

# Chromium picolinate and conjugated linoleic acid do not synergistically influence diet- and exercise-induced changes in body composition and health indexes in overweight women<sup>☆,☆☆</sup>

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## Abstract

This study assessed the effects of combined chromium picolinate (CP) and conjugated linoleic acid (CLA) supplementation on energy restriction and exercise-induced changes in body composition, glucose metabolism, lipid lipoprotein profile and blood pressure in overweight, premenopausal women. For 12 weeks, 35 women [age  $36 \pm 1$  years (mean  $\pm$  S.E.M.); BMI  $28.0 \pm 0.5$  kg/m<sup>2</sup>] were counseled to consume a 2092 kJ/day (500 kcal/day) energy deficit diet and performed 30 min of moderate-intensity walking or jogging 5 days/week. The women were randomly assigned to ingest either CP-CLA [400  $\mu$ g chromium (Cr), 1.8 g CLA in 2.4 g tonal oil,  $n = 19$ ] or placebo ( $<0.1$   $\mu$ g Cr, 2.4 g canola oil,  $n = 16$ ). Compared to baseline, urinary Cr excretion increased 22-fold, plasma CLA isomer 18:2 (c9,t11) content increased 79% and plasma CLA isomer 18:2 (t10,c12) became detectable in CP-CLA and were unchanged in Placebo. Over time, body weight decreased  $3.5 \pm 0.5\%$  (CP-CLA  $-2.6 \pm 0.5$ ; placebo  $-2.5 \pm 0.5$  kg) and fat mass decreased  $8.9 \pm 1.3\%$  (CP-CLA  $-2.7 \pm 0.5$ , placebo  $-2.4 \pm 0.5$  kg), with no differences in responses between groups. Fasting blood hemoglobin A<sub>1c</sub>, plasma glucose and insulin, a homeostatic assessment of insulin resistance, serum total cholesterol (CHOL), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol, triacylglycerol (TG), CHOL/HDL ratio, TG/HDL ratio and sitting systolic and diastolic blood pressures were not changed over time or influenced by CP-CLA. The use of a combined CP and CLA supplement for 3 months does not affect diet- and exercise-induced changes in weight and body composition or improve indexes of metabolic and cardiovascular health in young overweight women.

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## 1. Introduction

Moderate energy restriction (2092–4184 kJ/day; 500–1000 kcal/day) and aerobic exercise ( $\geq 30$  min/day on  $\geq 5$  days/week) are considered central components of effective programs to control body weight and maintain

health [1]. Many people use dietary supplements to hopefully achieve weight loss or enhance diet and exercise-induced weight loss. Results from the Behavioral Risk Factor Survey indicate that 14.3% of people trying to lose weight use nonprescription weight loss products [2]. Chromium picolinate (CP) and conjugated linoleic acid (CLA) are two supplements promoted for use in weight control.

Claims that a dietary supplement effectively causes or promotes a desired change in body composition, metabolism or health should be supported by independent scientific research. The 1997 Federal Trade Commission [3] ruling that claims for CP can only be made if, “at the time the representation is made, respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation” underscores the need for more research to critically evaluate the efficacy of CP. Possible benefits of

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chromium supplementation include increased lean body mass, decreased body fat and increased resting energy expenditure [4,5]. Chromium might also retard the loss of lean body mass that usually accompanies weight loss [6]. However, as summarized in several reviews [5,7–9], the majority of research indicates that chromium does not affect body weight or body composition. Positive [10] and null [11] results were reported regarding the effect of chromium to decrease total cholesterol and low-density lipoprotein cholesterol (LDL) and increase high-density lipoprotein cholesterol (HDL) (also see reviews [5,7–9]). Limited research indicates that chromium does not affect blood pressure [12].

*Conjugated linoleic acid* is a term used to describe a mixture of isomers either in the *cis*-9, *trans*-11 form or the *trans*-10, *cis*-12 form [13]. CLA at doses ranging from 1.7–6.8 g/day, especially the t10,c12 isomer, is suggested to positively affect body composition (decreased fat mass and increased fat-free mass) [13–15] and to possess anticarcinogenic, antiatherogenic and antidiabetogenic properties [13,16]. Other research with null results [17,18] raises questions about the efficacy of CLA on these outcomes. The short-term effect of CLA on blood lipid lipoprotein profile is questioned by findings that supplementation for 12 weeks did not affect plasma triacylglycerol (TG), cholesterol or LDL or HDL concentrations [19].

