an in vitro study in rats (38). Furthermore, in an in vivo study by Murphy et al (39) it was suggested that GIP mediates increased postprandial lipoprotein lipase activity in humans; however, neither a differential effect of various fatty acids on incretin concentrations nor an effect of GLP-1 on postprandial lipid concentrations was shown previously in humans.

Many factors control the circulating concentrations of triacylglycerol; chylomicron secretion by the intestine, VLDL secretion by the liver, conversion of triacylglycerol-rich lipoproteins to triacylglycerol-depleted lipoproteins, and tissue uptake of triacylglycerol-depleted lipoproteins are all processes that could be

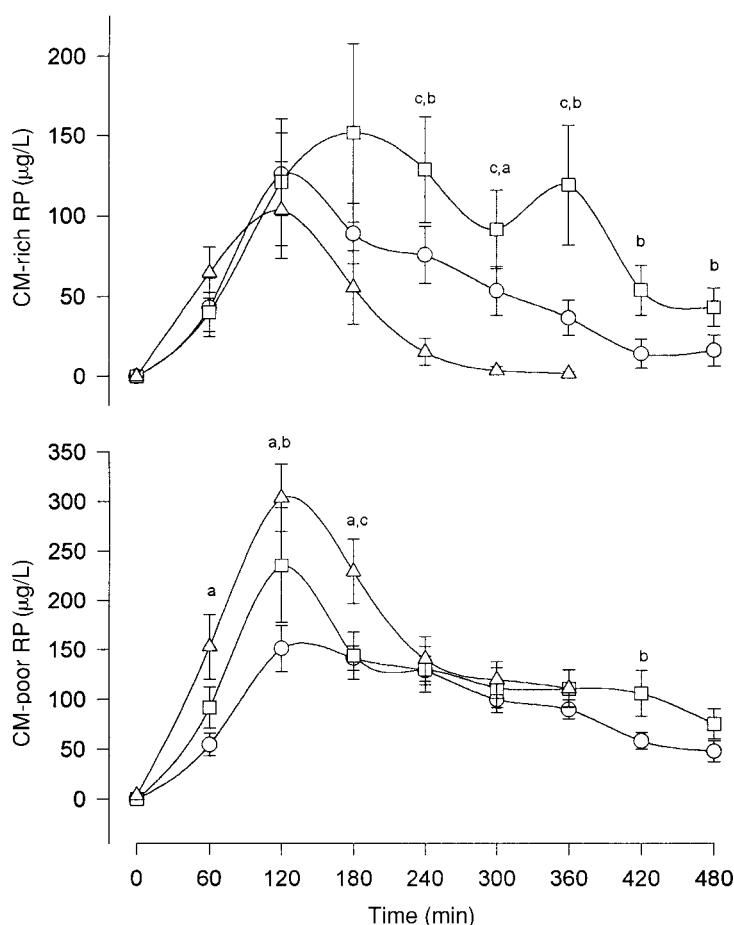


FIGURE 4. Mean (\pm SE) retinyl palmitate (RP) responses in the chylomicron (CM)-rich fraction and the CM-poor fraction in 10 healthy subjects to a control meal of soup plus 50 g carbohydrates (Δ), the control meal plus 80 g olive oil (\circ), and the control meal plus 100 g butter (\square). a: olive oil \neq control; b: butter \neq olive oil; c: butter \neq control (repeated-measures ANOVA).

responsible for fluctuations in postprandial triacylglycerol concentrations (40). Oleic acid is well absorbed in humans (41) and in this study we found no indications of a delayed absorption of olive oil (Figure 2). Factors responsible for the clearance of postprandial triacylglycerol are many (42). First, the activity of lipoprotein lipase, as described above, affects triacylglycerol clearance. Second, receptor-mediated remnant removal may be a determinant of triacylglycerol metabolism. VLDL remnants are clearly dependent on the expression of the LDL receptor, whereas chylomicron remnants seem to be cleared mainly via the LDL-receptor-related protein (43). However, an acute effect on receptor expression has not been reported and seems unlikely in this kind of experiment.

A hormonal fine-tuning during the postprandial state may be another factor responsible for postprandial triacylglycerol metabolism. In insulin-resistant situations, insulin concentrations can be insufficient for suppression of VLDL secretion by the liver (44). However, a difference in insulin sensitivity after the 2 fat-rich meals in our study seems unlikely because of the identical insulin and glucose responses. Furthermore, infusion of GLP-1 in healthy subjects has been shown to not acutely affect insulin sensitivity (45). A possible positive influence of GLP-1 or GIP on this hormonal fine-tuning may explain, at least in part, the accelerated clearance of postprandial triacylglycerol after olive oil ingestion.

