Conjugated Linoleic Acid Supplementation for 8 Weeks Does Not Affect Body Composition, Lipid Profile, or Safety Biomarkers in Overweight, Hyperlipidemic Men\textsuperscript{1–4}

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Abstract

The usefulness of conjugated linoleic acid (CLA) as a nutraceutical remains ambiguous. Our objective was, therefore, to investigate the effect of CLA on body composition, blood lipids, and safety biomarkers in overweight, hyperlipidemic men. A double-blinded, 3-phase crossover trial was conducted in overweight (BMI \(\geq 25\) kg/m\(^2\)), borderline hypercholesterolemic (LDL-cholesterol (C)) \(\geq 2.5\) mmol/L) men aged 18–60 y. During three 8-wk phases, each separated by a 4-wk washout period, 27 participants consumed under supervision in random order 3.5 g/d of safflower oil (control), a 50:50 mixture of trans 10, cis 12 and cis 9, trans 11 (c9, t11) CLA:Clarinol G-80, and c9, t11 isomer:c9, t11 CLA. At baseline and endpoint of each phase, body weight, body fat mass, and lean body mass were measured by DXA. Blood lipid profiles and safety biomarkers, including insulin sensitivity, blood concentrations of adiponectin, and inflammatory (high sensitive-C-reactive protein, TNF\(_a\), and IL-6) and oxidative (oxidized-LDL) molecules, were measured. The effect of CLA consumption on fatty acid oxidation was also assessed. Compared with the control treatment, the CLA treatments did not affect changes in body weight, body composition, or blood lipids. In addition, CLA did not affect the ß-oxidation rate of fatty acids or induce significant alterations in the safety markers tested. In conclusion, although no detrimental effects were caused by supplementation, these results do not confirm a role for CLA in either body weight or blood lipid regulation in humans. J. Nutr. 141: 1286–1291, 2011.

Introduction

Nutraceutical and functional food approaches are being investigated as viable options to help combat the obesity epidemic. Positional and geometric isomers of linoleic acid, known as conjugated linoleic acid (CLA),\textsuperscript{9} have shown promise with respect to modulation of body composition, but the majority of the evidence is from in vitro and animal models. In mice, CLA induces as large as a 60% reduction in body fat mass (1). Less dramatic results have been observed in other animal models, including hamsters (2). It has been established that the trans 10, cis 12 isomer (t10, c12 CLA), rather than the cis 9, trans 11 (c9, t11 CLA, rumenic acid) isomer, is primarily responsible for these effects [reviewed in (3)]. CLA supplements for humans promoting weight loss and increased lean body mass are currently being marketed in the form of a 50:50 mixture of the t10, c12 and c9, t11 isomers based on these animal data and limited clinical evidence (4–6). However, CLA does not perform consistently in humans and therefore its purported antiobesity effects remain unconfirmed. In fact, a growing number of studies suggest a lack of effect of CLA on body composition (7,8). In addition, CLA’s effect on risk markers of cardiovascular disease (CVD) also remains inconclusive. CLA has been shown to have hypocholesterolemic, hypoglycemic, and antiatherosclerotic properties in animals (9). CLA supplementation for 8 wk in normolipidemic men and women lowered plasma TG and VLDL.

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\textsuperscript{3} This study was registered at www.clinicaltrials.gov as NCT01047280.

\textsuperscript{4} Supplemental Tables 1–3 and Supplemental Figures 1–3 are from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at jn.nutrition.org.

\textsuperscript{9} Abbreviations used: ß-OHB, ß-hydroxybutyrate; C, cholesterol; c9, t11, cis 9, trans 11; CLA, conjugated linoleic acid; CRP, C-reactive protein; CVD, cardiovascular disease; HOMA-IR, homeostasis model insulin resistance index; hs, high sensitive; Ox-LDL, oxidized LDL; RCFFN, Richardson Center for Functional Foods and Nutraceuticals; t10, c12, trans 10, cis 12.

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cholesterol (C) (10). However, other studies showed that CLA supplementation at varying doses either in the form of naturally enriched foods or industrially produced supplements did not affect blood lipids (7,8,11). The discrepancy observed between the effectiveness of CLA in animal and in vitro models and human studies may be due to differences in dose and duration of supplementation, species-specific physiology, gender, or the initial metabolic status of the study sample (12).

In addition, controversy surrounds the safety of CLA as a dietary supplement. In mice, CLA causes liver enlargement due to steatosis (13). In humans, CLA has been shown to induce insulin resistance in overweight men (14), possibly due to increases in inflammatory molecules [C-reactive protein (CRP), TNFα, and IL-6] (15–17).

