review

Efficacy and safety of dietary supplements containing CLA for the treatment of obesity: evidence from animal and human studies

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Abstract **Dietary supplements containing conjugated linoleic acid (CLA) are widely promoted as weight loss agents available over the counter and via the Internet. In this review, we evaluate the efficacy and safety of CLA supplementation based on peer-reviewed published results from randomized, placebo-controlled, human intervention trials lasting more than 4 weeks. We also review findings from experimental studies in animals and studies performed in vitro. CLA appears to produce loss of fat mass and increase of lean tissue mass in rodents, but the results from 13 randomized, controlled, short-term (<6 months) trials in humans find little evidence to support that CLA reduces body weight or promotes repartitioning of body fat and fat-free mass in man. However, there is increasing evidence from mice and human studies that the CLA isomer *trans*-10, *cis*-12 may produce liver hypertrophy and insulin resistance via a redistribution of fat deposition that resembles lipodystrophy. CLA also decreases the fat content of both human and bovine milk. In conclusion, although CLA appears to attenuate increases in body weight and body fat in several animal models, CLA isomers sold as dietary supplements are not effective as weight loss agents in humans and may actually have adverse effects on human health.**—Larsen, T. M., S. Toubro, and A. Astrup. **Efficacy and safety of dietary supplements containing CLA for the treatment of obesity: evidence from animal and human studies.** ***J. Lipid Res.*** **2003.** 44: **2234–2241.**

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DIETARY SOURCES OF CONJUGATED LINOLEIC ACID

Conjugated linoleic acid (CLA) is a collective term used to describe the mixture of positional and geometric isomers of linoleic acid with conjugated double bonds (i.e., the two double bonds are separated by one single bond). The double bonds, each of which may be in the *cis* or *trans* configuration, can be in any position on the carbon chain. They are, however, most frequently found in positions 8 and 10, 9 and 11, 10 and 12, or 11 and 13. CLA is marketed commercially in the US in products such as Natrol®, Your Life®, Vitamin World®, Nature's Way®, and Nature's Plus®. These products are available over the counter in supermarkets, drug stores, and health food stores, and can be bought from wholesalers throughout the US. CLA is also sold in Asia, Canada, Europe and Japan (1). Most of the CLA products sold as dietary supplements for human consumption contain 60–90% CLA in the form of either free fatty acids or triglycerides, and they usually contain a mixture of isomers, predominantly *cis*-9, *trans*-11 (c9,t11) and *trans*-10, *cis*-12 (t10,c12) isomers (2).

The major sources of CLA in the human diet are meat and dairy products derived from ruminants, and in these products the predominant CLA isomer (>90%) is c9,t11.

The amount of CLA present in dairy products varies according to the animal breed and the processing of the product, but the major determinant appears to be livestock feeding conditions (3, 4). Various livestock feeding strategies have been used for increasing the CLA content of cow's milk. Data on CLA content of animal food products have recently become available, allowing estimation of human intakes. Recent studies suggest average intakes of ~150–200 mg/day (5, 6), and consumption of a diet rich in high-fat animal products can increase the daily intake to at least 650 mg/day (7). In comparison, CLA dietary supplements marketed for weight loss purposes constitute an intake of 3–4 g/day (8). Dietary CLA is recovered in human milk, serum lipids, and in adipose tissue. A sig-

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Abbreviations: CLA, conjugated linoleic acid; c9,t11, *cis*-9, *trans*-11; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; MUFA, monounsaturated fatty acid; SCD1, stearoyl-CoA desaturase 1; SFA, saturated fatty acid; t10,c12, *trans*-10, *cis*-12; TG, triglyceride.

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nificant correlation between the proportion of c9,t11 CLA in adipose tissue and milk fat intake has been found, and c9,t11 CLA can comprise 0.5% by weight of total fatty acids in human adipose tissue (5).

ISOMER-SPECIFIC EFFECTS OF CLA ON BODY COMPOSITION

CLA has been studied extensively in various animal species, and in general, it is now widely recognized that feeding CLA (various mixtures of isomers) to different animals (including mice, hamsters, rats, chickens, and dogs) results in changes in body composition, i.e., lowering of body weight and fat mass (FM) and a relative increase in lean body mass [as reviewed in ref. (9)]. For example, 6 weeks' administration of CLA (1% CLA added by weight to a low-fat diet, ~1.5g CLA/kg body weight) has been shown to decrease body weight by ~10% and body fat by ~70% when compared with placebo in mice (10). Furthermore, it has been shown, using accurate dual energy X-ray scanning methods, that CLA dose-dependently decreases fat accretion in growing pigs (11).

It appears that the effects on body composition are largest when CLA is given to the animal during growth periods, but the effects also depend on several other factors, including species, age, gender, dosage, and duration of CLA feeding, but perhaps most importantly, the CLA isomer composition. In the majority of the animal studies performed, the CLA preparations used have been mixtures of CLA isomers, i.e., usually a mixture composed of 30–40% of each of the c9,t11 and t10,c12 isomers, the residue consisting of various less-common isomers.

Although CLA has effects when given as a mixture, recent studies in mice and hamsters have identified the t10,c12 isomer, rather than the c9,t11 isomer, as being responsible for the attenuation of body weight gain and for the reduction of body fat (12, 13). In a study on Zucker Diabetic Fatty (ZDF) rats, c9,t11 CLA had no significant effects, whereas a mixture of c9,t11 and t10,c12 lowered body weight, although this was partly a result of a decreased energy intake (14).

EFFECTS OF CLA ON ATHEROSCLEROSIS AND GLUCOSE TOLERANCE IN ANIMALS

In general, the CLA-induced changes in cardiovascular risk factors, glucose tolerance, blood levels of free fatty acids, triglycerides, total-, LDL-, HDL- and/or VLDL-cholesterol, and liver metabolism observed in the various animal studies are conflicting.

There is considerable evidence that feeding CLA may affect liver metabolism and have adverse effects on glucose homeostasis in mice. Early studies in mice found that CLA induces peroxisome proliferation in the liver (15). In mice and chickens, CLA supplementation has been associated with increases in liver weight, possibly as a result of triglyceride accumulation (16–18).

In hamsters, the t10,c12 isomer causes enlargement of both liver and kidney, despite a lower body weight (19). In rats, however, CLA does not act as a classic peroxisome proliferator, despite moderate increases in liver weight (20–22).