Collectively, consensus is lacking with respect to whether CP and CLA supplementation positively influence changes in body composition and indexes of cardiovascular and metabolic health. A novel research area is the combined supplementation of CP-CLA. Recently, combined CP-CLA supplementation was reported to decrease body weight and fat mass and differentially affect plasma insulin in high-fat-fed Balb C mice [20].

The purpose of this research project was to assess the effects of a supplement containing CP and CLA on changes in body weight, body composition and indexes of metabolic (blood hemoglobin A<sub>1c</sub>, plasma glucose and insulin and a homeostatic assessment of insulin resistance (HOMA-IR)) and cardiovascular [maximal oxygen uptake capacity (VO<sub>2</sub> maximum), lipid lipoprotein profile, blood pressure] health in overweight and class I obese [body mass index (BMI) of 25–34 kg/m<sup>2</sup>] premenopausal women during a 12-week period of moderate energy restriction and exercise intervention. It was hypothesized that the women who consumed the supplement would achieve greater body fat loss, fat-free mass preservation and enhanced positive changes in indexes of metabolic and cardiovascular health, compared to women who consumed a placebo.

## 2. Methods and materials

### 2.1. Subjects

Fifty-nine overweight to moderately obese women (BMI between 25–34 kg/m<sup>2</sup>) aged 21–50 years were recruited in

the communities of West Lafayette and Lafayette, IN, USA. Prior to acceptance into the 14-week study, participants signed an informed consent form, completed a medical history questionnaire and gained written approval from their primary healthcare provider. Also, a screening that included a fasted blood sample to test for liver and kidney functions, protein and iron status, blood glucose, electrolytes and a urine sample to test for pregnancy was performed in order to exclude women with medical conditions that might place them at risk while participating in the study or interfere with successful completion of the study protocol. The institutional review board at Purdue University reviewed and approved the study protocol, and each subject received a monetary stipend for participating in the study.

Thirty-eight women (64%) completed the study. Of the 21 women who dropped out, 14 were in the placebo group, and seven were in the CP-CLA group. Reasons for dropping out included not having enough time to participate ( $n=5$ ), compliance issues ( $n=5$ ), trying to get pregnant ( $n=2$ ), physician request ( $n=1$ ), personal issues ( $n=1$ ), nausea possibly related to taking supplement ( $n=1$ ) and other unspecified reasons ( $n=6$ ). Data from three women who completed the study were excluded from analyses because they were identified to be noncompliant with the prescribed diet and exercise program (excessive exercise and weight loss,  $n=2$ ) or not consuming the CP-CLA supplement [low urinary chromium (Cr) excretion and no change in plasma CLA isomer profile,  $n=1$ ]. Thus, the final sample size of this study was 35 women (19 CP-CLA and 16 placebo).

Sample size calculations performed prior to starting the study based on data from Blankson et al. [21] indicated that  $n=11$  subjects per group were theoretically required to statistically confirm a differential body fat mass response of 3.2 kg (and a within-group variability of 2.4 kg) to consuming CLA vs. placebo with 80% power at the  $P=.05$  level. Based on data from Kaats et al. [22],  $n=34$  subjects per group would have been required to show a differential response of body fat mass to consuming CP vs. placebo with 80% power at the  $P=.05$  level. A sample size of  $n=16$  per group was chosen to detect changes due to CP-CLA, based on the assumption that the CLA in the supplement would promote any differential body composition response. Subjects were purposefully overrecruited ( $n=59$ ) to account for an expected 25–35% dropout rate and to achieve the minimum planned group size.

