

Efficacy and safety of dietary supplements containing Conjugated Linoleic Acid (CLA) for the treatment of obesity – evidence from animal and human studies.

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Abbreviations: CLA, Conjugated Linoleic Acid; c9,t11, cis9, trans11; t10,c12, trans10, cis12, TG, triglycerides; FM, fat mass; FFM, fat free mass; SCD1, stearoyl-CoA desaturase 1; MUFA, monounsaturated fatty acids; SFA, saturated fatty acids; DXA, dual-energy x-ray absorptiometry;

Abstract

Dietary supplements containing 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 t10,c12 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.

Supplementary key words: Obesity, fat mass, fat free mass, insulin resistance, t10,c12, clinical trial, human

Dietary sources of CLA

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 U.S. 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 Japan¹. 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) isomers².

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 approximately 150-200 mg per day^{5,6}, and consumption of a diet rich in high-fat animal products can increase the daily intake to at least

650mg/day⁷. In comparison, CLA dietary supplements marketed for weight loss purposes constitute an intake of 3-4 grams/day⁸. Dietary CLA is recovered in human milk, serum lipids, and in adipose tissue. A significant 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 tissue⁵.

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 and a relative increase in lean body mass (reviewed by Roche et al.)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 to placebo in mice¹⁰. Furthermore, it has been shown, using accurate dual energy x-ray scanning methods, that CLA dose-dependently decreases fat accretion in growing animals in the pigs¹¹.

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, though this was partly a result of a decreased energy intake¹⁴.

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 liver¹⁵. In mice and chickens CLA supplementation has been associated with increases in liver weight, possibly as a result of triglyceride accumulation¹⁶⁻¹⁸.

In hamsters the t10,c12 isomer causes enlargement of both liver and kidney, despite a lower body weight¹⁹. In rats, however, CLA does not act as a classical peroxisome proliferator despite moderate increases in liver weight²⁰⁻²².

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-cholesterol²³. However, others have found

an increase in arterial fatty streak formation in c57BL/6 mice after CLA supplementation²⁴.

Normalization of impaired glucose tolerance (using a glucose tolerance test) has been shown in Zucker rats fed a mixture of CLA²⁵, and the trans-10,cis-12 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 rats²⁷.

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 FFA²⁹. 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, though this was associated with the development of insulin resistance resulting in a metabolic state resembling lipotrophic diabetes^{30,31}. Similar observations have been reported by other researchers, showing that mice fed purified t10,c12 CLA or CLA mixtures develop hyperinsulinaemia 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* studies³⁵. SCD1 desaturates saturated fatty acids into monounsaturated fatty acids, resulting in a higher delta-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 ratios³⁶. Similarly, t10,c12 decreased SCD1 mRNA expression and activity in 3T3-L1 adipocytes, and resulted in cells with smaller lipid droplets³⁷. 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 (MFD), which occurs when cows are fed diets containing large amounts of unsaturated oils such as plant and fish oils⁴. 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 production⁴⁰⁻⁴². 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 synthesis³⁹. It has also been observed recently that CLA supplements may decrease mammary milk fat production in several other animal models, including mice, pigs⁴³ and humans⁴⁴. Early studies found that CLA significantly reduced the density of the

branching mammary epithelium in rats⁴⁵. 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 content⁴⁶ in hens' eggs, causing yolk hardening and inducing chick embryonic mortality⁴⁷. However, in rats no effect 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, reduced levels of plasma insulin and leptin, but developed signs of hepatic steatosis when fed a high fat diet⁴⁸. In summary, though 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 mice¹⁰ and rats¹⁴, yet CLA seems to have effects on body composition in mice independent of changes in energy intake⁵⁰.

Despite these suggestions that an increased energy expenditure and a decreased energy intake occurs 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 gamma, which is a strong inducer of adipocyte differentiation^{53,54}. Several *in vivo* studies support these findings. Sprague-Dawley rats fed have been seen to have a decreased body weight, with the reduced fat mass apparently accomplished by a decrease of adipocyte cell size, rather than cell number, when fed a CLA mixture⁵⁵. 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, whilst 7 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 et al.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 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 (BW) was found in any of the 13 studies. Fat mass (FM) was assessed in 10 studies and 3 of these found a decrease in fat mass (FM). FFM was assessed in 7 studies, but only 1 of these studies found a slight increase in body fat free mass⁵⁹ (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 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 a 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-alpha and 15-keto-dihydro-PGF₂-alpha, which are in vivo markers of non-enzymatic and enzymatic lipid peroxidation and oxidative stress, processes which may contribute to insulin resistance⁶².

