

Conjugated Linoleic Acids

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CAMPBELL, B. and R.B. KREIDER. Conjugated linoleic acids. *Curr. Sports Med. Rep.*, Vol. 7, No. 4, pp. 237–241, 2008. *Conjugated linoleic acid (CLA) has been studied extensively in both animal and human models. CLA supplementation has been attributed to provide several health benefits that are based largely upon animal and in vitro studies. Recent literature suggests that CLA supplementation possesses an anti-adipogenic role. However, the results of studies in humans have not been as consistent in this regard as anticipated from animal models. In addition to body composition, CLA also recently has been investigated in terms of exercise performance. The following review summarizes the most recent scientific investigations relative to CLA supplementation and its effects upon body composition and exercise performance. Additionally, recent investigations into the safety of CLA supplementation also are reviewed.*

INTRODUCTION

Conjugated linoleic acid (CLA) has been purported to promote health benefits as well as fat loss. For this reason, CLA has become a popular dietary supplement for those interested in weight loss, including athletes. CLA refers to a family of stereo and positional isomers of linoleic acid. As the name implies, the double bonds of CLA are conjugated (in which at least one pair of double bonds is separated by only one single bond). There are multiple isomers of CLA, but most of the animal studies with CLA have used mixtures of isomers that are mostly cis-9, trans-11 CLA (CLA-9) and trans-10, cis-12 CLA (CLA-10) in approximately equal amounts (1). To observe the differences of these two common isomers of CLA, refer to the Figure. There are two primary forms in which CLA is ingested, either as triacylglycerol or free fatty acids. Foods such as dairy products and meat contain relatively large amounts of CLA, with cheeses, homogenized milk, fresh ground beef, and lamb possessing some of the highest dietary sources of CLA (2). Conversely, vegetable fats and seafood generally are not rich sources of CLA (1,2).

Over the last decade, research has indicated that CLA may possess a number of health and performance-enhancing benefits. For this reason, CLA has been marketed as a

supplement that may promote health as well as provide ergogenic value to athletes. Although most research on CLA has been conducted on animals, there have been a number of recent studies that provide greater insight as to how CLA may be beneficial to enhance health and exercise performance in humans. Relative to the health benefits of CLA ingestion, there are several studies indicating (mostly in animal models) that CLA supplementation may prevent certain diseases and cancers. In particular, CLA has been shown to be anticarcinogenic (3) and antiatherosclerotic (4,5), and it appears to have insulin-sensitizing effects as well (6) (although some data exist to refute the insulin-sensitizing effects) (7). For these reasons, CLA is being developed for use in functional foods. While these aspects of CLA supplementation should not be overlooked, a thorough discussion of these health benefits is outside the scope of this article. The health benefits of CLA are well summarized in reviews by Bhattacharya *et al.* (8) and Tricon *et al.* (9). What follows are the latest findings relative to the effectiveness of CLA with regards to exercise performance and body composition, followed by the safety of CLA supplementation. It is of interest that multiple clinical studies using human subjects have been performed to assess these variables in the past several years.

CLA SUPPLEMENTATION AND EXERCISE AND BODY COMPOSITION

The relationship between body composition and exercise performance is correlated highly. Possessing a healthy, low body fat will enable an athlete or physically active individual to perform at a higher level. Additionally, achieving a healthy, low body fat is conducive for general

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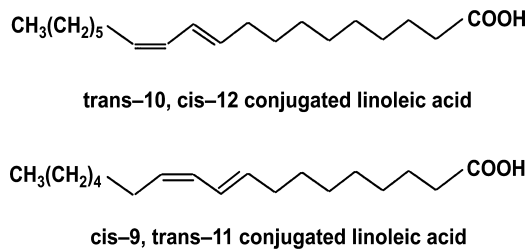


Figure. Structures of the common isomers of conjugated linoleic acid (CLA).

health. For this reason, CLA supplementation has been studied within both of these contexts: its effects upon both exercise performance and body composition. Following is a review of the more recent investigations (the last 2 yr) that have assessed these parameters.