### 2.2. Experimental design and supplementation

This was a randomized, double-blind, placebo-controlled study with a 2-week “baseline” period and a 12-week diet, exercise and supplementation intervention period (designated weeks 1–12). The women were instructed to discontinue taking medications and supplements not prescribed by their doctors for 2 weeks prior to and throughout the study. Randomized assignments to the placebo group or the CP-CLA supplement group were made based on the date the women qualified to participate in the study. The subjects

were not matched based on any physical, metabolic or lifestyle characteristic at the time of randomization. At baseline, the women remained sedentary and did not consume any experimental supplement. During the 12-week intervention period, each woman received dietary counseling and instruction to perform moderate exercise and was provided with the placebo or CP-CLA supplements to consume daily. Testing and evaluations were done at designated weeks, as described below, for each category.

### 2.3. Supplementation

During Weeks 1–12, each woman consumed, once daily in the morning, three soft-gel capsules. Each CP-CLA capsule was manufactured to contain 133  $\mu\text{g}$  Cr as CP and 0.59 g CLA in 0.8 g tonaloin oil, and each placebo capsule, <0.1  $\mu\text{g}$  Cr and 0.8 g canola oil. Thus, each subject was to consume daily 400  $\mu\text{g}$  Cr and 1.8 g CLA (CP-CLA group) or <0.3  $\mu\text{g}$  Cr and 2.4 g canola oil (placebo group). The 400  $\mu\text{g}$  Cr as CP is the same dose used by Kaats et al. [22,23], and the 1.8-g CLA dose is similar to the 1.7 g-CLA dose used by Blankson et al. [21] who reported efficacy with respect to improved body composition. The CP-CLA and placebo capsules were provided by Nutrition 21 (Purchase, NY, USA), placed in coded bottles by a technician otherwise not involved with the research project and provided to the subjects in blinded fashion. All other research staff remained blinded with respect to the subject's group assignment until after all testing and sample analyses were completed. The certificate of chemical analysis of the CP-CLA supplement provided by Nutrition 21 documented that each capsule contained 149  $\mu\text{g}$  Cr and 0.64 g CLA. Gas-liquid chromatography-based analyses of the supplements at Purdue University, which was not quantitative, documented that the CLA in the CP-CLA supplement was ~50% 18:2 (c9,t11) and 50% 18:2 (t10,c12) and that the canola oil in the placebo supplement was void of CLA isomers.

### 2.4. Diet

Each subject's energy requirement was determined to be 1.6 times their resting energy expenditure, estimated using the Harris–Benedict equation for women [24]. After baseline testing was completed, each subject received dietary counseling based on the American Diabetes Association/American Dietetic Association Exchange Lists for Weight Management [25] to achieve a 2092 kJ/day (500 kcal/day) energy deficit, with a macronutrient distribution of 15–20% protein, 50–55% carbohydrate and 30–35% fat. The subjects were provided with a listing of allowable food exchanges, a scale to help with portion sizes and were instructed to record each day the number of exchanges from all foods and beverages consumed. Detailed food records were kept by the subjects on three nonconsecutive days during baseline and Intervention Weeks 1–2 and 11–12. The energy and nutrient contents of these records were estimated using Nutritionist Pro software (Version 2.2, San Bruno, CA, USA). At baseline

only, a cutoff value of 1.0 times resting energy expenditure was used to assess food record acceptance.

### 2.5. Exercise intervention

All women were instructed to perform 30 min of unsupervised walking or jogging exercise at moderate-intensity (rating of perceived exertion=12 on a scale of 6–20 [26]) 5 days/week. A daily log of exercise activities was kept throughout the study.

At baseline and Week 12, the Stanford 3-mph treadmill protocol was used to determine heart rate responses to graded submaximal exercise, and maximum oxygen uptake was estimated from American College of Sports Medicine equations [26]. Blood pressure was recorded at rest, at 3-min intervals during the exercise test and at 4 min post test.

### 2.6. Body composition

Fasting-state nude body weight (total weight minus robe weight) was measured to  $\pm 0.01$  kg using an electronic scale (model ES200L; Ohaus, Pine Brook, NJ, USA) at baseline and Week 12. Height was measured using a wall-mounted stadiometer to the nearest 0.1 cm without shoes. Body mass index was calculated using the equation: [body weight (kg)/height<sup>2</sup> (m<sup>2</sup>)]. Whole body fat and fat-free masses were measured at baseline and Week 12 using dual X-ray absorptiometry (GE Lunar Prodigy with EnCORE software version 5.60, Madison, WI, USA).

