Conjugated Linoleic Acids Reduce Body Fat in Healthy Postmenopausal Women¹⁻³

Marianne Raff,⁴⁺ Tine Tholstrup,⁴ Søren Toubro,⁴ Jens M. Bruun,⁵ Pia Lund,⁶ Ellen M. Straarup,⁶ Robin Christensen,⁷ Maria B. Sandberg,⁸ and Susanne Mandrup⁹

¹Department of Human Nutrition, Faculty of Life, University of Copenhagen, Frederiksberg 1958, Denmark; ²Department of Endocrinology and Metabolism C, Aarhus University Hospital, DK-8000 Aarhus C, Denmark; ³Biochemistry and Nutrition Group, BioCentrum-DTU, Technical University of Denmark, Lyngby 2800, Denmark; ⁴Parker Institute, Musculoskeletal Statistics Unit, Frederiksberg Hospital, Frederiksberg C 2000, Denmark; and ⁵Department of Biochemistry and Molecular Biology, University of Southern Denmark, Odense 5000, Denmark

Abstract

Isomers of conjugated linoleic acids (CLA) reduce fat mass (FM) and increase insulin sensitivity in some, but not all, murine studies. In humans, this effect is still debatable. In this study, we compared the effect of 2 CLA supplements on total and regional FM assessed by dual energy X-ray absorptiometry, changes in serum insulin and glucose concentrations, and adipose tissue (AT) gene expression in humans. In a double-blind, parallel, 16-wk intervention, we randomized 81 healthy postmenopausal women to 1) 5.5 g/d of 40/60% of cis9,trans11-CLA (c9,t11-CLA) and trans10,cis12-CLA (t10,c12-CLA) (CLA-mix); 2) cis9, trans11-CLA (c9,t11-CLA); or 3) control (olive oil). We assessed all variables before and after the intervention. The CLA-mix group had less total FM (4%) and lower-body FM (7%) than the control (P = 0.02 and < 0.001, respectively). Post hoc analyses showed that serum insulin concentrations were greater in the CLA-mix group (34%) than the control group (P = 0.02) in the highest waist circumference tertile only. AT mRNA expression of glucose transporter 4, leptin, and lipoprotein lipase was lower, whereas expression of tumor necrosis factor-α was higher in the CLA-mix group than in the control group (P < 0.04). In conclusion, a 50:50 mixture of c9,t11- and t10,c12-CLA isomers resulted in less total and lower-body FM in postmenopausal women and greater serum insulin concentrations in the highest waist circumference tertile. Future research is needed to confirm the insulin desensitizing effect of the CLA mixture and the effect on the mRNA expression of adipocyte-specific genes in humans.


Introduction

Conjugated linoleic acid (CLA)⁹ is a collective term for a group of naturally occurring and industrially produced linoleic acid (C18:2) isomers with conjugated double bonds. cis9, trans11-CLA (c9,t11-CLA), found in dairy products and ruminant meat, is the most abundant naturally occurring isomer (1), whereas other isomers only occur naturally in negligible amounts. The majority of CLA studies in humans and animals have examined the effect of a mixture containing primarily the trans10, cis12-CLA isomer (t10,c12-CLA) and the c9,t11-isomer in equal amounts. This mixture is promoted and sold worldwide as a weight-loss agent, because supplementation with the CLA mixture and t10,c12-CLA has been shown to reduce fat mass (FM) in mice (2,3). In humans, the results are inconclusive in that some studies (4,5), but not all (6,7), have confirmed the fat-reducing effect of a CLA mixture. The rodent studies also found that adipose tissue (AT) in different regions differed in their responsiveness to a CLA mixture (8,9), the retroperitoneal region being the most sensitive. In addition to the fat-reducing effect, the CLA mixture also increased insulin sensitivity in rats (10), whereas decreased insulin sensitivity has been found in mice (2). In humans, both a CLA mixture and the c9,t11- and t10,c12-isomers separately have been reported to reduce insulin sensitivity (7,11,12) or to have no effect on fasting insulin and glucose concentrations (13,14), whereas only a single study reported improved insulin sensitivity in young participants after treatment with a CLA mixture (15).

