Comparison of the effects of medium-chain triacylglycerols, palm oil, and high oleic acid sunflower oil on plasma triacylglycerol fatty acids and lipid and lipoprotein concentrations in humans.\textsuperscript{1–3}

Nilo B. Cater, Howard J. Heller, and Margo A. Denke

ABSTRACT Although medium-chain triacylglycerols (MCTs, composed of medium-chain fatty acids 8:0 and 10:0) have long been described as having neutral effects on serum cholesterol concentrations, experimental evidence supporting this claim is limited. In a randomized, crossover, metabolic-ward study, we compared the lipid effects of a natural food diet supplemented with either MCTs, palm oil, or high oleic acid sunflower oil in nine middle-aged men with mild hypercholesterolemia. Rather than having a neutral effect, MCT oil reduced total cholesterol concentrations that were not significantly different from those produced by palm oil (MCT oil: 5.87 ± 0.75 mmol/L; palm oil: 5.79 ± 0.72 mmol/L) but significantly higher than that produced by high oleic acid sunflower oil (5.22 ± 0.52 mmol/L). Low-density-lipoprotein (LDL)-cholesterol concentrations paralleled those of total cholesterol. MCT oil tended to result in higher triacylglycerol concentrations than either palm oil or high oleic acid sunflower oil, but this difference was not significant. There were no differences in high-density-lipoprotein cholesterol concentrations. The palmitic acid and total saturated fatty acid content of plasma triacylglycerols in the MCT-oil diet was not significantly different from that in the palm oil diet. On the basis of percentage of energy, this study suggests that medium-chain fatty acids have one-half the potency that palmitic acid has in raising total and LDL-cholesterol concentrations. \textit{Am J Clin Nutr} 1997;65:41–5.

KEY WORDS Medium-chain triacylglycerols, medium-chain fatty acids, cholesterol-raising fat, cholesterol-raising fatty acids

INTRODUCTION Fatty acids are often classified according to their physical properties, such as degree of saturation: saturated, monounsaturated, or polyunsaturated. This classification has been useful for predicting how a dietary fatty acid will affect serum cholesterol concentrations in humans because the majority of the cholesterol-raising effects of a fat can be ascribed to its saturated fatty acid content (1). Another method for classifying fatty acids separates them according to chain length. The saturated fatty acids can be classified as short chain (4:0–6:0), medium chain (8:0–10:0), long chain (12:0–18:0), and very long chain (20:0–24:0). Chain length imparts important differences in absorption and metabolism (2–4). Specifically, medium-chain fatty acids are readily hydrolyzed from triacylglycerols by lingual and gastric lipases; long-chain and very-long-chain fatty acids require intestinal lipase for cleavage from triacylglycerols (5). Free medium-chain fatty acids are absorbed readily into gastrointestinal cells; free longer-chain fatty acids require the detergent action of bile to cross into the intestinal cell (6). Once inside, medium-chain fatty acids diffuse rapidly into the portal circulation; long-chain fatty acids are typically reesterified into triacylglycerols, which are in turn packaged into chylomicrons and secreted into the lymph (7, 8). After reaching the liver, medium-chain fatty acids are \(\beta\)-oxidized into acetyl coenzyme A (CoA); most longer-chain fatty acids mix with the hepatic fatty acid pool (3, 9).

Because medium-chain fatty acids are saturated, one might predict that medium-chain fatty acids will increase serum cholesterol concentrations compared with carbohydrate or monounsaturated fatty acids. However, because medium-chain fatty acids are rapidly oxidized, one might predict that medium-chain fatty acids will produce a neutral cholesterol response similar to that of carbohydrate or monounsaturated fatty acids. Support for this hypothesis comes from data showing that MCT feeding raises serum triacylglycerol concentrations, much like carbohydrate (10, 11). The present metabolic-ward investigation was designed to compare the effects on lipid and lipoprotein concentrations of MCT oil (a fat rich in medium-chain fatty acids) with that of palm oil (a fat rich in the long-chain saturate palmitic acid) and with that of high oleic acid sunflower oil (a fat rich in the long-chain monounsaturate oleic acid).