### 2.7. Blood and urine collection and analyses

Fasting-state blood samples were drawn from an antecubital vein using venipuncture on 2 consecutive days at baseline and Week 12 into tubes containing either heparin or no anticoagulant; the samples were processed and centrifuged at 3000g with refrigeration, and aliquots of the plasma and serum, respectively, were stored at  $-80^{\circ}\text{C}$ . Blood was also collected into EDTA tubes and kept at room temperature on a mechanical rocker until sent to a commercial laboratory (Mid-America Clinical Laboratory, Indianapolis, IN, USA) for hemoglobin A<sub>1c</sub> analysis using an immunoturbidimetric assay on a COBAS INTREGRA analyzer (Roche Diagnostic Systems, Indianapolis, IN, USA). Plasma glucose concentration was measured by an oxidase method on a COBAS Mira Plus analyzer. Plasma insulin concentration was measured with an enzyme-linked immunosorbent assay kit (Diagnostic Systems Laboratories, Webster, TX, USA). The HOMA-IR, an index of insulin sensitivity, was calculated using the equation:  $\text{HOMA-IR} = 405 / [\text{fasting glucose (mg/dl)} \cdot \text{fasting insulin } (\mu\text{U/ml})]$  [27]. Serum total cholesterol (CHOL), HDL and TG concentrations were measured using a COBAS analyzer. Low-density lipoprotein cholesterol was calculated to equal  $[\text{CHOL} - \text{HDL} - (\text{TG}/5)]$ .

The plasma fatty acid profile was determined as previously described [28]. Briefly, lipids were extracted with chloroform/methanol (2:1, v/v) and the fatty acid methyl esters prepared by sodium methoxide in methanol

Table 1

Dietary intakes at baseline and the start and end of 12-week period of diet and exercise-induced weight loss with or without CP and CLA supplementation

|                    | Placebo                |                        |                        | CP-CLA                 |                        |                        |
|--------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
|                    | Baseline               | Start                  | End                    | Baseline               | Start                  | End                    |
| Energy* (MJ/day)   | 8.63±0.57 <sup>a</sup> | 6.43±0.32 <sup>b</sup> | 6.52±0.38 <sup>b</sup> | 7.83±0.44 <sup>a</sup> | 6.59±0.36 <sup>b</sup> | 6.51±0.45 <sup>b</sup> |
| Protein (g/day)    | 81±8                   | 70±4                   | 62±5                   | 76±7                   | 70±4                   | 73±6                   |
| CHO (g/day)        | 245±15                 | 237±15                 | 254±19                 | 229±12                 | 229±17                 | 219±18                 |
| Fat* (g/day)       | 83±8 <sup>a</sup>      | 38±2 <sup>b</sup>      | 39±4 <sup>b</sup>      | 76±7 <sup>a</sup>      | 46±5 <sup>b</sup>      | 47±7 <sup>b</sup>      |
| Fiber* (g/day)     | 19±5 <sup>a</sup>      | 23±2 <sup>b</sup>      | 25±3 <sup>b</sup>      | 16±1 <sup>a</sup>      | 22±2 <sup>b</sup>      | 23±2 <sup>b</sup>      |
| Chromium* (µg/day) | 53±16 <sup>a</sup>     | 70±11 <sup>b</sup>     | 63±20 <sup>b</sup>     | 26±6 <sup>a</sup>      | 62±11 <sup>b</sup>     | 62±13 <sup>b</sup>     |

Values are mean±S.E.M. Means in a row with superscripts without a common letter differ.

\*  $P < .05$  (significant effect of time).

and analyzed by gas-liquid chromatography (HP 5890 series II, auto sampler 7673, HP 3365 ChemStation; Hewlett-Packard, Avondale, PA, USA).

Twenty-four-hour urine collections were made on two consecutive days during baseline and Intervention Weeks 1–2 and 11–12. All urine samples were collected, processed and stored using specialized procedures and supplies to minimize contamination [29]. Chromium concentration was measured using a graphite furnace atomic absorption spectrophotometer (model HGA500, Perkin-Elmer) [30].