The mechanisms underlying the effects of CLA are not yet established. However, there are clear indications that the adipogenic program is specifically inhibited by the t10, c12 CLA isomer. In vitro studies using murine adipocyte cell lines

1 Supported by the Danish Dairy Research Foundation and the Danish Research Development Program for Food Technology.
³ Supplemental Table 1 is available with the online posting of the paper at jn. nutrition.org.
⁴ Abbreviations used: AT, adipose tissue; BP, blood pressure; CE, cholesterol ester; CLA, conjugated linoleic acid; CLA-mix, mixture of cis9,trans11-CLA and trans10,cis12-CLA; c9,t11-CLA, cis9,trans11-CLA; CVD, cardiovascular disease; DEXA, dual energy X-ray absorptiometry; E%, percent of energy; EI, energy intake; FA, fatty acid; FM, fat mass; HOMA-R, homeostatic model assessment for insulin resistance; LBM, lean body mass; LPL, lipoprotein lipase; t10, c12-CLA, trans10,cis12-CLA; TNFα, tumor necrosis factor-α; wt%, relative weight content.
⁺ To whom correspondence should be addressed. E-mail: mrf@life.ku.dk.

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(16) as well as primary human adipocytes (17) show that t10, c12-CLA supplementation reduces triacylglycerol accumulation and adipocyte differentiation. These studies are supported by in vivo animal studies where t10,c12-CLA has been shown to reduce the transcription of several adipocyte-specific genes such as adiponectin, glucose transporter 4, leptin, and lipoprotein lipase (LPL) in white AT (16,18,19). The key adipogenic transcription factor PPARγ has been suggested to be involved in these effects of t10,c12-CLA on gene expression, because several of the adipogenic genes are PPARγ target genes.

Because the 50:50 mixture of CLA is the one commercially available to population groups interested in losing weight, we found it pertinent to examine the effect of this mixture and to compare this effect with the c9,t11-isomer and olive oil in a 16-wk intervention study of postmenopausal volunteers who were prone to changes in FM. The c9,t11-CLA isomer has not been as well examined as the t10,c12-isomer in humans. Because this is the one most abundant in natural foods and is possible to increase the content of this isomer in bovine milk via feeding strategies (20), we found it relevant to include this isomer in our study. Our main focus was on the in vivo changes in total and regional FM, as well as measures of glucose metabolism and gene expression of adipogenic genes. The effect of CLA on adipogenic genes in human AT samples has, to our knowledge, been examined in only 1 other study (21), which was published after the initiation of this human intervention trial.

Methods and Participants

This article is based on data from a large CLA supplementation study. Here we report effects on total and regional FM and lean body mass (LBM), insulin sensitivity, and the relative gene expression of adipose derived proteins. We have presented results from cardiovascular disease (CVD) markers, inflammation, and lipid peroxidation elsewhere (22). We performed a 16-wk, double-blind, randomized, dietary parallel study with dietary supplements that differed in fatty acid (FA) composition. The participants were stratified according to their blood pressure (BP), waist circumference, and smoking habits to 1 of the 3 supplements. We assessed all outcome variables at the start and end of the intervention and fully explained the protocol and aim of the study to the participants (orally and in writing) before they gave their written informed consent.

Participants. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The Scientific Ethics Committee of the City of Copenhagen and Frederiksberg Municipality (KF) 01–166/03 approved the research protocol.

We recruited 81 postmenopausal women by advertising in local newspapers and from a list obtained from the Danish central national register. Exclusion criteria were: BMI >35 kg/m², hypertension, chronic disease, regular use of medication, and <1 y since last menstruation. All women were apparently healthy as indicated by a medical and lifestyle questionnaire. The baseline characteristics did not differ between the groups (Supplemental Table 1). All participants agreed to refrain from donating blood 2 mo prior to and during the study and from taking dietary supplements and medication that might interfere with study measurements (e.g. acetylsalicylic acid). We assessed physical activity by a questionnaire and instructed all participants to maintain the same level of physical activity throughout the study.