Our primary objective in this study was to evaluate the effectiveness of 2 forms of CLA in modulating body weight and body composition, as well as blood lipids, in overweight, hyperlipidemic men in a free-living environment. Our secondary objective was to study the effect of the CLA supplementation on selected inflammatory and oxidative markers and insulin sensitivity, considered as safety biomarkers in the sample population.

**Participants and Methods**

**Participants.** Healthy male volunteers aged 18–60 y with a BMI ≥ 25 kg/m² were recruited from the city of Winnipeg, Manitoba. Men responded to radio and newspaper advertisements and were initially screened for eligibility by answering a phone-based questionnaire. Individuals were considered ineligible for participation in the study if they were smokers; consumed ≥ 2 alcoholic drinks/d; took medication that affects lipid metabolism, such as cholestyramine, colestipol, niacin, clofibrate, gemfibrozil, probucol, or HMG-CoA reductase inhibitors; or took high-dose (4 g/d) dietary supplements, including fish oil capsules, within 6 mo prior to the start of the intervention. The diagnosis of diabetes mellitus, liver disease, kidney disease, or heart disease precluded participation in the study. Potential participants from this initial stage were invited to the Richardson Center for Functional Foods and Nutraceuticals (RCCFN) at the University of Manitoba to undergo further screening based on anthropometry and a blood draw to determine fasting blood lipid profile. Subsequently, suitable candidates were invited for assessment of their overall health and fitness involving a second blood draw for routine biochemistry and hematology and a complete history and physical examination taken by the study physician. Signed informed consent was obtained from participants prior to any procedure performed on them for study purposes. The study protocol was approved by Health Canada and the Research Ethics Boards of the University of Manitoba and Dalhousie University.

**Diet and treatments.** The 3 treatments tested in the study were: 3.5 g/d of safflower oil (control), 3.5 g/d of a 50:50 mixture of t10, c12 and t11 CLA oil (Clarinol G-80, containing 8 g of total CLA), and 3.5 g/d of C9, t11 CLA (C9, t11 CLA oil, containing 2.7 g of total CLA). The 3 experimental oils were kindly provided by Lipid Nutrition. The fatty acid composition of the experimental fats is presented in **Supplemental Table 1**. The CLA and control treatments were administered to participants in the form of liquid oil, which was mixed into a constant amount (150 g) of fat-free, sugar-free fruit yogurt. This study was conducted under free-living conditions wherein the men were able to maintain their usual dietary habits and physical activity level during the intervention phases as well as the washout periods. Study volunteers were required to be present at the RCCFN during weekday evening mealtimes when treatment yogurts were administered under the supervision of the clinical coordinator, ensuring strict compliance. Participants were strongly encouraged to partake of a complementary supper buffet that was offered to them during their daily visits. Weekend treatments were provided as take away and empty or unused containers were returned on the following Monday to monitor compliance on the weekends.

**Study protocol.** This study was designed as a double-blinded, crossover clinical intervention in which participants received the 2 experimental CLA treatments and a control treatment in random order. The clinical trial comprised 3 treatment phases of 8 consecutive weeks each alternated with 4-wk washout periods. The crossover nature of the study ensured minimal variability, as each participant served as his own control. The men were instructed by the clinical coordinator to maintain their regular dietary habits and physical activity during the treatment phases, as well as during the washout periods. Physical activity questionnaires and 24-h dietary recalls provided a general idea of any changes in diet and physical activity that may have occurred during the study. Blood biochemistry and hematology were conducted at the end of each phase to ensure that no health abnormalities had occurred as a result of the experimental treatments.

**Measurement of body weight and body composition.** Participants weighed themselves on a clinical weighing scale during their daily visits to the RCCFN. BMI was calculated as weight (kg)/height (m²). Body composition (including overall body fat mass and lean body mass) was analyzed at the beginning and end of each phase using DXA. We conducted the DXA scan series by using General Electric’s Lunar Digital Prodigy Advance and the General Electric Prodigy Body Composition software program, EnCore 2005, to analyze the scans and generate body composition data.

**Blood sampling.** On d 1, 2, 56, and 57 of each phase, venous blood samples were collected following a 12-h overnight fast. Participants were also asked to abstain from alcohol 24 h prior to blood draw. Evacuated blood collection tubes containing disodium EDTA were used for obtaining plasma, whereas serum samples were obtained from blood drawn into uncoated tubes. Blood samples were centrifuged at 2000 × g for 20 min and plasma and serum were separated and stored at −80°C until further analysis. All analyses on the stored samples were completed within 24 mo of initial collection.