## 2.8. Statistics

Values are reported as means±S.E.M. and are based on samples sizes of  $n=16$  in the placebo group and  $n=19$  in the CP-CLA group. Statistical significance was assigned at  $P < .05$ . Unpaired  $t$  tests were used to assess group differences at baseline. The main effect of time (diet+exercise) and supplementation (CP-CLA vs. placebo) and the time by supplement interactions were assessed using two-factor repeated-measures analysis of variance. Statistical analyses of data were done using JMP Statistical Discovery Software (version 3, SAS Institute, Cary, NC, USA).

## 3. Results

At baseline, there were no differences between the placebo and CP-CLA groups for any of the variables reported below.

### 3.1. Dietary energy and nutrient intakes

Compared to baseline, at Weeks 1–2 and 11–12 of intervention, dietary energy and fat intakes were lower, protein and carbohydrates intakes were not different and fiber and chromium intakes were higher in both groups, with no differences between groups (Table 1).

### 3.2. Aerobic fitness

Resting heart rate was not changed over time for either group (Table 2). Heart rate at 3 mph and 5° grade decreased, consistent with a modest training response.  $\text{VO}_2$  maximum increased over time when expressed in relation to body weight, with no difference in response between groups. For all subjects combined,  $\text{VO}_2$  maximum ( $\text{ml O}_2 \cdot \text{kg BW}^{-1} \cdot \text{min}^{-1}$ ) increased by  $8.3 \pm 3.1\%$  (median 5.9%). When expressed in relation to fat-free mass, the apparent change in  $\text{VO}_2$  maximum (mean  $4.2 \pm 3.0\%$ , median 2.6%) was not statistically significant ( $P = .16$ ).

### 3.3. Supplement compliance

Urinary Cr excretion in the CP-CLA group increased 22-fold from baseline (Fig. 1). There was no change over time in urinary Cr excretion in the placebo group. From baseline to Week 12, plasma concentration of the 18:2 c9,t11 CLA isomer increased 79% (baseline  $0.38 \pm 0.02\%$ , post  $0.60 \pm 0.03\%$ ,  $P < .001$ ), and the 18:2 t10,c12 CLA isomer became detectable (baseline not detected; post  $0.18 \pm 0.01\%$ ) in the CP-CLA group and were unchanged in the placebo

Table 2

Aerobic fitness and body composition

|  | Placebo  |          |          | CP-CLA   |          |          |
|--|----------|----------|----------|----------|----------|----------|
|  | Baseline | Post     | Change   | Baseline | Post     | Change   |
| Aerobic Fitness  |          |          |          |          |          |          |
| Heart rate, rest (bpm)   | 78±3     | 78±3     | 0±3      | 79±2     | 76±2     | −3±3     |
| Heart rate*, 3 mph, 5° grade (bpm)   | 127±4    | 123±3    | −4±3     | 127±3    | 123±3    | −4±2     |
| $\text{VO}_2$ maximum* ( $\text{ml O}_2 \cdot \text{kg BW}^{-1} \cdot \text{min}^{-1}$ ) | 35.7±0.9 | 39.5±1.6 | 3.8±1.5  | 35.9±1.2 | 37.8±1.7 | 1.9±1.3  |
| $\text{VO}_2$ maximum ( $\text{ml O}_2 \cdot \text{kg FFM}^{-1} \cdot \text{min}^{-1}$ ) | 63.2±1.7 | 67.7±2.8 | 4.5±2.5  | 66.2±1.9 | 66.7±2.4 | 0.5±2.5  |
| Body composition   |          |          |          |          |          |          |
| Body weight* (kg)  | 73.4±1.6 | 70.9±1.9 | −2.5±0.5 | 75.4±2.3 | 72.8±2.5 | −2.6±0.5 |
| Fat mass* (kg)   | 29.2±1.4 | 26.8±1.5 | −2.4±0.5 | 32.0±1.7 | 29.3±1.8 | −2.7±0.5 |
| Fat-free mass (kg)   | 41.5±1.1 | 41.5±1.0 | 0±0.5    | 40.8±1.1 | 40.9±1.1 | 0.1±0.2  |

Values are mean±S.E.M.

\*  $P < .05$  (significant effect of time).