Thus, after the butter meal, an excessive increase in VLDL particles superimposed on chylomicrons could contribute to the augmented triacylglycerol concentrations (42), exceeding the capacity of the common triacylglycerol removal mechanism for chylomicron and VLDL particles (46, 47). In contrast, signs of this phenomenon were not seen after the ingestion of olive oil. The fatty acid composition of chylomicrons is known to reflect the composition of the ingested meal (48). A higher affinity of chylomicrons and chylomicron remnants for receptor-associated removal and hepatic lipase (12) after ingestion of olive oil would result both in lower postprandial triacylglycerol concentrations and higher postprandial HDL-cholesterol concentrations. Other mechanisms, eg, activity of cholesteryl ester transfer protein, may influence the observed differences in triacylglycerol metabolism, but have yet to be investigated. Future studies using fat loads could also investigate potential relations between incretin responses and different amounts of carbohydrate loads, gastric emptying, and lipoprotein lipase activity in plasma and in fat tissue.

Olive oil induced a beneficial lipid profile, ie, lower triacylglycerol concentrations and higher HDL-cholesterol concentrations than were induced by butter, without eliciting significant differences in glucose, insulin, or fatty acid concentrations. Furthermore, olive oil induced higher concentrations of GLP-1 and GIP than did butter, which may point to a relation between fatty

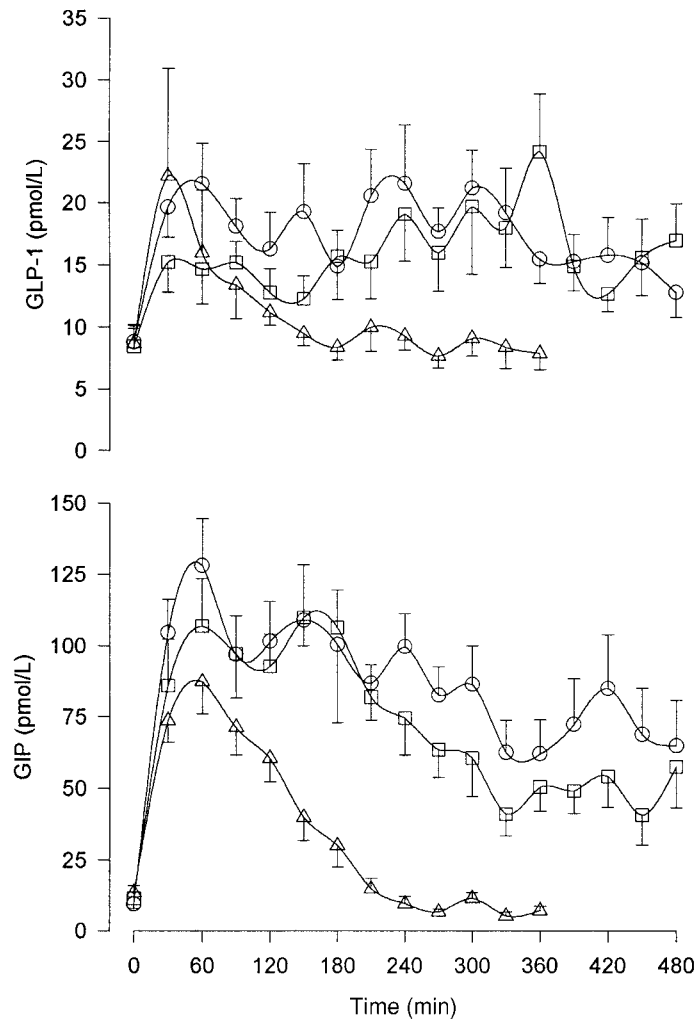



FIGURE 5. Mean (\pm SE) postprandial glucagon-like peptide 1 (GLP-1) and gastric inhibitory polypeptide (GIP) responses in 10 healthy subjects to a control meal of soup plus 50 g carbohydrates (Δ), the control meal plus 80 g olive oil (\circ), and the control meal plus 100 g butter (\square).

acid composition, incretin responses, and triacylglycerol metabolism in the postprandial phase. 

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