**Estimation of plasma lipids and lipoproteins.** Commercially available enzymatic assays were used to quantify C (Roche Diagnostics) and TG (Sigma-Aldrich) in plasma samples and lipoprotein gradient fractions. Plasma lipoproteins in 1000 μL of sample were separated by density gradient ultracentrifugation at 311,000 × g for 20 h in a SW60 Ti rotor following pretreatment of samples as described previously (18). Twenty fractions of 200 μL each were then collected starting from the top of the gradients. Fractions were defined as VLDL = 1–4 and HDL = 11–20. The C concentration of each class of lipoproteins was calculated as the AUC of the corresponding density gradient profile (18). LDL-C concentrations were calculated using the Friedewald equation (19).

**Assessment of atherogenicity of LDL-C.** Oxidation of LDL-C is considered to be one of the key events in the development of atherosclerosis. There is some evidence that CLA can beneficially influence the susceptibility of LDL to oxidation. The plasma concentration of oxidized LDL (Ox-LDL) was measured using a commercially available, solid phase, 2-site enzyme immunoassay (Mercodia) with murine monoclonal antibody mAb-4E6. The assay was performed according to the manufacturer’s instructions.

**Assessment of insulin sensitivity.** The insulin sensitivity of the men was determined by the homeostasis model insulin resistance index (HOMA-IR) (20). The HOMA index was calculated using the formula: fasting insulin concentration (μU/mL) × fasting glucose concentration (mmol/L/22.5). Plasma insulin and glucose concentrations were measured by RIA (21) and enzymatic methods (22), respectively.

**Estimation of inflammatory biomarkers (high sensitive-CRP, TNF-α, and IL-6).** Plasma concentrations of high sensitive (hs)-CRP were measured using Behring latex enhanced high-sensitivity assays, which were conducted on a Behring BN—100 nephelometer (Behring Diagnostic), by using calibrators provided by the manufacturer (N rheumatology standards SL). We measured serum IL-6 and TNFα concentrations with commercially available ELISA kits (Quantikine HS immunoassay kits; R&D Systems).
Measurement of plasma adiponectin. Plasma concentrations of adiponectin were measured with a commercially available ELISA kit according to manufacturer’s instructions (Linco Research).

Estimation of 13C-linoleate β-oxidation. CLA is known to be a ligand for PPARα and therefore might increase the rate of β-oxidation of fatty acids in muscles. For this purpose, a subset of 10 men from the study was orally administered a dose of uniformly carbon 13-labeled linoleic acid on d 56 of each phase. During the breakfast mealtime, participants consumed a single dose of 50 mg of 13C-linoleate (Cambridge Isotope Laboratories), which was mixed into butter and spread on half a bagel. β-Oxidation of the tracer was measured by recovery of 13CO2 in breath samples collected in duplicate at baseline and every hour for the next 12 h using a breath collection device (EasySampler, Quinton Instrument) and 10 mL evacuated glass tubes (Exetainer, Labco). A final breath sample was collected at 24 h after 13C-linoleate administration. Enrichment of 13C in breath CO2 following the ingestion of 13C-linoleate was analyzed by isotope ratio MS (Europa 20–20, Sercon) using He as the carrier gas (Praxair Canada) and 100% CO2 gas was used as the reference. Additionally, fasting plasma concentrations of FFA, TG, and β-hydroxybutyrate (β-OHB), the most stable plasma ketone and possibly another marker of β-oxidation, were estimated at the end of each phase. Commercially available reagent kits were used for the analysis of β-OHB (RX Daytona kit; Randox Laboratories), FFA (Wako Diagnostics), and TG (Dade Behring) using an automated clinical chemistry analyzer (Dimension Xpand Plus, Dade Behring).

Statistical analyses. A sample size of 28 was determined based on a power level corresponding to 80% in detecting an anticipated difference in our primary outcome, which was body fat mass, to \( P < 0.05 \) (23). Taking into account a dropout rate of -25%, the target sample size for recruitment was determined to be 36. We therefore recruited a final sample of 36. The sample size for the measurement of fatty acid oxidation rate was calculated to be 8 based on the change in the AUC with an \( a = 0.05 \) and a \( \beta = 0.8 \) (24). A total sample of 10 men randomly selected from the main study group of 36 ensured that we obtained complete information on β-oxidation of at least 8 participants.