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SUBJECTS AND METHODS

Subjects

The research protocol was approved by the Subcommittee of Human Studies of the Dallas Veterans Administration Medical Center and informed consent was obtained from each patient. Nine men with mild hypercholesterolemia aged 55–75 y (mean: 66 y) were recruited for study. The mean body mass index (in kg/m²) was 27 ± 5. At baseline, mean (± SD) fasting total cholesterol was 5.69 ± 0.54 mmol/L (219 ± 21 mg/dL) and fasting triacylglycerol was 1.52 ± 0.77 mmol/L (135 ± 68 mg/dL). Three men had documented coronary artery disease but were asymptomatic at the time of study. All were medically stable without evidence of gastrointestinal, renal, or untreated endocrine diseases or evidence of glucose intolerance, defined as a randomly measured glucose concentration > 7.2 mmol/L (> 130 mg/dL) or a fasting glucose concentration > 5.5 mmol/L (> 100 mg/dL).

Diet

In this metabolic-ward study, a randomized, crossover design was used. Each diet was administered for 3 wk on the metabolic ward. The inpatient diet periods were separated by an outpatient ad libitum period ≈ 1 wk. Patients lived in the metabolic ward during each diet period and were provided with all foods and fat supplements.

The daily base diet was a low-fat, natural-food diet comprising lean meats, skim milk, and 28 g (2 Tbsp) margarine to provide essential fatty acids. This base diet contributed all of the daily energy from carbohydrate (35%) and protein (12%) and contributed 19% of the total daily energy from fat (3% saturated, 4% monounsaturated, and 3% polyunsaturated fatty acids), with dietary cholesterol averaging 91 mg/d. In addition to this base diet, patients were provided with daily fat supplements that contributed 43% of daily energy. Thus, the overall energy composition of the diet was 53% fat, 35% carbohydrate, and 12% protein.

The daily fat supplements provided to each patient during each of the three dietary periods consisted of palm oil (RBD Palm Oil; Anderson-Clayton, Memphis), high oleic acid sunflower oil (Trisol 90 High Oleic Sunflower Oil; SVO Enterprises, Eastlake, OH), or medium-chain triacylglycerol oil (MCT oil; Mead Johnson, Evansville, IN). The fatty acid composition of the three fat supplements is given in Table 1.

The medium-chain fatty acid content of the MCT oil was twice that of the palmitic acid content of the palm oil. The weight of the MCT-oil supplement was adjusted for its lower energy value so that the same amount of energy was provided during all periods. In addition, energy intake was adjusted as necessary in order for each patient to maintain a constant weight throughout the study.

Each patient was instructed to add the test fat to soups, cereals, breads, and vegetables. Patients were interviewed daily and trays were examined to ensure that all food was consumed and that oil was not remaining on the plate. Patients were allowed to walk around the hospital grounds but were not allowed to engage in strenuous physical activity. During each of the final 5 d of each period, blood was drawn after a 14-h fast.

Lipid and lipoprotein analyses

Plasma cholesterol (12) and triacylglycerol (13) concentrations were determined by enzymatic assay. Plasma high-density-lipoprotein (HDL) cholesterol was measured after precipitation of apolipoprotein B–containing lipoproteins by heparin-manganese (14). Very-low-density lipoproteins (VLDLs) (density < 1.006 kg/L) were isolated by ultracentrifugation (105 000 × g for 18 h at 12–16 °C) and cholesterol was measured in the VLDL fraction and the infranate. LDL cholesterol was calculated by determining the difference between infranate cholesterol and the HDL fraction. Results were adjusted according to percentage recovery based on the differences between total cholesterol and VLDL plus infranate cholesterol. The means of the lipid and lipoprotein measurements during the final 5 d of each period were taken as the subject’s lipid and lipoprotein responses to diet.

Plasma fatty acid analysis

The specific fatty acids in plasma triacylglycerols were measured in each sample according to the methods of Lepage and Roy (15). Fasting plasma lipids were extracted and triacylglycerols separated by thin-layer chromatography on silica-gel G plates (250-μm thick) with hexane diethyl:ether:acetic acid (80:19:1, by vol) serving as the solvent system. The triacylglycerol band was scraped into glass tubes and resuspended in 2-mL volumes of methanol:benzene (4:1, by vol) solution. Fatty acids were then transesterified by heating the samples at 100 °C for 1 h, after 200 μL acetyl chloride had been added. The fatty acid composition was determined by gas-liquid chromatography (Hewlett-Packard, Palo Alto, CA) and capillary column.