A few recent investigations have evaluated whether CLA alone promotes fat loss. Lambert and colleagues (10) studied the effects of CLA ingestion upon body composition in regularly exercising individuals. Sixty-four regularly exercising participants (consisting of both men and women) were assigned randomly to either a CLA group (3.9 g consisting of 30% each of CLA-9 and CLA-10) or a control supplement, (3.9 g high-oleic sunflower oil). Both supplements were to be ingested on a daily basis for a 12-wk period. After the intervention, it was discovered that CLA supplementation was not associated with any statistically significant changes in body mass or body composition in men or women. In addition to the body composition measurements in this investigation, an oral glucose tolerance test was also administered before and after the 12-wk intervention. It was reported that mean plasma insulin concentrations (at 0, 30, and 120 min) were statistically lower in women taking CLA as compared with the women in the control group. Additionally, mean serum nonesterified free fatty acid concentrations were significantly attenuated in response to the oral glucose load after 12 wk of supplementation in the CLA group compared with the control group.

In contrast, Gallier and coworkers (11) reported favorable effects of CLA supplementation in terms of body fat mass. In this clinical investigation, a total of 118 subjects were included in a double-blind, placebo-controlled trial. CLA supplementation was administered at a dose of $3.4 \text{ g}\cdot\text{d}^{-1}$ for a 6-month period. The CLA oil was a mixture containing 37.5% CLA-9 and 38% CLA-10. At the end of the 6-month intervention, it was reported that CLA supplementation significantly decreased body fat mass at month 3 and at month 6 compared with placebo. Furthermore, it was reported that the reduction in fat mass was located mostly in the legs (as compared with arm fat mass and abdominal fat mass) (11).

Other investigations have evaluated the effectiveness of CLA plus additional compounds upon body composition and exercise performance. Most recently, CLA has been combined with other performance-enhancing (creatine monohydrate) (12) and purported weight-loss aid (chromium picolinate) (13) supplements to determine the cumulative effects that they exert upon exercise performance and body composition. Diaz *et al.* (13) assessed the

effects of combined chromium picolinate and CLA supplementation upon energy restriction and exercise-induced changes in body composition. For 12 wk, 35 overweight women (average age, 36 yr) were counseled to consume a hypocaloric diet (creating a $500 \text{ kcal}\cdot\text{d}^{-1}$ energy deficit) while performing 30 min of moderate-intensity walking or jogging $5 \text{ d}\cdot\text{wk}^{-1}$. The dosages of each supplement were as follows: chromium picolinate = $400 \mu\text{g}\cdot\text{d}^{-1}$, CLA = $1.8 \text{ g}\cdot\text{d}^{-1}$ (in 2.4 g of tonalin oil). After 12 wk of supplementation and exercise, it was reported that body weight decreased by 2.6 kg in the chromium picolinate and CLA group and by 2.5 kg in the placebo group. Fat mass decreased by 2.7 kg in the chromium picolinate and CLA group and by 2.4 kg in the placebo group. Because there were no differences between the chromium picolinate-CLA and placebo groups, the authors conclude that the use of a combined chromium picolinate-CLA supplement for 3 months does not affect diet and exercise-induced changes in body weight and body composition. Relative to the safety of the chromium picolinate-CLA supplement, the 12-wk intervention period was found to neither improve nor adversely affect metabolic syndrome markers or blood pressure.