The study participants received the dietary supplements (and returned leftover capsules) at monthly visits to the Department of Human Nutrition. Within a period 2 wk prior to, and in wk 8 of the intervention, the participants completed a 3-d weighted food record on 2 weekdays and 1 d the following weekend to assess potential difference in dietary intake between the groups before or during the intervention. We gave each participant detailed instructions on how to fill out the food records. A clinical dietician coded all records before evaluating them. She also calculated the energy intake (EI) and dietary composition by using a national database (Dankost; National Food Agency). Habitual dietary intake before the intervention did not differ between the 3 groups (22).

Test fats. During the intervention, we supplemented the participants with either a commercial mix of CLA-isomers (CLA-mix) or a synthetic preparation of the isofrom found in milk (c9,t11-CLA). Olive oil, which is considered neutral or slightly beneficial to blood lipids (and possibly to new CVD risk markers, as well), was selected as control. The FA composition of the supplements has been presented elsewhere (22). The test fats were provided as 6 capsules/d and the participants received a total of 5.5 g test fat/d, which corresponded to 2.3 g of c9,t11-CLA + 2.2 g t10,c12-CLA (mixture of 41.2 and 39.9% wt of either isomer) or 4.7 g c9t11-CLA. The control group received 5.5 g/d of olive oil, which corresponded to 4.2 g of oleic acid [18:1(n-9)].

Compliance. We provided all participants with surplus capsules once per month (exact number known to staff) and leftover capsules were counted when returned the following month. A participant was considered compliant when >75% of the expected capsules were taken. We used the relative weight content (wt%) of c9,t11-, and t10,c12-CLA in the AT and plasma cholesterol esters (CE) as a biomarker of compliance.

Fatty acid composition. We determined the FA composition in plasma CE and in AT. Total lipids were extracted as described elsewhere (22). We isolated CE by TLC, solvent system heptane: isopropanol:acetic acid 95:5:1 (v:v), and prepared the lipid fractions FAME (Nu-Chek Prep). Further details are presented elsewhere (22).

Body weight and composition. We used a regularly calibrated electronic scale (SCALE; Lindells) to measure the participants’ body weight to the nearest 0.1 kg while they were wearing underwear, with no subtractions for clothes. Height was measured without shoes to the nearest 0.5 cm. Body composition was measured by dual energy X-ray absorptiometry (DEXA; Lunar Radiation) with LUNAR PRODIGY software (version 4.6c; Lunar Radiation); CV = 0.1%. In total, the scan took 45 min/person and provided a maximum radiation of 19.3 mRem (0.193 mSv) (both visits included).

Blood sampling and analysis. We collected venous blood after a 12-h overnight fast on the first and last day of the intervention. Blood for serum adiponectin and FA analyses was collected in tubes containing EDTA kept on ice and the samples were centrifuged at 3000 × g; 15 min 4°C. We assessed the serum concentration of adiponectin by a specific highly sensitive human ELISA. The adiponectin assay (B-Bridge International) had an intra-assay CV of 5.0% (n = 12). We collected blood for
serum insulin and glucose concentrations into dry tubes and after coagulation, the samples were centrifuged at 3000 \( \times g \); 15 min at 20\(^\circ\)C. Serum (500 \( \mu L \)) was stored at \(-20\)^\(\circ\)C. Insulin concentration (pmol/L) was assessed by solid 2-site fluorimunometric assay (Insulin kit B080–101, Wallac 04) on an AutoDELFI A system (1235–514, Wallac), CV = 3.2\%. We assessed glucose concentrations (mmol/L) by a hexokinase endpoint procedure in serum (Gluco-quant Glucose/HK kit, Roche Diagnostics) using a Cobas Mira Plus analyzer (Roche Diagnostic Systems), CV = 1.2\%. The homeostatic model assessment for insulin resistance (HOMA-R) was calculated using the following equation: fasting serum insulin (pmol/L) \( \times \) fasting serum glucose (mmol/L)/1.35.

**AT biopsies and gene expression analysis.** We took subcutaneous AT biopsies from the upper outer quadrant of a buttoc k with a needle (16 or 17 \( \mathrm{G} \)) attached to a vacuum tube. We left the samples (~35 mg) in the connector and placed both needle and connector in a marked tube filled with nitrogen and stored the samples at \(-80\)^\(\circ\)C (23). Many of our biopsies could not be analyzed for the relative mRNA level of the AT-specific and inflammatory genes due to the small size of the adipose biopsies. In total (before/after): 14/10, 12/12, and 14/11 samples were analyzed from the CLA-mix, c9,t11-CLA, and control groups, respectively. RNA was isolated from biopsies and used for quantitative RT-PCR analysis. We performed RNA isolation, cDNA synthesis, and real time quantitative RT-PCR as described by Brown et al. (17). The relative expression of the AT-specific genes was calculated after normalization to glyceraldehyde-3-phosphate dehydrogenase.