Positive findings awakened interest in the health benefits of CLA. It was found that feeding rabbits a CLA mixture caused a substantial regression of established atherosclerosis, despite a significant increase in serum total cholesterol and decrease in HDL-cholesterol (23). However, others have found an increase in arterial fatty streak formation in c57BL/6 mice after CLA supplementation (24). Normalization of impaired glucose tolerance (using a glucose tolerance test) has been shown in Zucker rats fed a mixture of CLA (25), and the t10,c12 isomer has been shown to lower body weight and attenuate the development of insulin resistance in rats, though partly as a result of a decreased energy intake (14, 26). In contrast, CLA supplementation has been found to increase serum insulin levels in rats (27).

In mice and hamsters, CLA supplementation has been associated with increases in plasma insulin levels (10, 28). Similarly, despite resulting in decreased body weight, t10,c12 supplementation in mice was associated with increased serum glucose and insulin levels, whereas the c9,t11 supplementation group showed no weight loss, but lowered triglycerides and FFA (29). This study is in line with other studies in mice showing that CLA supplementation (36% t10,c12 isomer) results in marked reductions in body fat, although this was associated with the development of insulin resistance, resulting in a metabolic state resembling lipoatrophic diabetes (30, 31). Similar observations have been reported by other researchers, showing that mice fed purified t10,c12 CLA or CLA mixtures develop hyperinsulinemia and fatty liver (29, 32–34). However, the degree of fatty liver may depend to some extent on the total amount of fat in the diet, i.e., a higher dietary total fat content is associated with a lower degree of hepatic steatosis (20, 31).

THE T10,C12 ISOMER AFFECTS FATTY ACID METABOLISM AND LIPID SYNTHESIS

There is accumulating evidence that CLA may regulate lipid metabolism in addition to its effects on body composition per se. The t10,c12 isomer has been shown to inhibit the transcription and activity of stearoyl-CoA desaturase 1 (SCD1) in porcine adipose tissue in ex vivo studies (35). SCD1 desaturates saturated fatty acids (SFAs) into monounsaturated fatty acids (MUFAs), resulting in a higher δ-9 desaturase index, i.e., a higher MUFA/SFA ratio. In vitro studies have also delineated isomer-specific effects on SCD1 activity. The t10,c12 isomer seems to inhibit the expression of SCD1 mRNA in liver cells from mice fed the isomer and in mice liver cell lines, leading to decreased C16:1/C16:0 and C18:1/C18:0 ratios (36). Similarly, t10,c12 decreased SCD1 mRNA expression and activity in 3T3-L1 adipocytes, and resulted in cells with smaller lipid droplets

(37). This modulation of the ratio of MUFA/SFA (presumably by the t10,c12 isomer) has also been observed in milk fat from cows fed t10,c12 supplements (38, 39). In addition, the t10,c12 isomer seems to be responsible for the reduced milk fat production observed in cows, also known as milk fat depression syndrome, which occurs when cows are fed diets containing large amounts of unsaturated oils, such as plant and fish oils (4). Hence, in cows fed either a purified t10,c12 diet or a known milk fat-depressing diet, the de novo fatty acid synthesis and/or the utilization of circulating fatty acids is severely inhibited, resulting in a markedly lower milk fat production (40–42). By studying the transcription of several lipogenic enzymes in isolated mammary fat biopsy tissue, it has been found that t10,c12 feeding inhibits transcription of enzymes involved in de novo fatty acid synthesis, desaturation of fatty acids, and triglyceride synthesis (39). It has also been observed recently that CLA supplements may decrease mammary milk fat production in several other animal models, including mice, pigs, (43) and humans (44). Early studies found that CLA significantly reduced the density of the branching mammary epithelium in rats (45). This decrease in milk fat content may influence the growth of the offspring. It has been reported that dietary CLA decreases yolk 18:1(n-9) and increases SFA content (46) in hens' eggs, causing yolk hardening and inducing chick embryonic mortality (47). However, in rats, no effects on litter growth were seen when lactating rats were fed t10,c12 CLA. Mice with a targeted disruption of the gene encoding SCD1, shown to be resistant to diet-induced weight gain, had increased lipid oxidation and plasma levels of ketone bodies, and reduced levels of plasma insulin and leptin, but developed signs of hepatic steatosis when fed a high-fat diet (48). In summary, although CLA-induced decreases of the MUFA/SFA ratio seem to be involved in the general inhibition of adipogenesis, we do not yet know exactly how this may otherwise influence health in animals and humans.

THE T10,C12 ISOMER AFFECTS ADIPOCYTE DIFFERENTIATION AND FAT CELL TRIGLYCERIDE SYNTHESIS

The mechanism of action of the peripheral body fat-decreasing effect of CLA has not yet been fully elucidated. CLA does not seem to enhance energy expenditure acutely, but has been shown to increase energy expenditure in mice fed CLA for 6 weeks, despite a significant weight loss (10, 49). There is also controversy as to whether CLA affects energy intake, and some studies suggest that CLA may induce feeding aversion in mice (10) and rats (14); yet CLA seems to have effects on body composition in mice independent of changes in energy intake (50).

Despite these suggestions that an increased energy expenditure and a decreased energy intake occur with CLA intake, most of the evidence suggests that the major part of the effect on body fat changes can be explained by the attenuation of fat cell differentiation by the t10,c12 isomer.

In vitro studies of primary cultures of stromal vascular cells from human adipose tissue have shown that t10,c12 can lower triglyceride incorporation in these cells (i.e., inhibit lipogenesis), whereas the c9,t11 isomer increases the triglyceride content (51, 52). Similarly, the t10,c12 isomer has consistently been shown to decrease the differentiation of 3T3-L1 adipocytes, possibly via a decrease in the expression and/or activation of the peroxisome proliferator-activated receptor γ, which is a strong inducer of adipocyte differentiation (53, 54). Several in vivo studies support these findings. Sprague-Dawley rats have been seen to have a decreased body weight, with the reduced FM apparently accomplished by a decrease of adipocyte cell size, rather than cell number, when fed a CLA mixture (55). However, others have reported that CLA supplementation can inhibit both adipocyte number and adipocyte size in mice (56, 57). Finally, the t10,c12 isomer has been shown to induce apoptosis in mouse adipose tissue (30, 50, 57).