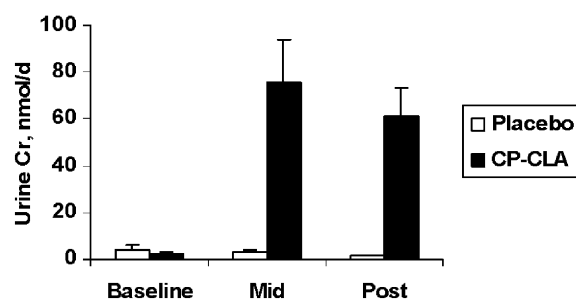


Fig. 1. Mean ( $\pm$ S.E.M.) 24-h urinary chromium excretion before (baseline) and Weeks 1–2 (mid) and 11–12 (post) of a 12-week period of diet and exercise-induced weight loss with (CP-CLA) or without (placebo) CP and CLA supplementation. Chromium excretion at mid and post was higher in the CP-CLA group than the placebo group; group-by-time,  $P < .0001$ .

group (18:2 c9,t11 baseline  $0.34 \pm 0.03\%$ , post  $0.29 \pm 0.04\%$ ; 18:2 t10,c12 not detectable at baseline and post). The other fatty acid methyl esters identified in plasma did not change over time in the control group and in the CP-CLA supplementation group (data not shown).

### 3.4. Body composition

Over time, with the energy restriction and exercise intervention, body weight and body fat decreased, and fat-free mass was not changed in both groups, with no differences in responses between groups (Table 2).

### 3.5. Metabolic and cardiovascular health indexes

A woman who has three or more of the following components may be identified as having the metabolic syndrome: fasting plasma glucose  $\geq 5.55$  mmol/L (100 mg/dl), fasting serum TG  $\geq 1.69$  mmol/L (150 mg/dl), fasting serum HDL  $\leq 1.29$  mmol/L (50 mg/dl), resting systolic/diastolic blood pressure  $\geq 130/85$  bpm and waist circumference  $\geq 88$  cm (35 in.). Among all 35 subjects at baseline, zero had elevated glucose, 13 (37%) had elevated TG, 11 (31%) had low HDL and zero had elevated blood pressure.

Waist circumference was not measured, and all of the women were overweight or obese. Only four women had both elevated TG and low HDL and would be classified as having the metabolic syndrome if their waist circumference was high.

Fasting hemoglobin A<sub>1c</sub> percentage, plasma glucose and insulin, insulin sensitivity (HOMA-IR), CHOL, HDL, LDL, TG, total cholesterol-to-HDL ratio and TG to HDL ratio and diastolic and systolic blood pressures were not changed over time or differentially affected by CP-CLA supplementation (Table 3).

## 4. Discussion

The results from this study support that combined CP and CLA supplementation for 12 weeks does not influence body weight, body composition and the selected metabolic and cardiovascular health indexes, in conjunction with a dietary energy restriction and exercise program. Strengths of this study included the randomized, placebo-controlled, double-blind experimental design; documentation that the subjects in the CP-CLA group consumed the supplements via the 22-fold increase in urinary chromium excretion and the altered plasma CLA isomer profile and evidence that the subjects complied with the diet and exercise programs via decreased energy intake, body weight and heart rate response to controlled-intensity exercise.

The foundation of the decision to test the efficacy of a supplement containing both CP and CLA rests on the literature supporting that these two supplements, independently, positively influence body composition (CP: Refs. [22,31]; CLA: Refs. [15,21,32,33]), glucose metabolism (CP: Ref. [34]) and cardiovascular health (CP: Ref. [12]; CLA: Ref. [33]). It is important to note that not all research supports the efficacy of these supplements (see below). The report [20] that coadministration of chromium (as chromium tricarboxylate) and CLA enhanced reductions in body