Statistical analysis

A repeated-measures analysis of variance was performed to compare the mean values obtained during the three dietary periods. When the analysis of variance found the results of the diets to be different, paired t tests with Bonferroni correction for multiple comparisons were performed (16). Because there were three dietary periods, significance was reached at a P value < 0.05/3 (or, 0.0167) with Bonferroni correction.

RESULTS

The plasma triacylglycerol fatty acid composition for each of the three diets is presented in Table 2. Whereas the plasma

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**TABLE 1**

<table>
<thead>
<tr>
<th>Fatty acid composition of oils</th>
<th>Palm</th>
<th>Sunflower</th>
<th>MCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>% by wt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8:0</td>
<td>ND</td>
<td>ND</td>
<td>67.6</td>
</tr>
<tr>
<td>10:0</td>
<td>ND</td>
<td>ND</td>
<td>32.2</td>
</tr>
<tr>
<td>12:0</td>
<td>ND</td>
<td>ND</td>
<td>0.1</td>
</tr>
<tr>
<td>14:0</td>
<td>1.1</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>16:0</td>
<td>48.3</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>16:1</td>
<td>0.2</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>18:0</td>
<td>4.4</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>18:1</td>
<td>35.0</td>
<td>87.0</td>
<td></td>
</tr>
<tr>
<td>18:2</td>
<td>7.6</td>
<td>5.0</td>
<td></td>
</tr>
</tbody>
</table>

1 Measured by gas chromatography. MCT, medium-chain triacylglycerol; ND, not detected.
triaclylglycerol fatty acid pattern observed during the palm oil and high oleic acid sunflower oil diets reflected dietary fatty acid intake, the plasma triacylglycerol fatty acid pattern during the MCT diet did not reflect dietary fatty acid intake. The plasma triacylglycerol fatty acid composition during the MCT diet was not significantly different from that seen during the palm oil diet, with only a small amount of medium-chain fatty acids detected. During both the MCT-oil diet and the palm oil diet, the majority of saturated fatty acids were palmitic acid (16:0). Both the MCT-oil and palm oil diets had significantly higher concentrations of saturated fatty acids than the high oleic acid sunflower oil diet. The MCT-oil diet contained a larger amount of stearic acid (18:0) than the other two diets.

The unsaturated plasma triacylglycerol fatty acid content of the MCT-oil diet was not significantly different from that of the palm oil diet. The amount of unsaturated fatty acids in the plasma triacylglycerols during these two periods was significantly lower than that found during the high oleic acid sunflower oil diet period. The MCT-oil diet had significantly more 16:1 than either diet.

The mean lipid and lipoprotein concentrations during each dietary period are presented in Table 3. Both the palm oil and MCT-oil diets produced total cholesterol concentrations significantly higher than those obtained during the high oleic acid sunflower oil diet. The total cholesterol concentration of 5.79 mmol/L (224 mg/dL) during palm oil feeding was statistically indistinguishable from the total cholesterol concentration of 5.87 mmol/L (227 mg/dL) during the MCT-oil feeding. LDL-cholesterol changes largely reflected changes in total cholesterol. Both the palm oil and MCT-oil diets produced LDL-cholesterol concentrations that were not significantly different and that were significantly higher than those obtained during the high oleic acid sunflower oil diet.

Triacylglycerol concentrations during the MCT-oil diet were higher than those during either the palm oil or high oleic acid sunflower oil diets. VLDL-cholesterol concentrations were highest during the MCT-oil diet. HDL-cholesterol concentrations did not differ among the three diets.