THE EFFICACY AND SAFETY OF CLA IN HUMAN INTERVENTION STUDIES

Literature and data on human clinical trials with CLA supplementation for the present review were obtained from searching ISI Web of Science, MEDLINE, Science Citation Index, and patent databases, with the key words *human*, *conjugated linoleic acid* and *CLA* (latest access July 10, 2003). Other data sources include published indexes, patent databases (accessed at www.uspto.gov), abstract booklets, and references identified from bibliographies of pertinent articles and books.

Our initial search identified 19 randomized, double-blinded, placebo-controlled studies on CLA supplementation in humans where changes in body weight or body composition had been reported. Of the studies found, 12 are published in peer-reviewed journals, while seven are only reported in abstract form. Of these 19 studies, 12 studies met the selection criteria (duration of >4 weeks, published in peer-reviewed journals). A thirteenth study did not meet the selection criteria but was included due to its duration—a 6-month study by Atkinson (58) had the longest duration of all but was not published in a peer-reviewed journal. The studies were not eligible for a formal meta-analysis, due to insufficient reporting of important data and substantial differences in design. For example, the studies found differed significantly in CLA-isomer composition and dosage, study duration, subject characteristics, and measurement methods. The studies were therefore interpreted individually, and comparisons between studies had to be conducted with caution, inasmuch as they differed in several aspects. Whenever possible only P values <0.05 for the treatment effect between study groups (CLA vs. placebo) are considered and presented as significant effects. The findings of the 13 selected studies are summarized in **Table 1**.

No effect of CLA consumption on body weight was found in any of the 13 studies. FM was assessed in 10 studies, and three of these found a decrease in FM. Fat-free

TABLE 1. Human intervention studies of conjugated linoleic acid

Study Subjects (Women/Men)	Intervention Period and Dose	CLA Composition and Provider	Placebo Supplementation	Author Conclusion	Blood Lipids or Other[a]	Comments	Reference
17 Subjects (17/0) BMI ~22	64 Days 3.9 g/day	65% CLA t10,c12, 22.6%; c9,t11,17.6%; c11,t13, 23.6%; t8,c10,16.6%; t9,t11+t10,t12, 7.7%; others: 11.9%; Tonalin™, Pharmanutrients, Inc	Sunflower oil (73% linoleic acid)	No effect on BW, FFM, or FM.	No change in lipids.	FM determined by bioimpedance and DXA.	(75, 76)
20 Subjects (10/10) BMI ~23	12 Weeks 1.8 g/day	60% CLA t10,c12, ~50%; c9,t11, ~50%; Tonalin™, Natural ASA	Hydrogel (1.8 g/day)	No effect on BW. Decrease in FM.	NA	FM determined by NIR. FFM NA.	(77)
53 Subjects (26/27) BMI~25	12 Weeks 4.2 g/day	75.9% CLA t10,c12, ~50%; c9,t11, ~50% others; Minor Natural ASA	Olive oil (4.2 g/day)	No effect on BW. Decrease in FM.	No change in lipids or glucose.	FM determined by skin fold thickness. FFM NA.	(62, 78)
22 Subjects (10/14) BMI~23	8 Weeks 0.7–1.4 g/day	69% CLA t10,c12, 51%; c9,t11, 49% CLA 70; TrofoCell	Soybean oil	No effect on BW or FM.	Decrease in HDL.	FM determined by skin fold thickness. FFM NA.	(79)
52 Subjects (35/17) BMI~29	12 Weeks 1.7–6.8 g/day	75% CLA t10,c12, ~50%; c9,t11, ~50%; Tonalin™, Natural ASA	Olive oil (9 g/day)	No effect on BW or FFM. Decrease in FM (CLA groups compared with placebo).	No change in lipids.	FM and FFM determined by DXA.	(80)
24 Subjects (0/24) BMI~32	4 Weeks 4.2 g/day	75% CLA t10,c12, ~37.0%; c9,t11, 36.9% CLA 80; Natural ASA	Olive oil (4.2 g/day)	No effect on BW. Decrease in sagittal abdominal diameter.	No change in lipids or glucose.	FM and FFM NA.	(81)
60 Subjects (0/60) BMI~30	12 Weeks 3.4 g/day	*1*) Isomer mixture, 80%; CLA t10,c12, 35%; c9,t11, 35.4%; *2*) t10c12 preparation, 75% CLA t10,c12, 76.5%; c9,t11, 2.9%; Natural ASA	NA	No effect on BW, FM, or FFM.	Isomer mixture decreased HDL. t10,c12 decreased HDL, increased glucose and CRP, and decreased insulin sensitivity.	FM and FFM determined by bioimpedance.	(60, 61)
60 Subjects (NA) BMI~30	12 Weeks 3.4 g/day	75% CLA, Composition, NA; Tonalin™, Natural ASA	Olive oil (4.5 g/day)	No effect on BW, FM, or LBM.	No change in lipids.	FM and FFM determined by bioimpedance.	(64)
23 Subjects (NA)	28 Days 6 g/day	65% CLA Composition = Reference (75); Tonalin™, Pharmanutrients	Olive oil (9 g/day)	No effect on BW, FM, or FFM.	NA	Exercise study. FM and FFM determined by DXA.	(82)
51 Subjects (23/28) BMI ~23	8 Weeks 3.0 g/day	*1*) 67% CLA, 50:50 mix; c9,t11, 50%; t10,c12, 50%; *2*) 59% CLA, 80:20 mix; c9,t11, 80%; t10,c12, 20%; Loders Croklaan B.V.	Linoleic acid (3 g/day)	No effect on BW.	50:50 Mix reduced fasting TG. 80:20 Mix reduced VLDL. No change in glucose.	FM and FFM NA.	(83)
21 Subjects (NA)	8 Weeks 8 g/day	76% CLA t10,c12, 39%; c9,t11, 37%; Pharmanutrients	Safflower oil (8 g/day)	No effect on BW.	Decrease in fasting glucose.	FM and FFM NA.	(84)
80 Subjects (NA) BW = 94 kg	6 Months 2.7 g/day	NA	NA	No effect on BW, FM, or FFM.	No change.	Weight loss study. FM and FFM determined by underwater weighing.	(58, 63)
56 Subjects (26/28) 25<BMI<30	13 Weeks 1.8 or 3.6 g/day	CLA 75% TG; Tonalin™, Natural ASA, Hovdebygda	Oleic oil (1.8 or 3.6 g/day)	Increased regain of FFM. No effect on FM, BW, or % BW regain.	No change in glucose, insulin, or TG.	Weight loss/regain study. FM and FFM determined by hydrodensitometry and deuterium dilution.	(59)

BMI, body mass index; BW, body weight; c9,t11, *cis*-9, *trans*-11; CLA, conjugated linoleic acid; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; NA = not available; NIR, near-infrared technique; t10,c12, *trans*-10, *cis*-12; TG, triglycerides.