Tarnopolsky and coworkers (12) examined whether creatine monohydrate and CLA supplementation could enhance strength gains and improve body composition after a resistance training program in older adults. Elderly men (75 yr old) and women (68 yr old) followed a resistance training program twice weekly for 6 months (using 12 resistance exercises in a circuit-set system that trained the upper and lower body). These elderly subjects were randomized into either a supplementation group or a placebo group. The supplementation consisted of 5 g creatine monohydrate plus 6 g CLA (at a ratio of 45% CLA-9 and 45% CLA-10). After the 6 months of resistance training and supplementation protocol, it was reported that the creatine monohydrate-CLA group experienced a significant increase in fat-free mass (2.1 kg) as compared with the placebo group (0.9 kg). Additionally, there was a significantly greater reduction in fat mass in the creatine monohydrate-CLA group after training (-1.9 kg) as compared with the placebo group (-0.4 kg). The creatine monohydrate-CLA group did not enhance further isometric strength measurements after training; however, a significant increase was observed relative to isokinetic strength and most measures of muscular endurance for those in the creatine monohydrate-CLA group as compared with the placebo group. In relation to side effects, the subjects tolerated the supplementation protocol well, with only one report of gastrointestinal distress in the creatine monohydrate-CLA group, but this did not lead to discontinuance of the study. The major findings of this study were the improvements in body composition (increase in fat-free mass and reduction in fat mass) and muscular endurance in those subjects ingesting the creatine monohydrate-CLA supplement. However, because of the design of the supplementation protocol, it is not possible to determine what proportion of the observed body composition and muscular endurance benefits can be attributed to creatine monohydrate and what may have been attributed to CLA intake.

There have been two well-designed clinical studies investigating the effects of CLA supplementation during resistance training. Kreider and colleagues (14) randomly assigned experienced, resistance-trained men to ingest either 6 g CLA with 3 g other fatty acids or 9 g of an olive oil placebo. During the 28-d intervention, the subjects maintained their usual individualized training programs and their normal diets. After the 28-d supplementation period, it was reported that the CLA supplementation did not significantly affect total body mass, fat-free mass, percent body fat, or muscular strength. As a result, the authors conclude that CLA does not appear to possess significant ergogenic value for experienced resistance-trained athletes. However, it is important to consider the short intervention period of 28 d used in this investigation. It is plausible that 28 d of CLA supplementation may not be of sufficient duration to detect physiological changes in body composition and strength indices.

A recent investigation involving resistance-trained athletes reports favorable changes in exercise performance resulting from CLA supplementation (15). In this study, 76 subjects (comprising both males and females) were randomized to receive 5 g·d⁻¹ of CLA (containing approximately equal amounts of CLA-9 and CLA-10) or a placebo (sunflower oil). During the 7-wk intervention, the participants performed resistance training 3 d·wk⁻¹. At the end of the 7-wk protocol, the CLA group demonstrated a significant increase in lean tissue mass (1.3 kg) as compared with the placebo group (0.5 kg). Additionally, the CLA group demonstrated a significant reduction in fat mass (-0.8 kg) and body fat percentage (-1.3%) as compared with the placebo group (+0.4 kg and +0.2%, respectively). Urinary 3-methylhistidine (a marker of myofibrillar breakdown) was found to be increased in the placebo group with no change in the CLA group. This is a plausible mechanism for the increase in lean tissue mass. This finding may indicate that CLA exerts an anticatabolic effect upon skeletal muscle tissue during resistance training. Elbow and knee flexor muscle strength and muscle thickness was not significantly different between groups. At the end of the 7-wk interval, 17 of the subjects crossed over to the opposite group for an additional 7 wk. In this 7-wk crossover study, there were no significant differences between the CLA and placebo groups in relation to body composition variables and strength and muscle tissue measurements. Although the results of the first 7-wk intervention yielded significant improvements in body composition for the CLA group, the changes in the CLA group were small and prompted the authors to question the clinical significance of these findings (15).

SAFETY OF CLA SUPPLEMENTATION

It is imperative that any dietary supplement purported to improve exercise performance is safe for consumption. Even if short-term improvements in physical performance are actualized, if the safety of the sports supplement is in question or is deleterious to long-term health, then the benefits do not outweigh the risks, and such supplements should not be recommended. In relation to CLA supplementation in humans, clinical investigations have administered dosages ranging from 2 to 6.8 g for periods

