Differential effects of saturated and monounsaturated fat on blood glucose and insulin responses in subjects with non-insulin-dependent diabetes mellitus

Ole Rasmussen, Finn Friis Lauszus, Christian Christiansen, Claus Thomsen, and Kjeld Hermansen

ABSTRACT To compare the metabolic effect of coingestion of saturated and monounsaturated fats with potato, 12 subjects with non-insulin-dependent diabetes mellitus (NIDDM) received 300 g mashed potato alone or in combination with 40 g olive oil, 80 g olive oil, 50 g butter, or 100 g butter, respectively. The blood glucose response area to potatoes with 100 g butter (448 ± 68 mmol·240 min/L) was significantly lower than after the four other meals: 596 ± 63 (potato alone), 649 ± 82 (potato + 40 g olive oil), 587 ± 80 (potato + 50 g butter), and 604 ± 81 (potato + 80 g olive oil) mmol·240 min/L, P < 0.05, respectively. The insulin response was significantly increased by adding 50 and 100 g butter, whereas addition of 40 and 80 g olive oil had no effect. The fatty acid concentration was higher when 100 g butter was added to the potato meal than when it was not (0.67 ± 0.05 compared with 0.48 ± 0.07 mmol/L; P < 0.05). Fatty acid concentrations were similar to those found for the other meals. The triacylglycerol response increased in a dose-dependent manner with the fat content of the meals irrespective of the type of fat. We conclude that butter increases the insulin response more than does olive oil, and large amounts of butter also increase fatty acid and triacylglycerol concentrations. Am J Clin Nutr 1996;63:249–53.

KEY WORDS Non-insulin-dependent diabetes mellitus, NIDDM, potato, saturated fat, monounsaturated fat, blood glucose, insulin, fatty acids, olive oil

INTRODUCTION

Fat constitutes 40–45% of total energy consumption in some Western countries. Whereas saturated fat is the most commonly consumed fat in northern Europe and the United States, the monounsaturated fat of olive oil dominates consumption in the Mediterranean region (1). Current dietary recommendations for diabetic subjects prescribe a reduction in total fat, saturated fat in particular, which should be replaced by carbohydrate (2–4). However, monounsaturated fat may also be used as an alternative to saturated fat. Thus, clinical studies with high-fat diets rich in monounsaturated fatty acids (MUFAs) showed improved lipoprotein composition in normal subjects (5, 6), improved glycemic control (7, 8), and subdued 24-h ambulatory blood pressure in subjects with non-insulin-dependent diabetes mellitus (NIDDM) (8), compared with the recommended high-carbohydrate diet. These results indicate that an isoenergetic, high-MUFA, low-carbohydrate diet can be consumed by NIDDM patients without deleterious effects on lipid and glucose metabolism. However, no information on the acute effect of different types of fat on glucose, insulin, and triacylglycerol concentrations in NIDDM subjects is available.

In normal subjects, coingestion of 50 g butter reduces the glycemic responses to potato and bread without altering the insulin response (9–11). This may be due to reduced gastric emptying caused by higher concentrations of gastric inhibitory peptide (GIP) after fat ingestion (11), but the mechanism is still uncertain. The increased GIP concentration obtained after fat intake has been proposed to be an incretin (11, 12), which may explain the enhanced insulin secretion. In NIDDM subjects, however, a stepwise increase in saturated fat from 5 to 45 g had no influence on the glycemic response to potato (13), whereas insulin concentrations increased after consumption of 15 g fat. Surprisingly, Gatti et al (14) found no effect on the postprandial blood glucose response area after adding 35 g saturated fat to a white bread meal, whereas coingestion of 35 g olive oil or corn oil reduced the glycemic response in normal subjects by 70% compared with white bread, without altering the insulin responses. This may be explained by differential effects of saturated and unsaturated fats on the glycemic response to a starch-rich meal. So far, no reports comparing the acute effect of unsaturated and saturated fat on the blood glucose, insulin, and lipid responses in NIDDM subjects are available. In the present investigation we studied the effect of adding 40 and 80 g saturated and monounsaturated fat to a starch-rich meal on blood glucose, insulin, and lipid concentrations in NIDDM subjects.