[a] Significance level for difference between CLA and placebo groups set at $P < 0.05$.

mass (FFM) was assessed in seven studies, but only one of these studies found a slight increase in body FFM (59) (FFM assumed to correspond to lean body mass). Three studies assessed neither FM nor FFM. With respect to cardiovascular risk factors, either no or very small changes in cholesterol levels were reported, and no consistent changes were observed.

Only one study included direct insulin sensitivity measurements. In this study by Riserus et al., for 12 weeks, supplementation with 3.4 g/day of purified (75%) t10,c12 resulted in a significant decrease in insulin sensitivity (using an intravenous glucose tolerance test), an increase in fasting plasma glucose, and a significant increase in the concentration of C-reactive protein, a marker of inflammation and a strong predictor of cardiovascular risk (60, 61). CLA supplementation in humans has been shown to increase urinary levels of 8-iso-PGF2-α and 15-keto-dihydro-PGF2-α, which are in vivo markers of nonenzymatic and enzymatic lipid peroxidation and oxidative stress, processes that may contribute to insulin resistance (62).

To summarize, the present data from human trials does not support any weight loss-inducing effect of CLA, and there is no unequivocal evidence of an effect on body fat percentage. In addition, it seems that CLA may actually induce adverse effects, including insulin resistance, in subjects susceptible to type 2 diabetes.

DISCUSSION

CLA supplements sold as slimming agents over the counter and via the internet do not seem to affect body weight in humans, contrary to results from animal studies and in contrast to the claims made in the commercials promoting the products. It should be noted that many animal studies have used direct measures of body composition (i.e., weighing of individual organs after slaughter), whereas human studies have used indirect measures, such as bioimpedance or dual-energy X-ray absorptiometry (DXA) scanning. Whether these methodological differences also play a role in the apparent differences between animal and human studies regarding changes in body composition is unknown.

Also, when comparing animal and human studies, it should be noted that the doses of 25–80 mg/kg/day CLA used in humans are much lower than those used in animals, i.e., one-tenth of the dose given to pigs and often only approximately one-fiftieth of that given to rats per kg body weight (63). The efficacious doses used in rat studies would correspond to a daily CLA intake of 130g/day in humans. However, the cases of liver hypertrophy and insulin resistance reported in many animal studies using large doses of CLA indicate major concerns about administering higher doses of CLA to humans. One recent study of a 3.4 g/day CLA supplementation (CLA mixture) in humans found no effect on body composition and no adverse effects on a broad selection of traditional liver parameters and plasma lipids (64). However, some data suggest that CLA preparations may actually decrease fat deposition in adipose tissues. It can therefore be argued that efficacious doses (i.e., high enough to cause changes in body composition) may lead to higher blood lipid levels, succeeded by increased fat deposition in other tissues such as liver and/or muscle. Assuming that total energy intake and fat oxidation remain unchanged, this could possibly lead to some degree of lipotoxicity and insulin resistance.

There is increasing evidence that a high intake of trans fatty acids adversely affects the plasma lipid profile, increasing the LDL/HDL ratio, and may increase the risk of cardiovascular disease (65). CLAs should be classified structurally as trans fatty acids, and thus it could be argued that CLA may cause an increased cardiovascular risk. However, despite recent evidence that high levels of trans isomers of linoleic acid (identified as trans-C18:2, i.e., 9c,12t or 9t,12c fatty acids) in red blood cell membranes are associated with increased risk of primary cardiac arrest (66), further studies are required to evaluate whether CLA (or t10,c12) could exert similar effects.

Studies in rats and in vitro studies have suggested that CLA may decrease insulin resistance in a manner similar to that of the thiazolidinedione (TZD) class of insulin-sensitizer compounds, acting through stimulation of the peroxisome proliferator-activated receptor γ (67, 68). However, TZD drugs ameliorate insulin resistance by enhancing adipocyte differentiation and by depleting TG and FFAs from the blood while inducing body fat gain (69, 70), whereas CLA seems to induce a reduction in body fat in animal models. Thus, conditions with increased lipid supply to fat tissues may not necessarily lead to insulin resistance. In one study, transgenic mice with overexpression of phosphoenolpyruvate carboxykinase (a positive regulator of glyceroneogenesis in adipose tissue) developed obesity, but unlike other mice models, these obese mice did not develop insulin resistance (71). In contrast, transgenic mice with selective overexpression of lipoprotein lipase (a rate-controlling enzyme involved in triglyceride hydrolysis in liver and muscle) did not become obese but had an accumulation of intracellular fatty acid-derived metabolites in liver and muscle and subsequent insulin resistance in these tissues (72). Hence, the site of lipid deposition is an important determinant of the development of abnormal lipid metabolism.

While there is circumstantial evidence that CLA isomers may affect lipid metabolism and decrease body fat gain, suggestions that CLA supplementation may be used to treat type 2 diabetes (67, 68) may be overly optimistic, in particular in light of the significant decrease in insulin sensitivity found after t10,c12 supplementation for 12 weeks (60).

Furthermore, it has recently been shown that the quality of the commercially available CLA products is highly variable, in that the actual content of the various CLA isomers in the tablets varies substantially among the different preparations studied (73, 74). Finally, commercial CLA products (often CLA mixtures with high content of the c10,t12 isomer, together with other isomers) are usually considered dietary supplements. However, knowing that the natural dietary sources usually contain high levels of

the t9,c11 isomer and very low levels of the c10,t12 isomer, whether this is an appropriate classification should be reconsidered.

To evaluate the potential beneficial/adverse effects of CLA supplementation accurately, it is requisite that the isomer distributions in the CLA-preparations used be standardized.