**Statistics.** We used the SAS statistical package (version 9.1; SAS Institute) for all statistical analyses. We applied a mixed-effects model ANCOVA to compare the effects of the 3 supplements using the baseline value as a covariate. If we detected a significant treatment effect \((P < 0.05)\), we included the Tukey-Kramer adjusted test for multiple post hoc pair-wise comparisons. We transformed data logarithmically when necessary, e.g. to normalize the distribution of residuals and to obtain variance homogeneity. We performed statistical tests on the transformed data. Baseline BP (both systolic and diastolic BP), waist circumference, and smoking status were all tested for influence on the results. Waist circumferences influenced fasting insulin concentrations and HOMA-R and were therefore included in the statistical analysis. We analyzed fasting serum insulin concentrations post hoc on data that was divided into the following baseline waist circumference tertiles: low (71–87 cm), medium (88–92 cm), and high (93–109 cm). The Pearson correlation coefficient was determined from pairwise correlations of \( \Delta \) values (end – start values) from the total sample of women. The sparse number of available AT samples for relative mRNA analysis made formal model assumptions of a specific probability distribution speculative. Accordingly, we employed the Fisher’s exact test to determine whether the missing data varied between the 3 groups. Because data were missing completely at random (24), the computer-intensive method bootstrapping was applied, which enabled us to estimate some quantity (25). We calculated the mean median values following multiple bootstrap samples (10,000 samples with replacement), with the corresponding SE associated with this quantity. We have summarized data for baseline variables as mean \( \pm SD \) and for outcome variables as LSMean \( \pm \) SEM, unless noted otherwise.

We determined Pearson correlation coefficient from pairwise correlations of \( \Delta \) values (end – start values) from the total sample of women.

### Results

**Participants and compliance.** A total of 81 participants were included in our study and 75 completed the 16-wk intervention. Three of the 6 dropouts were caused by withdrawal of consent and 3 by noneverse side effects. The dropouts were distributed as 2, 3, and 1 in the CLA-mix, c9,t11-CLA, and control groups, respectively. The main intervention period was \((\text{mean} \pm \text{SD})\) 112 \( \pm 3 \) d. Capsule counting showed a mean compliance of 98.2 \( \pm 22.4\% \) in all groups together and of 98.8 \( \pm 1.9\% \), 98.7 \( \pm 1.4\% \), and 98.2 \( \pm 2.4\% \) in the CLA-mix, c9,t11-CLA, and control group, respectively. The number of returned capsules did not differ between the groups. The wt\% of the specific CLA isomers in the plasma CE and AT all reflected the dietary supplements after the intervention (Table 1). Similar results were obtained for wt\% of the specific CLA isomers in the plasma triacylglycerol and phospholipids (data not shown).

**Dietary intake.** The c9,t11-CLA group reported a lower EI at wk 8 than the CLA-mix group \((\text{LSMean} \pm \text{SEM})\) (7330 \( \pm 300 \) kJ vs. 8420 \( \pm 320 \) kJ; \( P = 0.01 \)) and lower fat intake compared with the control group \((31.5 \pm 1.0\% \text{of energy (E\%)} \) vs. 34.2 \( \pm 0.9 \) E\%; \( P = 0.03 \)).

However, when expressed as g/d, the fat intake did not differ between any of the 3 groups. Both the EI and the fat intake in the c9,t11-CLA groups at wk 8 were lower compared with their habitual intake. The intake of carbohydrate and protein did not differ between the 3 groups intake when expressed as E\% or g/d at wk 8.