### Table 2

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Palm oil</th>
<th>High oleic and sunflower oil</th>
<th>MCT oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:0</td>
<td>ND</td>
<td>ND</td>
<td>1.0 ± 0</td>
</tr>
<tr>
<td>10:0</td>
<td>ND</td>
<td>ND</td>
<td>1.5 ± 0</td>
</tr>
<tr>
<td>14:0</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>1.7 ± 0.7</td>
</tr>
<tr>
<td>16:0</td>
<td>28.6 ± 1.5</td>
<td>21.2 ± 3.5</td>
<td>26.8 ± 3.0</td>
</tr>
<tr>
<td>18:0</td>
<td>3.9 ± 0.8</td>
<td>3.2 ± 0.4</td>
<td>4.6 ± 0.72</td>
</tr>
<tr>
<td>Total saturates</td>
<td>33.6 ± 2.13</td>
<td>25.6 ± 4.2</td>
<td>34.3 ± 5.34</td>
</tr>
<tr>
<td>16:1</td>
<td>2.7 ± 1.2</td>
<td>2.7 ± 1.7</td>
<td>4.0 ± 1.6</td>
</tr>
<tr>
<td>18:1</td>
<td>45.7 ± 2.26</td>
<td>55.7 ± 6.9</td>
<td>43.1 ± 2.64</td>
</tr>
<tr>
<td>18:2</td>
<td>16.3 ± 1.9</td>
<td>14.8 ± 1.6</td>
<td>16.6 ± 3.5</td>
</tr>
<tr>
<td>20:4</td>
<td>1.4 ± 0.5</td>
<td>1.1 ± 0.3</td>
<td>ND</td>
</tr>
<tr>
<td>Total unsaturates</td>
<td>66.0 ± 2.76</td>
<td>74.3 ± 4.7</td>
<td>64.9 ± 5.73</td>
</tr>
</tbody>
</table>

1. ± SD. MCT, medium-chain triacylglycerol; ND, not detected. Because of rounding, numbers may not add up to 100% of the value listed.

2. *P < 0.001, 3. *P < 0.02 (nonsignificant after Bonferroni correction). 4. *P < 0.005, 5. *P < 0.001.

### Table 3

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Palm oil</th>
<th>High oleic acid sunflower oil</th>
<th>MCT oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol Total</td>
<td>(mmol/L)</td>
<td>5.79 ± 0.72</td>
<td>5.22 ± 0.52</td>
</tr>
<tr>
<td>VLDL</td>
<td>(mmol/L)</td>
<td>0.52 ± 0.18</td>
<td>0.57 ± 0.41</td>
</tr>
<tr>
<td>HDL</td>
<td>(mmol/L)</td>
<td>4.37 ± 0.70</td>
<td>3.72 ± 0.47</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>(mmol/L)</td>
<td>0.91 ± 0.16</td>
<td>0.93 ± 0.26</td>
</tr>
</tbody>
</table>

1. ± SD. MCT, medium-chain triacylglycerol.

2. *P < 0.001, 3. *P < 0.001, 4. *P < 0.001 (nonsignificant after Bonferroni correction).

### DISCUSSION

Although MCTs have long been described as neutral dietary constituents that have no effect on serum cholesterol concentrations, there is limited experimental evidence supporting this claim (17). In this metabolic-ward study, the lipid and lipoprotein effects of MCTs were systematically compared with two different fats: 1) palm oil, a fat rich in palmitic acid, a long-chain fatty acid known to raise serum cholesterol concentrations; and 2) high oleic sunflower oil, a fat rich in oleic acid, a long-chain fatty acid known to have neutral effects on serum cholesterol concentrations (1). Each feeding period was 3 wk in duration to ensure that lipid and lipoprotein concentrations had achieved a steady state. As observed previously (10, 11), we found that MCT-oil feeding resulted in higher triacylglycerol concentrations than did either long-chain fat. Unexpectedly, MCT-oil feeding produced total and LDL-cholesterol concentrations statistically indistinguishable from those after palm oil feeding and significantly higher than those after high oleic acid sunflower oil feeding. Because MCT oil contains almost exclusively medium-chain fatty acids, these results indicate that, contrary to widely held beliefs, medium-chain fatty acids raise total and LDL-cholesterol concentrations.