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 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. 1/10 of the dose given to pigs and often only ~1/50 of that given to rats pr. kg bodyweight⁶³. 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 lipids⁶⁴. 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 remains unchanged this may 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 LDL/HDL ratio, and may increase the risk of cardiovascular disease⁶⁵.

Conjugated linoleic acids should be classified structurally as trans fatty acids, and thus it could therefore 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 arrest⁶⁶, 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 gamma^{67,68}. However, TZD

drugs ameliorate insulin resistance by enhancing adipocyte differentiation and by depleting TG and FFA's from the blood whilst 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 over expression of phosphoenolpyruvate carboxykinase (PEPCK, a positive regulator of glyceroneogenesis) in adipose tissue developed obesity, but unlike other mice models these obese mice did not develop insulin resistance⁷¹. In contrast, transgenic mice with selective over expression of lipoprotein lipase (LPL, 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 tissues⁷². 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 the light of the significant decrease in insulin sensitivity found after t10,c12 supplementation for 12 weeks⁶⁰.

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 between the different preparations studied^{73,74}. Finally, commercial CLA products (often CLA mixtures with high contents 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, it

should be reconsidered whether this is an appropriate classification.

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 so far have several shortcomings such as small sample sizes, insufficient control

of the isomeric composition of the CLA preparation, imprecise assessment of body composition,

and 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 fat free mass. 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.

Table 1 Human Intervention Studies of Conjugated Linoleic Acid

Study subjects (women/men)	Intervention period & dose	CLA Composition & provider	Placebo Supplementation	Author conclusion	Blood lipids or other [#]	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 TM , 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 Zambell 2000 ⁷⁶ Benito 2001
20 subjects (10/10) BMI ~23	12 weeks 1.8g/day	60% CLA t10,c12: ~50%; c9,t11: ~50% Tonalin TM , Natural ASA	Hydrogel (1.8g/day)	No effect on BW. Decrease in FM	NA	FM determined by NIR. FFM NA.	⁷⁷ Thom 2001
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..	⁷⁸ Smedman 2001 ⁶² Basu 2000
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 <u>FM</u> .	Decrease in HDL	FM determined by skin fold thickness. FFM NA.	⁷⁹ Mougios 2001
52 subjects (35/17) BMI~29	12 weeks 1.7-6.8 g/day	75 % CLA t10,c12:~50%; c9,t11:~50% Tonalin TM , Natural ASA	Olive oil (9g/day)	No effect on BW or FFM. Decrease in FM <u>FFM</u> (CLA groups compared to placebo).	No change in lipids	FM and FFM determined by DXA.	⁸⁰ Blankson 2000

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 ¹⁶ Riserus 2001
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Table 1 cont. Human Intervention Studies of Conjugated Linoleic Acid

Study subjects (women/men)	Intervention period & dose	CLA Composition & provider	Placebo Supplementation	Author conclusion	Blood lipids or other [#]	Comments	Reference
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 decrease HDL, increase glucose and CRP and decrease insulin sensitivity	FM and FFM determined by bioimpedance.	⁶⁰ Riserus 2002 ⁶¹ Riserus 2002
60 subjects (NA) BMI~30	12 weeks 3.4 g/day	75% CLA, Composition: NA Tonalin TM 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 Berven 2000
23 subjects (NA)	28 days 6 g/day	65% CLA Composition = Reference ⁷⁵ Tonalin TM , Pharmanutrients	Olive oil (9g/day)	No effect on BW, FM or FFM.	NA	Exercise study. FM and FFM determined by DXA.	⁸² Kreider 2002
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 (3g/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 Noone 2002

Table 1 cont. Human Intervention Studies of Conjugated Linoleic Acid

Study subjects (women/men)	Intervention period & dose	CLA Composition & provider	Placebo Supplementation	Author conclusion	Blood lipids or other [#]	Comments	Reference
21 subjects (NA)	8 weeks 8 g/day	76% CLA t10,c12:39%; c9,t11:37% Pharmanutrients Inc.	Safflower oil (8g/day)	No effect on BW.	Decrease in fasting glucose.	FM and FFM NA.	⁸⁴ Belury 2003
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.	⁶³ Atkinson 1999 (Book) ⁵⁸ Atkinson 2002 (Abstract)
56 subjects (26/28) 25<BMI<30	13 weeks 1.8 or 3.6 g/day	Tonalin TM CLA 75 % TG 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 Kamphuis 2003

[#] Significance level for difference between CLA and placebo groups set at P<0.05 NA = Not Available.

BW, body weight; FFM, fat free mass; FM, Fat mass; DXA, Dual energy x-ray absorptiometry; NIR, Near Infrared technique; TG, triglycerides;

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