SUBJECTS AND METHODS

Subjects

Twelve patients with NIDDM participated in the study. The subjects were selected among outpatients of the Diabetes Clinic

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at Aarhus University Hospital in Aarhus, Denmark. Clinical characteristics for the 12 participants (8 men, 4 women) are given in Table 1. All patients were treated with their prescribed diabetic diets, in addition, seven required sulfonylurea hypoglycemic agents and three required metformin. No patients had clinical signs of neuropathy (judged by determination of the vibratory perception threshold with a Biothesiometer (Biomedical Instruments, Chagrin Falls, OH). No patients had retinopathy more severe than background. Participants were fully informed of the experimental nature of the study and the protocol was approved by the local ethics committee of Aarhus County.

**Study design**

Studies were performed on an outpatient basis. The five test meals were given within a 4–6-wk period. Patients were given test meals at 0830 after a 12-h overnight fast. A cannula was inserted into an antecubital vein of each subject, from which blood samples were collected 15 min before, at the beginning of the test meal, and 15, 30, 45, 60, 90, 120, 150, 180, 210, and 240 min after the meal. Test meals were ingested within 10 min; participants took their prescribed medicine at the same time. The patients were asked to urinate before meal intake and glucose loss was measured in the urine collected during the test period (0–240 min).

**Test meals**

The study included five test meals consisting of 300 g mashed potato (Sava cultivar) given alone or mixed with fat in the form of olive oil (40 or 80 g) or butter (50 or 100 g). The nutrient composition of the potato (Table 2) was calculated according to the Helms food tables (15). The nutrient contents of unsalted butter and olive oil were provided by the manufacturers. To ensure isoenergetic amounts of butter and olive oil, larger amounts of butter were given because of its water content. The olive oil contained predominantly MUFA (74%) and butter mainly saturated fatty acids (72%). The potatoes (without skin) were boiled in water with 5 g added salt for 20 min and then blended immediately for 4 min and served hot. The potato eaten alone was blended with 100 mL water, whereas the other meals had added oil or unmelted butter only. The meals were served in random order with 250 mL tap water and were ingested continuously over a 10-min period.

**Analytical techniques**

Blood and urinary glucose were determined by the glucose oxidase method, glycosylated hemoglobin (HbA1c) values by a commercial kit (Bio-Rad, Richmond, CA; normal values 3.5–5.5%), and serum insulin concentrations by a specific radioimmunoassay (16). Fatty acids and triacylglycerols were determined by standard enzymatic colorimetric assays using commercial kits (Waco Chemicals, Neuss, Germany and Boehringer Mannheim, Neckargemünd, Germany).

**Statistical methods**

The positive blood glucose and insulin response areas were calculated geometrically according to Jenkins and Wolever (17), and blood glycemias areas are given as percentages of the response to potato eaten alone. Values below the basal value were ignored. The basal value was calculated as the mean value at 15 and 0 min before ingestion of the test meals. Results are expressed as means ± SEM. Comparisons between response areas and mean values were made by two-way analysis of variance (ANOVA), followed by paired t tests of the means if the ANOVA indicated significant differences. The limit of significance was set at P < 0.05.

**RESULTS**

Twelve subjects completed the study and consumed the test meals within the prescribed time. There were no differences on the five different study days in fasting blood glucose, serum insulin, fatty acid, or triacylglycerol concentrations.

**Blood glucose and insulin concentrations**

The results are given in Table 3. Postprandial blood glucose and insulin responses to the meals are shown in Figure 1. The blood glucose response area to potatoes with 100 g butter (448 ± 68 mmol ∙ 240 min/L) was significantly lower than that after the other four meals: 596 ± 63 (potato alone), 649 ± 82 (40 g olive oil), 587 ± 80 (50 g butter), and 604 ± 81 (80 g olive oil) mmol ∙ 240 min/L, respectively (P < 0.05). The mean peak blood glucose concentration and the percentage glucose response to potato with 100 g butter were also lower than for the other meals (Table 3). No difference in glucosuria after the meals was detected. The insulin response area to potato alone (15.80 ± 3.80 mmol ∙ 240 min/L) was significantly increased by coinjection of 50 g butter (21.86 ± 4.56 mmol ∙ 240 min/L, P < 0.05) and 100 g butter (22.12 ± 4.56 mmol ∙ 240 min/L, P < 0.05), whereas addition of 40 and 80 g olive oil did not significantly increase insulin secretion (19.48 ± 4.32 and 19.13 ± 3.27 mmol ∙ 240 min/L, respectively).