encompassing 30 d to 2 yr. In 2003, Larsen and colleagues (16) published a comprehensive review on the safety and efficacy of dietary supplements containing CLA for the treatment of obesity. According to Larsen and coworkers (16), with respect to cardiovascular risk factors, either no or very small changes in cholesterol levels were reported in the studies that assessed these variables. One of the studies (7) assessed insulin sensitivity in abdominally obese men resulting from 12 wk of supplementation at 3.4 g·d⁻¹ CLA (predominantly comprising CLA-10). The results of this intervention reveal a significant decrease in insulin sensitivity, an increase in fasting glucose, and a significant increase in C-reactive protein. These findings are contrasted with a study of people with type II diabetes conducted by Belury and colleagues (6). In this study, CLA supplementation with a commercially available CLA mixture (8 g of an approximately 50:50 mixture of CLA-9 and CLA-10 consumed on a daily basis) for 8 wk led to a decrease in fasting blood glucose in 81% of the subjects with diabetes, suggesting that CLA may be beneficial in people with type II diabetes. Most of the studies reviewed in the Larsen paper (16) that assessed blood glucose report no changes after the CLA intervention (17–21). Another investigation (6) that instructed the participants to ingest 8 g·d⁻¹ of CLA (predominantly comprising CLA-10) for an 8-wk period resulted in a decrease in fasting blood glucose.

Since 2003, several more studies have been conducted on CLA supplementation with health outcomes reported. A recent investigation sought to assess the short-term safety of dietary CLA in overweight Japanese male volunteers (22). This study used CLA-9 and CLA-10 in approximately equal amounts at dosages of 3.4 and 6.8 g·d⁻¹ for 12 wk. Safety of CLA supplementation was assessed comprehensively via blood parameters, vital signs, and the reporting of adverse events. Adverse events were reported by 30% of the placebo group, 60% of the group ingesting 3.4 g, and 70% of the group ingesting 6.8 g·d⁻¹. All adverse events were mild to moderate. They included adenoiditis, diarrhea, cough, feelings of worthlessness, headache, fever, nasal inflammation, and abdominal distention. According to the authors, most adverse events disappeared spontaneously or were in remission after a few days. Blood pressure and heart rate did not differ significantly among the three groups at 12 wk (22). There was a slight increase in the level of liver enzymes (serum AST and ALT activities) in the high CLA group (6.8 g·d⁻¹) at 12 wk. The authors indicated that the changes were small and within normal ranges. Furthermore, statistical analysis of the population of apparently healthy volunteers who had normal blood parameters at the baseline revealed that serum AST and ALT activities did not differ significantly among the three groups at 12 wk, and hepatorenal contrast also remained unchanged in all groups during the experiment. The authors summarized the results of this comprehensive study with the following: "3.4 g of CLA (supplementation) daily for 12 [wk] was well tolerated in the Japanese overweight male population. In particular, overweight volunteers who had normal blood parameters at the baseline showed no significant clinical changes in blood parameters even when 6.8 g of CLA was ingested daily for 12 [wk]."

Gaullier *et al.* (23,24) published two studies that assessed the long-term safety of CLA supplementation. In the first of these studies (24), CLA was administered to male and female volunteers at a dosage of either 3.6 g·d⁻¹ in the free-fatty acid form (CLA-FFA) or at a dosage of 3.4 g·d⁻¹ in triacylglycerol form (CLA-Trig) for a 1-yr period. Each form of CLA possessed a 50:50 mixture of CLA-9 and CLA-10. A placebo group was given 4.5 g·d⁻¹ olive oil. In this 1-yr intervention, safety was assessed via comprehensive blood samples, vital signs, and adverse events. Adverse events were reported by 68% of all randomly assigned subjects and with similar frequency in all three study groups. All adverse events were rated as either “mild” or “moderate,” and the symptoms were transient. Abdominal discomfort or pain, loose stools, and dyspepsia were the most frequently reported adverse events. Only 11.4% of the reported adverse events were related to the supplementation. The lack of difference in adverse-events reports between the CLA groups and the placebo group indicates that the CLA was well tolerated. Of the numerous variables assessed systemically, three were elevated significantly in the CLA-FFA group as compared with the placebo group (no differences were reported between the CLA-Trig group and the placebo group). These three variables were lipoprotein a, thrombocytes, and AST. Despite these changes, the mean values were not outside of the normal ranges for these variables. Also, fasting blood glucose and insulin levels did not change in any of the groups. There were no significant differences between the groups for blood pressure and heart rate.