Data were subjected to repeated-measures ANOVA based on the comparison between the final data from the end of each phase with the data from the start of the phase. Due to the crossover nature of the study, possible carryover effects were tested by including a term in the statistical model referring to the sequence in which the experimental treatments were administered. However, a repeated-measures ANOVA was used to identify significant differences between the effects induced by the 3 treatments on changes in plasma adiponectin concentration as a result of CLA supplementation compared with the control treatment (Table 1). Similarly, at the end of 8 wk of supplementation, there was no significant effect of CLA treatments on changes in plasma oxidized-LDL concentrations compared with control (Table 1).

Circulating concentrations of inflammatory markers, oxidized-LDL, and adiponectin. Baseline to endpoint changes in the serum concentrations of hs-CRP, TNFα, or IL-6 did not differ among the 3 treatments (Table 1). There was no significant change from baseline to endpoint in the circulating adiponectin concentration as a result of CLA supplementation compared with the control treatment (Table 1). Similarly, at the end of 8 wk of supplementation, there was no significant effect of CLA treatments on changes in plasma oxidized-LDL concentrations compared with control (Table 1).

Discussion

Functional foods such as CLA may aid in controlling the increasing prevalence of obesity and related diseases. The amount of CLA in the diet ingested from ruminant meats, milk, and dairy products has been estimated to be -152 mg/d in women and 212 mg/d in men (27) and may be somewhat higher due to the endogenous conversion of vaccenic acid from these foods to CLA (28). However, dietary CLA alone is not sufficient to attain therapeutic levels (~3–6 g/d), necessitating the use of CLA supplements and CLA-enriched foods.
The present study showed that supplementation of CLA in overweight, hyperlipidemic men for a period of 8 wk did not alter body weight or body composition. Similarly, none of the CLA treatments improved blood lipid profiles. These results agree with other human data demonstrating a lack of effect of CLA (as either c9, t11 isomer, t10, c12 isomer, or c9, t11 and t10, c12 CLA mixture) on body mass or the different body compartments from recent clinical trials (7,8,11,29). However, a meta-analysis of 18 studies concluded that CLA supplementation (mainly as a 50:50 mixture of c9, t11 and t10, c12 isomers) at a dose of 3.2 g/d does reduce fat mass at a rate of 50 g/wk for up to 2 y in both men and women (30). More recently, the ability of CLA to elicit marked reductions in total (31) and regional (trunk and legs) fat mass was observed in women (31–33). Our study population consisted of only males, which could partly explain the lack of efficacy, but further work in females is required to establish if gender plays a role in determining the effectiveness of CLA in humans. Nevertheless, the results of the current study add to the growing body of evidence that CLA might not be a useful tool for weight management in men.

It has also been suggested that CLA possesses cardio-protective potential by regulating markers that are associated with the

![FIGURE 1 Cumulative oxidation curves of 13C-linoleate oxidation over 24 h following 8-wk control and CLA treatments in overweight, hyperlipidemic men. Data are means ± SEM, n = 10.](image-url)