Although our finding that MCT oil raises cholesterol concentrations contradicts current dogma that medium-chain fatty acids have neutral effects, it does not contradict the published findings of other investigators. In 1960, Hashim et al (18) published their results from a metabolic-ward investigation that is frequently cited to support the claim that medium-chain fatty acids have neutral effects on cholesterol concentrations. In this study, liquid-formula diets in which 40% of energy came from fat were used and each feeding period lasted 3–4 wk. In three subjects, the effects on cholesterol concentrations of a diet...
enriched with MCTs were compared with those of a diet enriched in butter. The MCT diet lowered total cholesterol concentrations by 0.52–1.29 mmol/L (20–50 mg/dL) compared with the butter diet, suggesting that medium-chain fatty acids did not raise cholesterol concentrations. However, this study also observed that MCTs raised total cholesterol concentrations 0.28 mmol/L (11 mg/dL) above the concentrations seen with corn oil feeding. Although this latter finding was attributed to the cholesterol-lowering effect of the polyunsaturated fatty acids in corn oil, a unique cholesterol-lowering property of polyunsaturated fatty acids has been refuted (1), suggesting that MCTs may have contributed to the higher concentrations observed. In addition, another study conducted by Roels and Hashim (19) also found that MCTs raised total cholesterol concentrations with an oil low in saturated fatty acids.

Two other MCT-feeding studies used feeding periods that were of insufficient length to ensure that lipid concentrations had reached a steady state (11, 20). However, their observations were consistent with our findings and those of Hashim et al. (18). In 1959, Beveridge et al. (20) compared the cholesterol-raising effects of coconut oil, a butter distillate fraction, and MCT in a parallel study in which all 83 participants were initially fed a liquid-formula diet that contained no fat. Total cholesterol concentrations during the coconut oil diet were 0.34 mmol/L (13 mg/dL) higher than those found on the MCT diet. Many interpreted this to mean that MCT is not a cholesterol-raising fat. However, the total cholesterol concentration found with MCT feeding was 0.26 mmol/L (10 mg/dL) higher than the concentration during the no-fat run-in period. In 1990, Hill et al. (11) reported the findings of a short-term crossover study comparing an MCT-oil diet with a soybean oil diet in which 10 volunteers were fed 150% of their daily energy needs. Total cholesterol concentrations obtained on the sixth day of the MCT feeding were higher than on the sixth day of the soybean oil feeding. Thus, contrary to current dogma, our findings and published findings in the literature suggest that MCTs and medium-chain fatty acids are in fact cholesterol-raising.

Studies in animals (21) and humans (22) have shown that MCT feeding results in increased thermogenesis, suggesting that medium-chain fatty acids are rapidly catabolized after ingestion. How then do MCTs raise cholesterol concentrations if their fatty acids are rapidly catabolized? We speculate that the acetyl CoA end products of MCT oxidation are resynthesized into long-chain fatty acids that then mix with the hepatic long-chain fatty acid pool. These newly synthesized long-chain fatty acids could then behave like dietary long-chain fatty acids.

Support for this hypothesis comes from three sources. First, we and others found that plasma triacylglycerol fatty acids during MCT feeding contain few medium-chain fatty acids (11, 23). Instead, most of the fatty acids are long-chain fatty acids. These findings, coupled with the observation that MCT feeding results in higher triacylglycerol concentrations, suggest that MCT either stimulates hepatic synthesis of fatty acids or stimulates release of fatty acids from adipose tissue.

Second, direct evidence that 8:0 components serve as precursors for long-chain fatty acids has been shown in infants fed 13C-labeled 8:0 (23). 13C-labeled 14:0 (myristic acid) and 16:0 (palmitic acid) appeared in plasma triacylglycerol fatty acids at enrichments of 53% and 91%, respectively, of that seen for plasma 8:0. This finding suggests that the source for these fatty acids was de novo synthesis from 8:0 components.

Lastly, the cholesterol-raising potency of the medium-chain fatty acids appears to be half that of palmitic acid (Tables 1 and 3). In a previous study we found that lauric acid (12:0) had two-thirds of the cholesterol-raising potential of palmitic acid (24). These relative cholesterol-raising potentials are coincidentally proportional to the number of carbons each fatty acid would contribute when forming a 16- or 18-carbon fatty acid.

In summary, the present metabolic-ward investigation found that contrary to current beliefs, MCT oil is a cholesterol-raising fat and that medium-chain fatty acids are cholesterol-raising fatty acids. We found that MCT oil raised total and LDL-cholesterol concentrations similarly to palm oil and that the cholesterol-raising potency of medium-chain fatty acids appears to be half that of palmitic acid. Our results also confirm previous findings that the medium-chain fatty acids have the additional disadvantage of raising triacylglycerol concentrations.

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LIPID EFFECTS OF MEDIUM-CHAIN TRIACYLGLYCEROLS