Studies conducted to date have several shortcomings, such as small sample sizes, insufficient control of the isomeric composition of the CLA preparation, and imprecise assessment of body composition; insulin sensitivity was measured in only one study. When evaluating the outcome of a study, it should be emphasized that any beneficial changes in body weight/body composition should be associated with beneficial findings on type-2 diabetes and/or cardiovascular risk factors. Long-term, large-scale studies including better estimates of body composition (e.g., DXA scanning) and indices of insulin sensitivity and cardiovascular fitness (e.g., arterial compliance) are required before firm conclusions can be drawn.

In conclusion, the evidence from human short-term studies suggests that CLA supplementation does not reduce body weight and body fat or increase FFM. There is evidence that CLA isomers sold as dietary supplements have marked biological effects, but there is accumulating evidence that the CLA t10,c12 isomer may adversely influence human health by producing lipodystrophy and insulin resistance and by decreasing milk fat production in lactating women. Hence, CLA supplementation for humans should not be recommended before studies showing more positive findings are available.

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REFERENCES

1. Web Links, D. 2. 2002. (Accessed July 10, 2003 at http://www.npicenter.com/index.asp?action=NBViewDoc&DocumentID=2704)
2. Web Links, D. 2. 2002. (Accessed July 10, 2003 at http://www. cognis.com/framescout.html?/cognis/nutritionandhealth/home. htm).
3. Lawson, R. E., and A. R. Moss. 2002. G.DI. The role of dairy products in supplying conjugated linoleic acid to man's diet: a review. *Nutr. Res. Rev.* **14:** 153–172.
4. Bauman, D. E., and J. M. Griinari. 2000. Regulation and nutritional manipulation of milk fat: low-fat milk syndrome. *Livest. Prod. Sci.* **70:** 15–29.
5. Jiang, J., A. Wolk, and B. Vessby. 1999. Relation between the intake of milk fat and the occurrence of conjugated linoleic acid in human adipose tissue. *Am. J. Clin. Nutr.* **70:** 21–27.
6. Ritzenthaler, K. L., M. K. McGuire, R. Falen, T. D. Shultz, N. Dasgupta, and M. A. McGuire. 2001. Estimation of conjugated linoleic acid intake by written dietary assessment methodologies underestimates actual intake evaluated by food duplicate methodology. *J. Nutr.* **131:** 1548–1554.
7. Park, Y., M. K. McGuire, R. Behr, M. A. McGuire, M. A. Evans, and T. D. Shultz. 1999. High-fat dairy product consumption increases delta 9c,11t-18:2 (rumenic acid) and total lipid concentrations of human milk. *Lipids.* **34:** 543–549.
8. Pharma Nord ApS Denmark. 2002. Bio-C.L.A. 80. (Accessed November 27, 2003, at http://www.pharmanord.dk/product.htm?l=dk&id=cla).
9. Roche, H. M., E. Noone, A. Nugent, and M. J. Gibney. 2001. Conjugated linoleic acid: a novel therapeutic nutrient? *Nutr. Res. Rev.* **14:** 173–187.
10. West, D. B., J. P. Delany, P. M. Camet, F. Blohm, A. A. Truett, and J. Scimeca. 1998. Effects of conjugated linoleic acid on body fat and energy metabolism in the mouse. *Am. J. Physiol.* **275:** R667–R672.
11. Ostrowska, E., D. Suster, M. Muralitharan, R. F. Cross, B. J. Leury, D. E. Bauman, and F. R. Dunshea. 2003. Conjugated linoleic acid decreases fat accretion in pigs: evaluation by dual-energy X-ray absorptiometry. *Br. J. Nutr.* **89:** 219–229.
12. Park, Y., J. M. Storkson, K. J. Albright, W. Liu, and M. W. Pariza. 1999. Evidence that the trans-10,cis-12 isomer of conjugated linoleic acid induces body composition changes in mice. *Lipids.* **34:** 235–241.
13. Gavino, V. C., G. Gavino, M. J. Leblanc, and B. Tuchweber. 2000. An isomeric mixture of conjugated linoleic acids but not pure cis-9, trans-11-octadecadienoic acid affects body weight gain and plasma lipids in hamsters. *J. Nutr.* **130:** 27–29.
14. Ryder, J. W., C. P. Portocarrero, X. M. Song, L. Cui, M. Yu, T. Combatsiaris, D. Galuska, D. E. Bauman, D. M. Barbano, M. J. Charron, J. R. Zierath, and K. L. Houseknecht. 2001. Isomer-specific antidiabetic properties of conjugated linoleic acid. Improved glucose tolerance, skeletal muscle insulin action, and UCP-2 gene expression. *Diabetes.* **50:** 1149–1157.
15. Belury, M. A., S. Y. Moya-Camarena, K. L. Liu, and J. P. Vanden Heuvel. 1997. Dietary conjugated linoleic acid induces peroxisome-specific enzyme accumulation and ornithine decarboxylase activity in mouse liver. *J. Nutr. Biochem.* **8:** 579–584.
16. DeLany, J. P., F. Blohm, A. A. Truett, J. A. Scimeca, and D. B. West. 1999. Conjugated linoleic acid rapidly reduces body fat content in mice without affecting energy intake. *Am. J. Physiol.* **276:** R1172–R1179.
17. Belury, M. A., and A. Kempa-Steczko. 1997. Conjugated linoleic acid modulates hepatic lipid composition in mice. *Lipids.* **32:** 199–204.
18. Cherian, G., T. B. Holsonbake, M. P. Goeger, and R. Bildfell. 2002. Dietary CLA alters yolk and tissue FA composition and hepatic histopathology of laying hens. *Lipids.* **37:** 751–757.
19. de Deckere, E. A., J. M. van Amelsvoort, G. P. McNeill, and P. Jones. 1999. Effects of conjugated linoleic acid (CLA) isomers on lipid levels and peroxisome proliferation in the hamster. *Br. J. Nutr.* **82:** 309–317.
20. Yamasaki, M., K. Mansho, H. Mishima, G. Kimura, M. Sasaki, M. Kasai, H. Tachibana, and K. Yamada. 2000. Effect of dietary conjugated linoleic acid on lipid peroxidation and histological change in rat liver tissues. *J. Agric. Food Chem.* **48:** 6367–6371.
21. Jones, P. A., L. J. Lea, and R. U. Pendlington. 1999. Investigation of the potential of conjugated linoleic acid (Cla) to cause peroxisome proliferation in rats. *Food Chem. Toxicol.* **37:** 1119–1125.
22. Moya-Camarena, S. Y., J. P. Van den Heuvel, and M. A. Belury. 1999. Conjugated linoleic acid activates peroxisome proliferator-activated receptor alpha and beta subtypes but does not induce hepatic peroxisome proliferation in Sprague-Dawley rats. *Biochim. Biophys. Acta.* **1436:** 331–342.
23. Kritchevsky, D., S. A. Tepper, S. Wright, P. Tso, and S. K. Czarnecki. 2000. Influence of conjugated linoleic acid (CLA) on establishment and progression of atherosclerosis in rabbits. *J. Am. Coll. Nutr.* **19 (Suppl.):** 472–477.
24. Munday, J. S., K. G. Thompson, and K. A. James. 1999. Dietary conjugated linoleic acids promote fatty streak formation in the C57BL/6 mouse atherosclerosis model. *Br. J. Nutr.* **81:** 251–255.
25. Houseknecht, K. L., J. P. Vanden Heuvel, S. Y. Moya-Camarena, C. P. Portocarrero, L. W. Peck, K. P. Nickel, and M. A. Belury. 1998. Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat. *Biochem. Biophys. Res. Commun.* **244:** 678–682. [Erratum. 1998. *Biochem. Biophys. Res. Commun.* **247:** 911.].
26. Henriksen, E. J., M. K. Teachey, Z. C. Taylor, S. Jacob, A. Ptock, K. Kramer, and O. Hasselwander. 2003. Isomer-specific actions of conjugated linoleic acid on muscle glucose transport in the obese Zucker rat. *Am. J. Physiol. Endocrinol. Metab.* **285:** E98–E105.
27. McCarthy-Beckett, D. O. 2002. Dietary supplementation with conjugated linoleic acid does not improve nutritional status of tumor-bearing rats. *Res. Nurs. Health.* **25:** 49–57.
28. Bouthegourd, J. C., P. C. Even, D. Gripois, B. Tiffon, M. F. Blouquit, S. Roseau, C. Lutton, D. Tome, and J. C. Martin. 2002. A CLA mixture prevents body triglyceride accumulation without affecting energy expenditure in Syrian hamsters. *J. Nutr.* **132:** 2682–2689.