Table 3  
Metabolic and cardiovascular health indexes

|                                  | Placebo         |                 | CP-CLA          |                 |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                  | Baseline        | Post            | Baseline        | Post            |
| <b>Glucose metabolism</b>        |                 |                 |                 |                 |
| Hemoglobin A <sub>1c</sub> (%)   | 5.1 $\pm$ 0.1   | 5.1 $\pm$ 0.1   | 5.1 $\pm$ 0.1   | 5.1 $\pm$ 0.1   |
| Fasting plasma glucose (mmol/L)  | 4.3 $\pm$ 0.1   | 4.2 $\pm$ 0.2   | 4.2 $\pm$ 0.1   | 4.3 $\pm$ 0.1   |
| Fasting plasma insulin (pmol/L)  | 61 $\pm$ 7      | 51 $\pm$ 7      | 60 $\pm$ 6      | 61 $\pm$ 5      |
| HOMA-IR                          | 0.86 $\pm$ 0.14 | 0.97 $\pm$ 0.16 | 0.88 $\pm$ 0.15 | 0.81 $\pm$ 0.13 |
| <b>Lipid lipoprotein profile</b> |                 |                 |                 |                 |
| Total cholesterol (mmol/L)       | 5.74 $\pm$ 0.31 | 5.69 $\pm$ 0.47 | 5.64 $\pm$ 0.28 | 5.48 $\pm$ 0.34 |
| HDL (mmol/L)                     | 1.63 $\pm$ 0.10 | 1.58 $\pm$ 0.16 | 1.55 $\pm$ 0.10 | 1.50 $\pm$ 0.10 |
| LDL (mmol/L)                     | 3.41 $\pm$ 0.18 | 3.54 $\pm$ 0.28 | 3.49 $\pm$ 0.23 | 3.39 $\pm$ 0.21 |
| TG (mmol/L)                      | 1.55 $\pm$ 0.19 | 1.24 $\pm$ 0.19 | 1.33 $\pm$ 0.15 | 1.33 $\pm$ 0.21 |
| Cholesterol:HDL                  | 3.61 $\pm$ 0.12 | 3.91 $\pm$ 0.23 | 3.78 $\pm$ 0.19 | 3.77 $\pm$ 0.18 |
| TG:HDL                           | 2.22 $\pm$ 0.26 | 1.76 $\pm$ 0.20 | 2.17 $\pm$ 0.32 | 2.13 $\pm$ 0.31 |
| <b>Blood pressure</b>            |                 |                 |                 |                 |
| Resting diastolic (mmHg)         | 71 $\pm$ 3      | 71 $\pm$ 2      | 110 $\pm$ 2     | 110 $\pm$ 3     |
| Resting systolic (mmHg)          | 110 $\pm$ 2     | 111 $\pm$ 3     | 74 $\pm$ 2      | 71 $\pm$ 1      |

Values are mean $\pm$ S.E.M.

weight and fat mass, compared to CLA only, in male Balb C mice fed a high-fat (20% corn oil) diet, also supports this decision, albeit retrospectively. Plasma glucose, insulin and leptin were decreased in the mice given CLA alone and increased when chromium was also given. These observations highlight the need for future studies to simultaneously test the independent and combined effects of these supplements in separate experimental groups. This type of study with an expanded experimental design is also needed to assess if combined chromium and CLA supplementation might blunt or antagonize their independent effects, as observed in the mice with the differential metabolic responses to CLA with and without chromium [20].

This study assessed the efficacy of the CP-CLA supplement while all subjects habitually consumed an energy-restriction diet and regularly performed moderate-intensity exercise. The findings that CP-CLA did not enhance the body weight and fat mass losses achieved with these recommended lifestyle behaviors supports similar types of studies with CP or CLA supplementation alone. Whigham et al. [35] reported no differential body weight or body composition responses in obese men and women who consumed either placebo or 6 g/day CLA over a 52-week period. This year-long study included an initial 12-week energy restriction weight loss phase (double-blind; primarily liquid low-energy diet), a 16-week weight maintenance phase (double-blind) and a 24-week open-label continuation of weight maintenance. For CLA supplementation studies that did not include energy restriction or exercise interventions, some studies support that CLA supplementation results in decreased fat mass [15,21,32,33]. However, the majority of studies support that CLA does not affect body weight [18,32,36,37], fat mass [17,18,37,38] or fat-free mass [18,21,37–39].