**TABLE 1** Body weight and body composition, plasma lipids, and safety biomarkers of overweight, hyperlipidemic men before and after 8-wk control and CLA treatment periods.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>c9, t11 + c10, c12 CLA</th>
<th>c9, t11 CLA</th>
<th>P&lt;sub&gt;r&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>Baseline</td>
<td>92.2 ± 3.0</td>
<td>90.0 ± 3.0</td>
<td>98.7 ± 3.0</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.7 ± 0.4</td>
<td>0.1 ± 0.4</td>
<td>0.3 ± 0.4</td>
<td>0.43</td>
</tr>
<tr>
<td>BMI, kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Baseline</td>
<td>31.3 ± 0.8</td>
<td>31.5 ± 0.8</td>
<td>31.4 ± 0.8</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.2 ± 0.1</td>
<td>0.0 ± 0.1</td>
<td>0.1 ± 0.1</td>
<td>0.53</td>
</tr>
<tr>
<td>Body fat mass, kg</td>
<td>Baseline</td>
<td>34.5 ± 2.2</td>
<td>34.8 ± 2.2</td>
<td>34.9 ± 2.2</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.2 ± 0.3</td>
<td>0.0 ± 0.3</td>
<td>-0.3 ± 0.3</td>
<td>0.58</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>Baseline</td>
<td>60.1 ± 1.2</td>
<td>60.6 ± 1.2</td>
<td>60.2 ± 1.2</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.6 ± 0.3</td>
<td>0.1 ± 0.3</td>
<td>0.6 ± 0.3</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Plasma lipids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total C, mmol/L</td>
<td>Baseline</td>
<td>6.31 ± 0.22</td>
<td>6.26 ± 0.22</td>
<td>6.02 ± 0.22</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.00 ± 0.22</td>
<td>-0.22 ± 0.22</td>
<td>0.00 ± 0.22</td>
<td>0.34</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>Baseline</td>
<td>3.23 ± 0.30</td>
<td>2.87 ± 0.30</td>
<td>2.95 ± 0.28</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.27 ± 0.16</td>
<td>-0.19 ± 0.12</td>
<td>-0.19 ± 0.12</td>
<td>0.56</td>
</tr>
<tr>
<td>VLDL-C, mmol/L</td>
<td>Baseline</td>
<td>1.16 ± 0.15</td>
<td>1.13 ± 0.15</td>
<td>1.14 ± 0.15</td>
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<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.46 ± 0.14</td>
<td>-0.29 ± 0.14</td>
<td>-0.28 ± 0.14</td>
<td>0.52</td>
</tr>
<tr>
<td>LDL-C, mmol/L</td>
<td>Baseline</td>
<td>2.28 ± 0.16</td>
<td>2.44 ± 0.16</td>
<td>2.32 ± 0.16</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.04 ± 0.12</td>
<td>-0.17 ± 0.12</td>
<td>-0.11 ± 0.12</td>
<td>0.73</td>
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<tr>
<td>HDL-C, mmol/L</td>
<td>Baseline</td>
<td>0.54 ± 0.05</td>
<td>0.57 ± 0.05</td>
<td>0.55 ± 0.05</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.05 ± 0.05</td>
<td>-0.09 ± 0.05</td>
<td>-0.05 ± 0.05</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Safety biomarkers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma hs-CRP, mg/L</td>
<td>Baseline</td>
<td>1.89 ± 0.29</td>
<td>2.17 ± 0.33</td>
<td>2.21 ± 0.45</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.12 ± 0.41</td>
<td>0.18 ± 0.31</td>
<td>0.96 ± 0.58</td>
<td>0.56</td>
</tr>
<tr>
<td>Serum TNFα, ng/mL</td>
<td>Baseline</td>
<td>1.63 ± 0.19</td>
<td>1.38 ± 0.17</td>
<td>1.32 ± 0.11</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.28 ± 0.19</td>
<td>-0.00 ± 0.14</td>
<td>0.16 ± 0.15</td>
<td>0.09</td>
</tr>
<tr>
<td>Serum IL-6, ng/mL</td>
<td>Baseline</td>
<td>1.15 ± 0.20</td>
<td>1.40 ± 0.25</td>
<td>1.32 ± 0.18</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.14 ± 0.13</td>
<td>-0.35 ± 0.15</td>
<td>0.00 ± 0.18</td>
<td>0.16</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>Baseline</td>
<td>4.6 ± 0.7</td>
<td>4.1 ± 0.4</td>
<td>4.7 ± 0.8</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.6 ± 0.4</td>
<td>-0.3 ± 0.3</td>
<td>-0.1 ± 0.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Plasma adiponectin, mg/L</td>
<td>Baseline</td>
<td>12.1 ± 1.2</td>
<td>12.3 ± 1.1</td>
<td>12.3 ± 1.3</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.0 ± 0.5</td>
<td>-0.8 ± 0.7</td>
<td>-0.5 ± 0.3</td>
<td>0.84</td>
</tr>
<tr>
<td>Plasma Ox-LDL, μg/L</td>
<td>Baseline</td>
<td>75.8 ± 3.2</td>
<td>74.7 ± 3.2</td>
<td>75.1 ± 3.2</td>
</tr>
<tr>
<td>Δ&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-3.5 ± 2.0</td>
<td>-0.7 ± 2.0</td>
<td>-1.9 ± 2.0</td>
<td>0.61</td>
</tr>
</tbody>
</table>

1 Data are means ± SEM, n = 27 or 26 (HOMA-IR).

2 Δ<sup>r</sup> refers to comparisons between absolute changes from baseline to phase end elicited by experimental treatments (repeated-measures ANOVA).