29. Roche, H. M., E. Noone, C. Sewte, S. McBennett, D. Savage, M. J. Gibney, S. O'Rahilly, and A. J. Vidal-Puig. 2002. Isomer-dependent metabolic effects of conjugated linoleic acid: insights from molecular markers sterol regulatory element-binding protein-1c and LXRalpha. *Diabetes.* **51:** 2037–2044.
30. Tsuboyama-Kasaoka, N., M. Takahashi, K. Tanemura, H. J. Kim, T. Tange, H. Okuyama, M. Kasai, S. Ikemoto, and O. Ezaki. 2000. Conjugated linoleic acid supplementation reduces adipose tissue by apoptosis and develops lipodystrophy in mice. *Diabetes.* **49:** 1534–1542.
31. Tsuboyama-Kasaoka, N., H. Miyazaki, S. Kasaoka, and O. Ezaki. 2003. Increasing the amount of fat in a conjugated linoleic acid-supplemented diet reduces lipodystrophy in mice. *J. Nutr.* **133:** 1793–1799.
32. Clement, L., H. Poirier, I. Niot, V. Bocher, M. Guerre-Millo, S. Krief, B. Staels, and P. Besnard. 2002. Dietary trans-10,cis-12 conjugated linoleic acid induces hyperinsulinemia and fatty liver in the mouse. *J. Lipid Res.* **43:** 1400–1409.
33. Degrace, P., L. Demizieux, J. Gresti, J. M. Chardigny, J. L. Sebedio, and P. Clouet. 2003. Association of liver steatosis with lipid oversecretion and hypotriglyceridaemia in C57BL/6j mice fed trans-10,cis-12-linoleic acid. *FEBS Lett.* **546:** 335–339.
34. Takahashi, Y., M. Kushiro, K. Shinohara, and T. Ide. 2003. Activity and mRNA levels of enzymes involved in hepatic fatty acid synthesis and oxidation in mice fed conjugated linoleic acid. *Biochim. Biophys. Acta.* **1631:** 265–273.
35. Smith, S. B., T. S. Hively, G. M. Cortese, J. J. Han, K. Y. Chung, P. Castenada, C. D. Gilbert, V. L. Adams, and H. J. Mersmann. 2002. Conjugated linoleic acid depresses the delta9 desaturase index and stearoyl coenzyme A desaturase enzyme activity in porcine subcutaneous adipose tissue. *J. Anim. Sci.* **80:** 2110–2115.
36. Lee, K. N., M. W. Pariza, and J. M. Ntambi. 1998. Conjugated linoleic acid decreases hepatic stearoyl-CoA desaturase mRNA expression. *Biochem. Biophys. Res. Commun.* **248:** 817–821.
37. Choi, Y., Y. C. Kim, Y. B. Han, Y. Park, M. W. Pariza, and J. M. Ntambi. 2000. The trans-10,cis-12 isomer of conjugated linoleic acid downregulates stearoyl-CoA desaturase 1 gene expression in 3T3–L1 adipocytes. *J. Nutr.* **130:** 1920–1924.
38. Baumgard, L. H., B. A. Corl, D. A. Dwyer, A. Saebo, and D. E. Bauman. 2000. Identification of the conjugated linoleic acid isomer that inhibits milk fat synthesis. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **278:** R179–R184.
39. Baumgard, L. H., E. Matitashvili, B. A. Corl, D. A. Dwyer, and D. E. Bauman. 2002. Trans-10, cis-12 conjugated linoleic acid decreases lipogenic rates and expression of genes involved in milk lipid synthesis in dairy cows. *J. Dairy Sci.* **85:** 2155–2163.
40. Piperova, L. S., B. B. Teter, I. Bruckental, J. Sampugna, S. E. Mills, M. P. Yurawecz, J. Fritsche, K. Ku, and R. A. Erdman. 2000. Mammary lipogenic enzyme activity, trans fatty acids and conjugated linoleic acids are altered in lactating dairy cows fed a milk fat-depressing diet. *J. Nutr.* **130:** 2568–2574.
41. Peterson, D. G., L. H. Baumgard, and D. E. Bauman. 2002. Short communication: milk fat response to low doses of tran-10, cis-12 conjugated linoleic acid (CLA). *J. Dairy Sci.* **85:** 1764–1766.
42. Baumgard, L. H., J. K. Sangster, and D. E. Bauman. 2001. Milk fat synthesis in dairy cows is progressively reduced by increasing supplemental amounts of trans-10, cis-12 conjugated linoleic acid (CLA). *J. Nutr.* **131:** 1764–1769.
43. Bee, G. 2000. Dietary conjugated linoleic acid consumption during pregnancy and lactation influences growth and tissue composition in weaned pigs. *J. Nutr.* **130:** 2981–2989.
44. Masters, N., M. A. McGuire, K. A. Beerman, N. Dasgupta, and M. K. McGuire. 2002. Maternal supplementation with CLA decreases milk fat in humans. *Lipids.* **37:** 133–138.
45. Thompson, H., Z. Zhu, S. Banni, K. Darcy, T. Loftus, and C. Ip. 1997. Morphological and biochemical status of the mammary gland as influenced by conjugated linoleic acid: implication for a reduction in mammary cancer risk. *Cancer Res.* **57:** 5067–5072.
46. Raes, K., G. Huyghebaert, S. De Smet, L. Nollet, S. Arnouts, and D. Demeyer. 2002. The deposition of conjugated linoleic acids in eggs of laying hens fed diets varying in fat level and fatty acid profile. *J. Nutr.* **132:** 182–189.
47. Aydin, R., M. W. Pariza, and M. E. Cook. 2001. Olive oil prevents the adverse effects of dietary conjugated linoleic acid on chick hatchability and egg quality. *J. Nutr.* **131:** 800–806.