### Table 1

Clinical characteristics of 12 non-insulin-dependent diabetic subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>56.0 ± 10.4 (37–67)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.6 ± 4.9 (21.9–35.8)</td>
</tr>
<tr>
<td>Duration of diabetes (y)</td>
<td>5.0 ± 3.5 (1–14)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.2 ± 2.4 (5.7–11.8)</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>9.9 ± 4.2 (4.8–17.7)</td>
</tr>
</tbody>
</table>

*1 ± SD; range in parentheses; n = 8 men, 4 women.

2 Hemoglobin A1c; normal range: 4.1–6.1%.

### Table 2

Test meal composition and portion size

<table>
<thead>
<tr>
<th>Test meal</th>
<th>Chemical composition</th>
<th>Portion size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>carbohydrates</td>
<td>Protein</td>
</tr>
<tr>
<td>P</td>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>P + 40 g O</td>
<td>53.1</td>
<td>5.4</td>
</tr>
<tr>
<td>P + 50 g B</td>
<td>54.1</td>
<td>5.6</td>
</tr>
<tr>
<td>P + 80 g O</td>
<td>53.1</td>
<td>5.4</td>
</tr>
<tr>
<td>P + 100 g B</td>
<td>55.1</td>
<td>5.8</td>
</tr>
</tbody>
</table>

1 P, potato; O, olive oil (cold-pressed virgin olive oil, Elanthy, Piraeus, Greece); B, Danish butter. All meals were served with 250 mL tap water.
TABLE 3
Metabolic responses in 12 non-insulin-dependent diabetic patients to meals of 300 g mashed potatoes eaten alone and with olive oil (40 and 80 g) and butter (50 and 100 g)

<table>
<thead>
<tr>
<th>Addition to potato</th>
<th>None</th>
<th>40 g Oil</th>
<th>50 g Butter</th>
<th>80 g Oil</th>
<th>100 g Butter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose area (mmol · 240 min/L)</td>
<td>596 ± 63</td>
<td>649 ± 82</td>
<td>587 ± 80</td>
<td>604 ± 81</td>
<td>448 ± 68&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Blood glucose (% of area after potato)</td>
<td>100</td>
<td>109 ± 10</td>
<td>102 ± 11</td>
<td>107 ± 14</td>
<td>78 ± 10&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Blood glucose peak (mmol/L)</td>
<td>15.9 ± 0.9</td>
<td>16 ± 1.3</td>
<td>14.8 ± 1.1</td>
<td>15.4 ± 1.2</td>
<td>13.9 ± 1.2&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fasting blood glucose (mmol/L)</td>
<td>9.9 ± 1.1</td>
<td>10 ± 10.3</td>
<td>9.6 ± 1.1</td>
<td>9.9 ± 1.2</td>
<td>10.2 ± 1.2</td>
</tr>
<tr>
<td>Insulin area (mmol · 240 min/L)</td>
<td>15.80 ± 3.80&lt;sup&gt;4&lt;/sup&gt;</td>
<td>19.48 ± 4.32</td>
<td>21.86 ± 4.56</td>
<td>19.13 ± 3.28</td>
<td>22.12 ± 4.56</td>
</tr>
<tr>
<td>Triacylglycerol area (mmol · 240 min/L)</td>
<td>---</td>
<td>77 ± 19&lt;sup&gt;1&lt;/sup&gt;</td>
<td>56 ± 16&lt;sup&gt;6&lt;/sup&gt;</td>
<td>133 ± 36</td>
<td>145 ± 29</td>
</tr>
<tr>
<td>Mean fatty acids (mmol/L)</td>
<td>0.48 ± 0.07&lt;sup&gt;6&lt;/sup&gt;</td>
<td>0.56 ± 0.04</td>
<td>0.57 ± 0.05</td>
<td>0.54 ± 0.05</td>
<td>0.67 ± 0.05</td>
</tr>
<tr>
<td>Urinary glucose (g)</td>
<td>11.6 ± 3.8</td>
<td>5.5 ± 1.6</td>
<td>8.6 ± 2.9</td>
<td>9.5 ± 3.9</td>
<td>10 ± 3.9</td>
</tr>
</tbody>
</table>