**Body weight and DXA scans.** Body weight tended to be less in the CLA-mix group than in the control \((P = 0.05)\) and the c9,t11-CLA group \((P = 0.09)\) (Table 2). Three DEXA scans were missing due to technical problems, 2 from the CLA-mix group and 1 from the c9,t11-CLA group. After the intervention, the CLA-mix group had a lower total FM than the control group \((P = 0.02)\) and tended to have lower total FM compared with the c9,t11-CLA group \((P = 0.07)\). Regional measurements showed that the CLA-mix group had less lower-body fat than both the control group \((P = 0.0008)\) and the c9,t11-CLA group \((P = 0.009)\). Lower-body LBM was higher in the CLA-mix group than in the control \((P = 0.02)\) and c9,t11-CLA \((P = 0.04)\) groups. None of the other DEXA scan data differed among the 3 groups.

**Table 1** Fatty acid composition in plasma CE and AT of fasting, postmenopausal women who where supplemented with CLA-mix, c9,t11-CLA, or olive oil for 16 wk\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>CLA-mix</th>
<th>c9,t11-CLA</th>
<th>Olive oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma CE, ( n )</td>
<td>25</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>18:1(n=9), %wt</td>
<td>19.81 ( \pm 0.26 ) &amp;</td>
<td>20.38 ( \pm 0.26 ) &amp;</td>
<td>21.33 ( \pm 0.26 ) &amp;</td>
</tr>
<tr>
<td>c9,t11-CLA, %wt</td>
<td>0.42 ( \pm 0.02 ) &amp;</td>
<td>0.76 ( \pm 0.04 ) &amp;</td>
<td>0.11 ( \pm 0.01 ) &amp;</td>
</tr>
<tr>
<td>t10c12-CLA, %wt</td>
<td>0.26 ( \pm 0.01 ) &amp;</td>
<td>0.11 ( \pm 0.01 ) &amp;</td>
<td>0.07 ( \pm 0.01 ) &amp;</td>
</tr>
<tr>
<td>AT, ( % )</td>
<td>n = 12</td>
<td>n = 13</td>
<td>n = 11</td>
</tr>
<tr>
<td>18:1(n=9), %wt</td>
<td>46.17 ( \pm 0.31 )</td>
<td>46.55 ( \pm 0.38 )</td>
<td>45.77 ( \pm 0.33 )</td>
</tr>
<tr>
<td>c9,t11-CLA, %wt</td>
<td>0.49 ( \pm 0.02 ) &amp;</td>
<td>0.68 ( \pm 0.03 ) &amp;</td>
<td>0.37 ( \pm 0.02 ) &amp;</td>
</tr>
<tr>
<td>t10c12-CLA, %wt</td>
<td>0.08 ( \pm 0.03 )</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

\(^1\) Data are L SVMean \( \pm \) SEM. Means in a row with superscripts without a common letter differ, \( P < 0.05 \) (ANCOVA following intervention; baseline values applied as covariates).

\(^2\) Due to the small amount of sample collected, it was not possible to analyze all FA composition in all AT biopsies. ND, Nondetectable.
Table 2: Weight, body composition, insulin sensitivity, and adiponectin of fasting, postmenopausal women who were supplemented with CLA-mix, c9,t11-CLA, or olive oil for 16 wk.

<table>
<thead>
<tr>
<th></th>
<th>CLA-mix</th>
<th>c9,t11-CLA</th>
<th>Olive oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>25</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>70.2 ± 0.3</td>
<td>71.0 ± 0.3</td>
<td>71.1 ± 0.3</td>
</tr>
<tr>
<td>Total FM, kg</td>
<td>24.6 ± 0.3a</td>
<td>25.5 ± 0.3b</td>
<td>25.6 ± 0.3b</td>
</tr>
<tr>
<td>Lower-body FM, kg</td>
<td>9.5 ± 0.2a</td>
<td>10.1 ± 0.2b</td>
<td>10.2 ± 0.1b</td>
</tr>
<tr>
<td>Upper-body FM, kg</td>
<td>11.1 ± 0.1</td>
<td>11.4 ± 0.1</td>
<td>11.3 ± 0.1</td>
</tr>
<tr>
<td>Total LBM, kg</td>
<td>43.3 ± 0.2</td>
<td>43.2 ± 0.2</td>
<td>43.1 ± 0.2</td>
</tr>
<tr>
<td>Lower-body LBM, kg</td>
<td>14.7 ± 0.1a</td>
<td>14.3 ± 0.1b</td>
<td>14.3 ± 0.1b</td>
</tr>
<tr>
<td>Upper-body LBM, kg</td>
<td>20.9 ± 0.2</td>
<td>21.0 ± 0.1</td>
<td>21.0 ± 0.1</td>
</tr>
<tr>
<td><strong>Serum measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>41.6 ± 2.4</td>
<td>40.9 ± 2.4</td>
<td>40.3 ± 2.3</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.1 ± 0.1</td>
<td>5.1 ± 0.1</td>
<td>5.1 ± 0.1</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>1.4 ± 0.1</td>
<td>1.4 ± 0.1</td>
<td>1.4 ± 0.1</td>
</tr>
<tr>
<td>Adiponectin, mg/L</td>
<td>11.9 ± 0.4</td>
<td>12.6 ± 0.5</td>
<td>12.5 ± 0.4</td>
</tr>
</tbody>
</table>