48. Ntambi, J. M., M. Miyazaki, J. P. Stoehr, H. Lan, C. M. Kendziorski, B. S. Yandell, Y. Song, P. Cohen, J. M. Friedman, and A. D. Attie. 2002. Loss of stearoyl-CoA desaturase-1 function protects mice against adiposity. *Proc. Natl. Acad. Sci. USA.* **99:** 11482–11486.
49. West, D. B., F. Y. Blohm, A. A. Truett, and J. P. DeLany. 2000. Conjugated linoleic acid persistently increases total energy expenditure in AKR/J mice without increasing uncoupling protein gene expression. *J. Nutr.* **130:** 2471–2477.
50. Hargrave, K. M., C. Li, B. J. Meyer, S. D. Kachman, D. L. Hartzell, M. A. Della-Fera, J. L. Miner, and C. A. Baile. 2002. Adipose depletion and apoptosis induced by trans-10, cis-12 conjugated linoleic acid in mice. *Obes. Res.* **10:** 1284–1290.
51. Brown, J. M., Y. D. Halvorsen, Y. R. Lea-Currie, C. Geigerman, and M. McIntosh. 2001. Trans-10, cis-12, but not cis-9, trans-11, conjugated linoleic acid attenuates lipogenesis in primary cultures of stromal vascular cells from human adipose tissue. *J. Nutr.* **131:** 2316–2321.
52. Brown, J. M., M. S. Boysen, S. S. Jensen, R. F. Morrison, J. Storkson, R. Lea-Currie, M. Pariza, S. Mandrup, and M. K. McIntosh. 2003. Isomer-specific regulation of metabolism and PPAR{gamma} signaling by CLA in human preadipocytes. *J. Lipid Res.* **44:** 1287–1300.
53. Kang, K., W. Liu, K. J. Albright, Y. Park, and M. W. Pariza. 2003. Trans-10,cis-12 CLA inhibits differentiation of 3T3-L1 adipocytes and decreases PPAR gamma expression. *Biochem. Biophys. Res. Commun.* **303:** 795–799.
54. Granlund, L., L. K. Juvet, J. I. Pedersen, and H. I. Nebb. 2003. Trans10, cis12 conjugated linoleic acid prevents triacylglycerol accumulation in adipocytes by acting as a PPARgamma modulator. *J. Lipid Res.* **44:** 1441–1452
55. Azain, M. J., D. B. Hausman, M. B. Sisk, W. P. Flatt, and D. E. Jewell. 2000. Dietary conjugated linoleic acid reduces rat adipose tissue cell size rather than cell number. *J. Nutr.* **130:** 1548–1554.
56. Bouthegourd, J. C., J. C. Martin, D. Gripois, S. Roseau, M. F. Blouquit, P. C. Even, and A. Quignard Boulange. 2002. Efficacy of dietary CLA and CLA plus Guarana (ADI Pill) on body adiposity, and adipocytes cell number and size (part 1, March 20, 2002). *FASEB J.* **16:** A370.
57. Xu, X., and M. W. Pariza. 2002. Dietary conjugated linoleic acid reduces mouse adipocyte size and number (part 1, March 20, 2002). *FASEB J.* **16:** A370.
58. Atkinson, R. L. 2002. Effects of CLA in Obese Subjects on a Weight Loss Diet: Wisconsin Data (Abstract). NIH seminar. Perspectives on Conjugated Linoleic Acid Research: Current Status and Future Directions. Bethesda, MD.
59. Kamphuis, M. M., M. P. Lejeune, W. H. Saris, and M. S. Westerterp-Plantenga. 2003. The effect of conjugated linoleic acid supplementation after weight loss on body weight regain, body composition, and resting metabolic rate in overweight subjects. *Int. J. Obes. Relat. Metab. Disord.* **27:** 840–847.
60. Riserus, U., P. Arner, K. Brismar, and B. Vessby. 2002. Treatment with dietary trans10cis12 conjugated linoleic acid causes isomer-specific insulin resistance in obese men with the metabolic syndrome. *Diabetes Care.* **25:** 1516–1521.
61. Riserus, U., S. Basu, S. Jovinge, G. N. Fredrikson, J. Arnlov, and B. Vessby. 2002. Supplementation with conjugated linoleic acid causes isomer-dependent oxidative stress and elevated C-reactive protein: a potential link to fatty acid-induced insulin resistance. *Circulation.* **106:** 1925–1929.
62. Basu, S., A. Smedman, and B. Vessby. 2000. Conjugated linoleic acid induces lipid peroxidation in humans. *FEBS Lett.* **468:** 33–36.
63. Atkinson, R. L. 1999. Chapter 27. Conjugated linoleic acid for altering body composition and treating obesity. *In* Advances in Conjugated Linoleic Acid Research. M. P. Yurawecz, M. M. Mossoba, J. K. G. Kramer, M. W. Pariza, and G. J. Nelson, editors. American Oil Chemists' Society Press, Champaign, IL. 348–353.
64. Berven, G., A. Bye, O. Hals, H. Blankson, H. Fagertun, E. Thom, J. Wadstein, and O. Gudmundsen. 2000. Safety of conjugated linoleic acid (CLA) in overweight or obese human volunteers. *Eur. J. Lipid Sci. Technol.* **102:** 455–462.
65. Ascherio, A., M. B. Katan, P. L. Zock, M. J. Stampfer, and W. C. Willett. 1999. Trans fatty acids and coronary heart disease. *N. Engl. J. Med.* **340:** 1994–1998.
66. Lemaitre, R. N., I. B. King, T. E. Raghunathan, R. M. Pearce, S. Weinmann, R. H. Knopp, M. K. Copass, L. A. Cobb, and D. S. Siscovick. 2002. Cell membrane trans-fatty acids and the risk of primary cardiac arrest. *Circulation.* **105:** 697–701.
67. Belury, M. A., and J. P. Vanden Heuvel. 1999. Chapter 32. Modulation of diabetes by conjugated linoleic acid. *In* Advances in Conjugated Linoleic Acid Research. M. P. Yurawecz, M. M. Mossoba,