<sup>1</sup> ± SEM.
<sup>2</sup> Significantly smaller than for all other conditions, P < 0.05.
<sup>3</sup> Significantly smaller than for all other conditions except potato alone, P < 0.05.
<sup>4</sup> Significantly smaller than for 50 and 100 g butter, P < 0.05.
<sup>5</sup> Significantly smaller than for 80 g oil, P < 0.05.
<sup>6</sup> Significantly smaller than for 100 g butter, P < 0.05.

Lipid concentrations

The postprandial fatty acid and triacylglycerol concentrations are given in Figure 2 and Table 3. Fatty acid concentrations declined after all five test meals (Figure 2). The average fatty acid concentration was higher when 100 g butter was eaten with the potatoes than without (0.67 ± 0.05 compared with 0.48 ± 0.07 mmol/L, P < 0.05). No difference in fatty acid concentration was detected after the other meals. In contrast, triacylglycerol concentrations and response areas increased in a dose-dependent manner after the meals containing both olive oil and butter (Figure 2, Table 3), whereas a slight decrease was seen after consumption of potato alone. Mean triacylglycerol concentrations after consumption of potato alone (1.5 ± 0.2 mmol/L) and after potato with 40 g olive oil (1.7 ± 0.2 mmol/L) were lower than after meals with 100 g butter (2.3 ± 0.3 mmol/L) and 80 g olive oil (2.1 ± 0.3 mmol/L)(P < 0.05). Plasma triacylglycerol concentrations at 240 min tended to be higher, although not significantly, after 100 g butter than after 80 g olive oil (2.7 ± 0.4 and 2.2 ± 0.4 mmol/L, respectively).

![FIGURE 1. Postprandial blood glucose and insulin responses in 12 patients with non-insulin-dependent diabetes mellitus after five different meals of mashed potato: ●, potato alone; ▼, + 40 g olive oil; ▼, + 80 g olive oil; □, + 50 g butter; and ■, + 100 g butter.](https://academic.oup.com/ajcn/article-abstract/63/2/249/4650563)
fatty acids appear to potentiate insulin release from isolated mouse islets through an increase in intracellular calcium and another, as yet unidentified, glucose-dependent mechanism (19). Because fat is the most potent dietary stimulus of GIP (11), an indirect effect via GIP-mediated glucose-dependent insulin secretion might also operate (12, 20, 21). The finding that olive oil apparently had no effect on insulin secretion appears puzzling. Whether this is a question of the amount of monounsaturated fat given is unknown.

The similar increase in insulin concentrations after consumption of 50 and 100 g butter compared with potato alone may be due to an incretin effect, which was found previously after addition of butter (10, 11) without a dose-response relation (13). Many factors might contribute to the reduction in glucose response stimulated by potato after addition of 100 g butter, because 50 and 100 g butter elevated insulin concentrations to the same degree. A more marked delay in gastric emptying may have contributed to the lower postprandial blood glucose response seen with the largest amount of butter (22). However, we cannot exclude the possibility that fat ingestion may alter the hepatic extraction of blood glucose, leading to a reduced postprandial blood glucose response.