1 Data are LSMeans ± SEM. Means in a row with superscripts without a common letter differ, P < 0.05 (ANCOVA following intervention; baseline values applied as covariate).

Discussion

This randomized, controlled, double-blind study showed that a 40:40 mixture of c9,t11- and t10,c12-CLA isomers significantly reduces total and lower-body FM compared with olive oil. This was supported by a similar tendency in body weight and, very interestingly, also by differences in the pattern of expression of adipogenic genes. The location-specific effect of CLA on the FM is interesting, as the FM in the lower-body was previously shown to correlate with insulin sensitivity (26).

The total body FM-reducing effect of CLA mixtures is supported by other human studies (4,5) as well as by a recently published meta-analysis (27), but there are also several studies that did not find this effect (6,7). The reason for the discrepancy is not clear. A recent study also found a lower-body FM reduction after supplementation with a CLA mixture when assessed by DEXA (28), whereas several others found no difference in hip circumference regardless of the effect on total FM (7,13). We speculate that differences in the measuring methods may explain the discrepancies. The changes in total and lower-body FM were significantly and inversely correlated to the changes in the relative content of t10,c12-CLA in plasma CE, which is consistent with the findings of others (29). We found no correlation between the change in FM and c9,t11-CLA in CE or AT. Mice and cell studies have found that the t10,c12-isomer is responsible for the fat-reducing effect of CLA (3,17). Only the CLA-mixture supplement contained the t10,c12-isomer; thus, the correlation to this isomer is consistent with our finding of FM reduction in this group only.

Notably, we found greater lower-body LBM in the CLA-mixture group than in the other 2 groups. This is in contrast to most human studies that find no significant difference between the effect of a CLA supplement and a placebo (5,7,30). However, 2 human studies (4,30) and some animal studies (9,31) found a similar increase in LBM in response to CLA mixtures. The effect of a CLA supplement on LBM may be small and thus more difficult to detect. This is partly supported by the fact that many of the studies that examine the effect of CLA on LBM find nonsignificant increases or smaller decreases in LBM than a control (5,7,30). However, because we did not assess physical activity during the intervention, we cannot rule out that the change in LBM in our CLA-mixture group was caused by change in physical activity.

We found no differences in the effect of the 3 supplements on fasting serum insulin or glucose concentrations or the calculated HOMA-R, but because the baseline waist circumference had a
significant influence on the insulin concentrations, we conducted a post hoc analysis where the women were divided into tertiles according to their waist circumference. In the women with the largest waists, we found a significantly greater serum insulin concentration in the CLA-mix group than in the other groups, whereas the supplementation groups did not differ in the leaner women. This finding was supported by similar results for the HOMA-R. A large waist circumference is a characteristic of metabolic syndrome and a risk factor for diabetes type II (32). Thus, our post hoc analysis indicates that participants with a large waist circumference are more sensitive to a negative effect of a CLA mixture on insulin metabolism. This is particularly interesting in light of the previous CLA studies in humans, as most studies with participants in the risk group (e.g. men with abdominal obesity or diabetes type II or suffering from metabolic syndrome) showed that supplementation with a CLA mixture or t10,12-CLA decreased insulin sensitivity (7,11). Abdominal obesity is a promoter of low-grade inflammation (33) and we speculate that participants with large waist circumferences may have increased potential for producing proinflammatory signals in response to a CLA mixture, which in turn mediates the insulin desensitizing effect.