Based on a meta-analysis of 10 randomized, double-blind and placebo-controlled CP supplementation studies, Pittler et al. [5] concluded that CP had a favorable, albeit modest (weighted mean difference  $-1.1$  kg; 95% confidence interval:  $-1.8$  to  $-0.4$  kg,  $n=489$ ) effect on body weight and no effect on lean body mass (weighted mean difference  $0.4$  kg; 95% confidence interval:  $-0.1$  to  $0.8$  kg,  $n=416$ ). Pittler et al. cautioned that the effect of CP on body weight was largely driven by the results from 1 [22] of the 10 studies, and that the clinical relevance of the effect is debatable when compared to the implementation of improved diet and exercise behaviors, a view shared by others [4]. The apparent lack of effect of CP on body weight and body composition is supported by findings from other reviews of literature [7–9,40].

The apparent lack of diet- and exercise-induced changes in the markers of metabolic and cardiovascular health measured in this study was contrary to a priori expectations but, in hindsight, plausible, based on the clinical normalcy of the subject's metabolic and cardiovascular markers at baseline and the modest body weight and aerobic fitness changes achieved. While overweight or obese, on a group

basis, these otherwise apparently healthy premenopausal women did not display the features of the metabolic syndrome. Our data support other shorter-term studies that supplementation with CP ([41–43]) or CLA ([18,19,36]) is not beneficial to people with clinically normal health profiles and extend this view to include overweight and obese premenopausal women who use moderate dietary energy restriction and aerobic exercise practices. Independent of the CP-CLA supplementation, these findings support that improvements in indexes of metabolic and cardiovascular health require greater (5–10%) reductions in body weight and improvement in aerobic fitness than were achieved and are more likely to occur in overweight women who also manifest markers of the metabolic syndrome [1].

The results from the dietary records indicate that, excluding the supplements, the women ( $n=35$ ) consumed  $\sim 65$   $\mu\text{g}$  Cr per day ( $\sim 42$   $\mu\text{g}/1000$  kcal of energy intake) during the intervention period. This amount of dietary Cr is well above the 25  $\mu\text{g}/\text{day}$  adequate intake recommended by the Institute of Medicine, Food and Nutrition Board [44] and consumed by American women [45], but comparable to controlled feeding diets previously developed by our research group ( $\sim 77$   $\mu\text{g}$  Cr per day) [29]. While direct analyses of the foods consumed by the subjects would be needed to confirm these food record data, adequate dietary chromium intake would likely negate the effects of a CP supplement [4,7].

The length of intervention and quantities of CP and CLA doses tested are additional issues of interest when interpreting the results of this and other studies. The 12-week intervention period used for the current study is comparable to most previous CP and CLA supplementation trials but has been questioned as too short by researchers interested in chromium [4] and CLA [46]. Limited CP [31] and CLA [17] studies support the possibility that the efficacy of CP and CLA supplements may require longer-duration studies ( $>6$  months). The 400  $\mu\text{g}/\text{day}$  Cr and 1.8 g/day CLA doses used in the current study are within the 200–1000- $\mu\text{g}/\text{day}$  Cr and 1.5–6-g/day CLA doses typically used in research. We are not aware of any systematic evaluations of dose-dependent responses of CP or CLA on the parameters measured in this study, and consensus is apparently lacking on the “optimum” doses of Cr and CLA to use in clinical research.

It is important to note that while these groups of overweight women achieved significant weight loss, it was less than the approximate 4.5–5.0 kg expected to occur over 12 weeks with a 2.1 MJ/day (500 kcal/day) energy deficit. Results from the food records indicate that overall, the women achieved an approximate 1.13 MJ/day (270 kcal/day) energy deficit. This should, theoretically, result in about 2.9-kg weight loss, which is close to the 2.5-kg weight loss achieved. The underachievement of the prescribed energy deficit likely reflects the difficulties of implementing a counseling-based diet plan with the expectation of quick and successful compliance.

## 5. Conclusion

The results of this study support that combined supplementation of CP-CLA (400 µg Cr and 1.8 g CLA) for 12 weeks by overweight but otherwise apparently healthy premenopausal women, in conjunction with moderate energy restriction and exercise, did not influence losses of body weight and body fat, compared to women who consumed a placebo. Independent of CP-CLA supplementation, the modest improvements in body weight (3.5%), body fat (8.9%) and aerobic fitness (4.2%) achieved by the women did not influence indexes of metabolic and cardiovascular health, including the lipid lipoprotein profile, glucose tolerance and blood pressure.

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