3 Change from baseline to end of phase.
development of heart disease. However, the failure to elicit a response in the plasma lipid and lipoprotein profiles following CLA supplementation in overweight, hyperlipidemic men in this study is in keeping with recent data indicating that CLA does not affect blood lipids (8,29). Furthermore, whether CLA in mixed or pure form is either naturally incorporated into dairy products such as milk (1.3 g CLA/d) (8) and butter (2.59 g CLA/d) (7) or is chemically synthesized, the results on blood lipids are apparently the same, suggesting no impact of the CLA dietary form. In an overweight male population similar to that in the current study (29), consumption of 4.5 g/d of c9, t11 and t10, c12 CLA mixture did not improve the blood lipid profile, which supports our finding.

Proposed mechanisms by which CLA, mainly the t10, c12 isomer, have been shown to reduce fat mass and body weight in animal and in vitro studies include decreased enzymatic activity of lipoprotein lipase and stearoyl CoA desaturase leading to decreased TG uptake by adipocytes. Inhibitory effects of CLA have been documented on preadipocyte differentiation via reduction in the expression of transcription factors regulating adipogenesis, such as PPARγ (34). In addition, CLA induces higher fat β-oxidation, leading to smaller adipocyte size (35), perhaps by increasing the activity of the rate-limiting enzyme, carnitine palmitoyl transferase. We therefore investigated if CLA consumption would increase linoleic acid β-oxidation in a subset of 10 men. Our results did not support our hypothesis, because neither of the 2 CLA treatments significantly increased cumulative β-oxidation. Similar results were observed in a recent study in men and women given 4 g/d of a c9, t11 and t10, c12 CLA mixture (36). Because cumulative β-oxidation was unchanged after treatment, the concentration of β-OHB in the blood also remained unaffected by treatment.

Evidence exists that CLA supplementation in humans, specifically with the t10, c12 isomer, increases concentrations of CRP, which is a marker of systemic inflammation (15,37). The current study did not show such an increase in circulating hs-CRP after 8 wk of both CLA treatments compared with control. This difference in results could be due to our use of safflower oil instead of olive oil as the control, which has been shown to have a strong antioxidative property as well as the ability to lower CRP concentrations (38). Olive oil was used as the control in studies in which CLA supplementation increased circulating CRP concentrations (15,37). None of the 2 other serum inflammatory markers analyzed in this study varied upon CLA intake and confirm observations reported in previous clinical trials (8,37). Taken together with the absence of an influence on blood lipid profile, the lack of an effect on inflammatory markers and adiponectin concentrations provides further evidence that CLA may have no negative impact on CVD risk.

There has been some evidence that CLA increases in vivo oxidant stress status. Ox-LDL, formed by the exposure of LDL to oxidizing agents, is also a widely used marker of in vivo oxidative stress. Ox-LDL particles are known to play a key role in atherosclerosis by being proinflammatory in nature; their concentrations in plasma have been correlated with the presence of insulin resistance and clinical CVD. In the present study, a positive correlation was indeed found between the baseline to phase end change in the Ox-LDL concentration and the change in the HOMA index in study participants. However, CLA supplementation for 8 wk did not modify plasma Ox-LDL, suggesting that under the present experimental conditions, CLA supplementation does not affect oxidative status in men.

The presence of insulin resistance represents an important step in the sequence of events leading to the development of type 2 diabetes. Early studies conducted in animals indicated that CLA can improve insulin sensitivity; however, these results have since been shown to be exclusive to rat models of diabetes (39). In fact, in both mice (13) and men (14), supplementation with a CLA mixture or t10, c12 isomer reportedly resulted in insulin resistance. In our study, 8 wk of supplementation with the 2 CLA treatments did not modify the HOMA index, a marker used to assess insulin sensitivity. These data suggest that under the current experimental conditions, CLA (c9, t11 isomer and c9, t11 and t10, c12 CLA mixture) appears not to affect glycemic control.

In our study, although we did not control the dietary intake of participants, no changes in body weight or in body composition were observed, suggesting that habitual dietary intake was maintained among the 3 dietary interventions. Physical activity was maintained as well during the study period (data not shown). Of particular interest in the context of the current study is that there is some evidence that additional physical exercise in conjunction with CLA supplementation could lead to beneficial changes in body composition (40).

In conclusion, the present study did not provide evidence to support the purported antioxidant and anti-CVD effects of CLA, which is in agreement with a substantial number of studies showing that CLA indeed has no impact on body weight and body composition or blood lipid concentrations. However, 8 wk of CLA intake did not alter any of the safety markers that were tested, supporting the concept that CLA-rich oil supplementation at a dose of 3.5 g/d (2.7–2.8 g/d of CLA isomers) is safe. Overall, the results of this study do not support a role for CLA per se as an effective weight loss nutraceutical for overweight or obese men.

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Literature Cited