In relation to the inflammatory response, TNFα mRNA expression was higher in AT in the CLA-mix group than in the control group. The isomer t10, c12 CLA has been shown to activate expression of proinflammatory genes in human adipocytes and our results indicate that t10,c12 CLA may have similar effects on adipocytes in vivo. The proinflammatory effect of CLA is supported by the finding of higher serum C-reactive protein concentrations, a well-established inflammatory marker, in the CLA-mix group in this (22) and at least 1 other study (30). However, not all studies found such proinflammatory effects (11,13).

Interestingly, when taken together, our results seem to support a delipidating effect of t10,c12 CLA by mechanisms reminiscent of those in animals (18) and in vitro studies with human adipocytes (17). Thus, like those studies, we found significantly lower relative AT expression of PPARγ target genes such as glucose transporter 4 and LPL and a significant induction of TNFα in the CLA-mix group compared with the control. In addition, there was a tendency for the AT expression of A-FABP and adiponectin, also PPARγ target genes, to be less in the CLA-mix group than in the control. The reduction in leptin expression contrasts with data from acute in vitro studies (17). The discrepancy between in vivo and in vitro studies in this case is likely to be due to the length of CLA exposure. TNFα and other proinflammatory cytokines have been found to suppress both activation and expression of PPARγ (34), the key adipocyte transcription factor. Studies using human adipocytes in culture indicate that repression of PPARγ expression and activity is involved in the delipidating and dedifferentiating effects of the t10,c12-isomers (17). Although our in vivo results are based on few samples, they support the relevance of the above-mentioned ex vivo results. It is of interest that the relative AT expression of TNFα tended to be lower in the c9,t11-CLA group than in the control group.

To our knowledge, only 1 other study has examined the effect of CLA on the relative expression of adipogenic genes in human AT (21). In contrast to our findings, they found greater PPARγ mRNA expression and no effect on body composition. The reason for the different results is not clear, because CLA dose, isomeric composition, participant bodyweight, and intervention length were similar to ours. Their study participants were of both genders and younger than ours, but because the fat-reducing effect has been found both in men (13) and in young participants (~30 y) (14), this is unlikely to account for the different results.

Adiponectin is expressed by the adipocytes and is inversely associated with body weight and insulin resistance (35). We found no difference in the effect of a CLA mixture or the c9,t11-isomer on serum adiponectin concentration, which is consistent with the findings of others (13).

A strength of this study is the high compliance and low dropout rate, which indicated good tolerance of the CLA supplements. The EI, examined using 3-d food records, did not differ significantly between the CLA-mix and the control group, which suggest that the observed differences between these 2 groups were independent of diet. The lower EI reported by the c9,t11-CLA group at wk 8 compared with the CLA-mix group would have been expected to reduce the FM in the c9,t11-CLA group, but the CLA-mix group had a lower FM than the c9,t11-CLA group; thus, the lower EI in the c9,t11-CLA group is not likely to have influenced our FM results.

This study included healthy, primarily normal-weight women for whom an increase in a risk parameter within the normal range may be less relevant than a change from normal to increased risk. However, the participating women had a small increased risk of developing CVD and diabetes type II due to their age and postmenopausal status and any change in a risk parameter that would indicate increased CVD risk may be considered unbeneficial.

Another concern may be the power in this study. The prestudy power calculation was based on differences in blood lipids and for the fasting serum insulin concentrations, we may have had too little power to detect a change caused by the c9,t11-isomer, as found by Risérus et al. (12). This also applies to the upper-body FM and LBM as well as serum adiponectin concentrations.

In conclusion, we found that a mixture of t10, c12- and c9,t11-CLA resulted in lower total and lower-body FM in healthy postmenopausal women. The change in FM was correlated with the content of t10, c12-isomer in CE and not the c9,t11-isomer. Future research is needed to confirm if a CLA mixture, as indicated by our current results, can reduce insulin sensitivity in women with large, but not lower, waist circumference and to further examine if a CLA mixture containing the t10,c12-CLA isomer reduces mRNA expression of adipocyte-specific genes and increases the mRNA expression of TNFα in AT in humans.

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Literature Cited