In a follow-up to their 1-yr CLA intervention study, Gaullier and colleagues (23) instructed a large percentage of the original participants in the previous study (24) to ingest 3.4 g of CLA (as part of a 4.5-g CLA-triacylglyceride supplement) daily for an additional 12 months (totaling 2 yr of CLA supplementation for a majority of the study participants). Even though all participants ingested 3.4 g of CLA in the year-long extension study, the participants remained in the original groups mentioned previously for statistical comparison (CLA-FFA, CLA-Trig, and placebo). As in the original study, the subjects consumed their food ad libitum without energy restrictions or changes in lifestyle, including exercise habits. After 2 yr of CLA supplementation, adverse events were reported by 50% of all randomized subjects with similar frequencies in the three study groups. All adverse events were rated as “mild,” and the most frequently reported adverse event was gastrointestinal complaints. As compared with the first 12 months of CLA ingestion, the adverse events rate decreased. The good compliance and low drop-out rates indicate that long-term CLA supplementation was well tolerated by the subjects. Gaullier *et al.* (23) concluded that CLA supplementation was well tolerated and the observed changes in the safety variables were all within the normal range, suggesting that CLA supplementation in healthy, overweight subjects for 2 yr is safe.

A composite survey of the clinical investigations that have assessed the safety of CLA supplementation seems to indicate that it is generally well tolerated and safe. While most problems reported with CLA supplementation are minor in nature, the most common problem reported is

related to gastrointestinal distress. The majority of the published data in humans does not lead one to the conclusion that CLA supplementation is diabetogenic, although more research is needed. The role of CLA in cardiovascular risk is equivocal. In perhaps the most comprehensive study (23) assessing the safety of CLA ingestion in humans (in which CLA supplementation was ingested over a 2-yr period), there were no changes in triglyceride and very small changes in total, high-density lipoprotein, and low-density lipoprotein cholesterol in all groups. However, there was an increase in some markers associated with inflammation and cardiovascular disease risk. Further studies are needed to determine whether there is an effect of CLA ingestion upon cardiovascular risk and inflammation in humans.

CONCLUSION

The previously mentioned studies summarize the most recently published articles relative to CLA supplementation and its effects upon body composition, exercise performance, and safety in humans. Some studies demonstrate that CLA supplementation improves body composition (23,25–27), while others indicate that such supplementation is not effective in improving body composition (28–31). Even though the data are conflicting, when CLA does impart favorable effects upon body composition, it has been determined that the CLA isomer that is primarily responsible in the body fat-lowering effect (and that is active in lipid metabolism) is the trans-10, cis-12 isomer (32). However, the results of studies in humans indicate that the effect of the CLA-10 isomer upon body fat is considerably less than that anticipated from mice studies.

Very few studies exist that have investigated CLA ingestion and its effects upon exercise performance. Most of the clinical investigations that have been published are those that have exercising individuals supplement with CLA for a period of time with the primary purpose of eliciting changes in body composition. Of the few studies that do exist relative to CLA supplementation and exercise performance, there also are conflicting results, with one investigation demonstrating that CLA supplementation improves performance (15) and one that did not show improvements (14). There appears to be a plethora of published papers on the effects of CLA upon body composition, but not on direct measures of exercise performance. Therefore, more research needs to be conducted in this area.

Long-term (12–24 months) clinical investigations have reported that CLA supplementation is well tolerated in healthy, overweight humans (23,24). When adverse reactions associated with CLA supplementation are reported, they are generally mild, with gastrointestinal distress being the most common problem reported. Recent studies investigating the safety of CLA supplementation (22–24) report that adverse events were mild to moderate, and occurrences were no different between the CLA supplementation and placebo groups.

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