The simultaneous increase in insulin and fatty acid concentrations after consumption of potato with 100 g butter may appear puzzling. However, our findings are consistent with previous data obtained in normal subjects. Infusion of triacylglycerol emulsions leads to an elevated fatty acid concentration, which is related to the activity of the enzyme lipoprotein lipase (23, 24). Even during insulin infusion rates that would normally suppress fatty acids and inhibit fat oxidation, a simultaneous infusion of triacylglycerol emulsion leads to maintenance of high plasma fatty acids and a substantial contribution to energy production (25). Furthermore, addition of 80 g fat to a carbohydrate-rich meal leads to increased fat oxidation and sparing of carbohydrate oxidation (26). The increased fat oxidation was associated with elevated fatty acid concentrations 2–4 h after the meals, at the same time glucose and insulin concentrations were also elevated. The fatty acids are derived presumably from chylomicron triacylglycerol (27) as a result of carbohydrate-stimulated lipoprotein lipase activity (via insulin release). The combination of elevated concentrations of glucose, fatty acids, and chylomicron triacylglycerols for a period of hours could provide a useful substrate mixture for muscular work.

The difference in postprandial fatty acid and triacylglycerol peaks after consumption of butter and olive oil may be explained in part by differences in fatty acid chain length. Thus, ~90% of olive oil is 18 carbon atoms or longer whereas 22% of butter is 14 carbon atoms or shorter. The short- and medium-chain fatty acids (which contain <10–12 carbon atoms) pass from mucosal cells into circulation without reesterification and are bound to albumin. Furthermore, the fact that no difference in fatty acid concentrations after consumption of potato and olive oil or potato alone could be detected may be due to differential effects on postprandial triacylglycerol concentration by olive oil and butter. Thus, the postprandial triacylglycerol concentrations after 80 g olive oil peaked after 120 min and then declined, whereas the triacylglycerol response to 100 g butter increased continuously over the entire 240-min observation period. The plasma triacylglycerol concentration at 240 min also tended to be higher after 100 g butter than after 80 g

DISCUSSION

The results demonstrate that the addition of saturated and monounsaturated fats to a carbohydrate-rich meal has different effects on blood glucose, insulin, and fatty acid concentrations. Interestingly, 100 g butter with potato suppressed the blood glucose response area in subjects with NIDDM whereas neither 40 nor 80 g olive oil had any influence. Furthermore, intake of butter but not olive oil stimulated insulin release. In contrast, Gatti et al (14) reported a large reduction in postprandial blood glucose response to white bread after addition of polyunsaturated and monounsaturated but not saturated fat in normal subjects, whereas similar insulin responses to the meals were found. The unchanged insulin concentrations after ingestion of olive oil corroborates the findings of the present study, whereas we found elevated insulin concentrations after intake of saturated fat. This agrees with the observation of Gannon et al (13) in NIDDM subjects. Their study showed an increase in insulin concentrations after a potato meal with 30 and 50 g butter despite similar blood glucose responses. In addition, they found an increase in C-peptide concentrations after the addition of saturated fat. This indicates that coinjection of saturated fat enhanced insulin secretion, a finding that also agrees with that of Collier et al (18). The mechanism by which saturated fatty acids increase insulin release is not known. However, saturated

![FIGURE 2. Postprandial fatty acid and triacylglycerol concentrations in 12 patients with non-insulin-dependent diabetes mellitus after five different meals of mashed potato: O, potato alone; \( \vee \), + 40 g olive oil; \( \triangledown \), + 80 g olive oil; \( \square \), + 50 g butter; and \( \blacksquare \), + 100 g butter.](https://academic.oup.com/ajcn/article-abstract/63/2/249/4650563)
olive oil. The finding of enhanced postprandial triacylglycerol concentrations after consuming potato in the present study corroborates the findings of Gannon et al (13), who found a dose-dependent increase in triacylglycerol after adding increasing amounts of butter to potato. Note that the triacylglycerol uptake and clearance after a large saturated fat load is far from complete after 4 h of observation (28, 29), and that 8–10 h of observation are required to cover the period of postprandial triacylglycerol absorption and clearance. However, the primary question under consideration was how the two types of fat influenced blood glucose and insulin responses. Further investigations with 8–10 h observation periods are needed to characterize the postprandial lipemia for the two fat types. Previous studies found lower chylomicron triacylglycerol responses to meals with polyunsaturated fatty acids than to meals with saturated fatty acids (30); however, no results focusing on MUFAs are available to our knowledge.

Butter increases the insulin response more than does olive oil and large amounts also increase fatty acid and triacylglycerol concentrations, which may lead to hyperlipemia and reduced insulin sensitivity in the long term.*

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REFERENCES