J. K. G. Kramer, M. W. Pariza, and G. J. Nelson, editors. American Oil Chemists' Society Press, Champaign, IL. 405–410.
68. Pariza, M. W. 2002. Conjugated linoleic acid may be useful in treating diabetes by controlling body fat and weight gain. *Diabetes Technol. Ther.* **4:** 335–338.
69. Oakes, N. D., P. G. Thalen, S. M. Jacinto, and B. Ljung. 2001. Thiazolidinediones increase plasma-adipose tissue FFA exchange capacity and enhance insulin-mediated control of systemic FFA availability. *Diabetes.* **50:** 1158–1165.
70. Larsen, T. M., S. Toubro, and A. Astrup. 2003. PPARgamma agonists in the treatment of type II diabetes: is increased fatness commensurate with long-term efficacy? *Int. J. Obes. Relat. Metab. Disord.* **27:** 147–161.
71. Franckhauser, S., S. Munoz, A. Pujol, A. Casellas, E. Riu, P. Otaegui, B. Su, and F. Bosch. 2002. Increased fatty acid re-esterification by PEPCK overexpression in adipose tissue leads to obesity without insulin resistance. *Diabetes.* **51:** 624–630.
72. Kim, J. K., J. J. Fillmore, Y. Chen, C. Yu, I. K. Moore, M. Pypaert, E. P. Lutz, Y. Kako, W. Velez-Carrasco, I. J. Goldberg, J. L. Breslow, and G. I. Shulman. 2001. Tissue-specific overexpression of lipoprotein lipase causes tissue-specific insulin resistance. *Proc. Natl. Acad. Sci. USA.* **98:** 7522–7527.
73. Adlof, R. O., L. C. Copes, and E. L. Walter. 2001. Changes in conjugated linoleic acid composition within samples obtained from a single source. *Lipids.* **36:** 315–317.
74. Gaullier, J. M., G. Berven, H. Blankson, and O. Gudmundsen. 2002. Clinical trial results support a preference for using CLA preparations enriched with two isomers rather than four isomers in human studies. *Lipids.* **37:** 1019–1025.
75. Zambell, K. L., N. L. Keim, M. D. Van Loan, B. Gale, P. Benito, D. S. Kelley, and G. J. Nelson. 2000. Conjugated linoleic acid supplementation in humans: effects on body composition and energy expenditure. *Lipids.* **35:** 777–782.
76. Benito, P., G. J. Nelson, D. S. Kelley, G. Bartolini, P. C. Schmidt, and V. Simon. 2001. The effect of conjugated linoleic acid on plasma lipoproteins and tissue fatty acid composition in humans. *Lipids.* **36:** 229–236. [Erratum. 2001. *Lipids.* **36:** 857.]
77. Thom, E., J. Wadstein, and O. Gudmundsen. 2001. Conjugated linoleic acid reduces body fat in healthy exercising humans. *J. Int. Med. Res.* **29:** 392–396.
78. Smedman, A., and B. Vessby. 2001. Conjugated linoleic acid supplementation in humans—metabolic effects. *Lipids.* **36:** 773–781.
79. Mougios, V., A. Matsakas, A. Petridou, S. Ring, A. Sagredos, A. Melissopoulou, N. Tsigilis, and M. Nikolaidis. 2001. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. *J. Nutr. Biochem.* **12:** 585–594.
80. Blankson, H., J. A. Stakkestad, H. Fagertun, E. Thom, J. Wadstein, and O. Gudmundsen. 2000. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J. Nutr.* **130:** 2943–2948.
81. Riserus, U., L. Berglund, and B. Vessby. 2001. Conjugated linoleic acid (CLA) reduced abdominal adipose tissue in obese middle-aged men with signs of the metabolic syndrome: a randomised controlled trial. *Int. J. Obes. Relat. Metab. Disord.* **25:** 1129–1135.
82. Kreider, R. B., M. P. Ferreira, M. Greenwood, M. Wilson, and A. L. Almada. 2002. Effects of conjugated linoleic acid supplementation during resistance training on body composition, bone density, strength, and selected hematological markers. *J. Strength Cond. Res.* **16:** 325–334.
83. Noone, E. J., H. M. Roche, A. P. Nugent, and M. J. Gibney. 2002. The effect of dietary supplementation using isomeric blends of conjugated linoleic acid on lipid metabolism in healthy human subjects. *Br. J. Nutr.* **88:** 243–251.
84. Belury, M. A., A. Mahon, and S. Banni. 2003. The conjugated linoleic acid (CLA) isomer, t10c12-CLA, is inversely associated with changes in body weight and serum leptin in subjects with type 2 diabetes mellitus. *J. Nutr.* **133:** 257S–260S.