Ingredient Spotlight: Conjugated Linoleic Acid

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CLA, or conjugated linoleic acid, is a mixture of 28 isomers-compounds with the same molecular formulas but different structural formulas. CLA is a naturally occurring fatty acid most commonly found in dairy and in beef from ruminant animals able to synthesize it from the omega-6 fatty acid linoleic acid. Average intake of CLA by humans is estimated at around 130 to 440 mg/day.(1) The largest percentage of CLA in the diet (about 90%) is composed of the cis-9-trans-11 isomer (c9,t11).(2)

CLA was discovered back in the late 1980s when Michael Pariza, PhD, and colleagues at the University of Wisconsin-Madison were investigating the carcinogenic properties of grilled beef.(3) To the surprise of Dr. Pariza, the fatty acids in the grilled beef exhibited significant anticarcinogenic, rather than procarcinogenic, properties. Since this discovery, CLA has been widely investigated and shown to have significant biological effects in animal models, cell culture, and humans. Most of the studies are related to CLA’s anticarcinogenic and antiadipogenic effects, and its ability to influence body weight, body fat, and lean body mass.(4)

Biological Effects of CLA

Carcinogenesis

Many reports using in vivo and in vitro models have shown that CLA suppresses the development of multistage carcinogenesis at different sites. CLA has been reported to affect initiation, promotion, and metastasis of breast, gastrointestinal, and prostate cancers in experimental animal models.(5,6) To date, there have only been a few case-control studies that have examined the relationship between CLA intake and cancer. Larsson and colleagues reported an inverse relationship between CLA intake and risk of colorectal cancer.(7) Significantly lower dietary intake and blood levels of CLA were found in individuals with breast cancer compared to those without breast cancer among postmenopausal women.(8) Two other studies showed no significant relationship between intake or adipose tissue concentration of CLA, and risk of breast cancer.(9,10) Several different cell lines have been studied as well as various animal models. Many of these studies show a benefit of the c9,t11 isomer of CLA in mammary cancer, but less conclusive results in gastrointestinal and prostate cancer. The antitumorogenic effects of purified c9,t11-CLA and t10,c12-CLA isomers (as found in many CLA supplements) seem to depend on tumor type as well as tumor location. T10,c12-CLA tends to reduce tumorigenesis in most cell types, but has also been shown to increase it in others. Some researchers suggest that the effects of CLA could be mediated through its ability to influence angiogenesis (growth of new blood vessels) via the reduction of VEGF (Vascular Endothelial Growth Factor) and bFGF (basic Fibroblast Growth Factor), both of which are involved in the angiogenic process, with bFGF also having an effect on DNA synthesis and cell proliferation.(11,12) Other mechanisms include CLA’s effects on COX-2 and 5-LOX activity, both of which influence cell growth, inflammation, induction of apoptosis (cell death), as well as cell proliferation.(13-15)

Also, the amount of CLA used in most animal and cell studies would be equivalent to about 5 to 50 g/day for an average 150-lb individual. This amount of CLA would only be attainable with supplements. More controlled human studies are needed to determine the risk:benefit ratio of using CLA as an adjuvant or chemopreventive therapy in humans.
CLA and Body Composition

Several studies have investigated the relationship between CLA and body composition, particularly body fat and lean body mass. Many of the CLA isomers have been studied, but the most potent with regard to impact on body composition seems to be the t10,c12 isomer. (16) Riserus and colleagues found that when given alone, t10,c12 causes an increase in insulin resistance in men with metabolic syndrome, which was offset by a 50:50 mixture of t10,c12:c9,t11-CLA. (17) This combination has been shown to reduce fat mass and increase lean body mass (fat-free mass) in animals.

The effect of CLA on fat mass is highly dependent upon length of time used, dose, and species, with mice showing the greatest response among lab animals. (4) Numerous clinical studies have been completed to date, with several demonstrating a positive effect of CLA on body fat and lean body mass. Most of these studies have used the 50:50 mixture t10,c12:c9,t11 of CLA.

Short-Term Studies

A 2001 study conducted at Uppsala University in Sweden showed that 4.2 g of CLA for four weeks significantly reduced abdominal fat (measured by sagittal abdominal diameter measure of visceral fat) in obese men with metabolic syndrome. (17) CLA (6.4 g/day for 12 weeks) significantly increased lean body mass in healthy obese humans compared with controls. (18) A six-month study by Gaultier and colleagues demonstrated the ability of CLA to increase lean body mass and decrease body fat mass and waist-to-hip ratio. (19) Researchers at the University of Wisconsin-Madison evaluated the effects of 3.2 g/day of CLA on overweight adults. CLA was effective in reducing body fat and, in addition, helped prevent the seasonal gain of weight that occurred in control subjects. (20) Recently, a seven-month study evaluated the effects of CLA in prepubertal children (53 completed the study) ages 6 to 10 years who were overweight or obese, but otherwise healthy. Compared to placebo, 3 g/day of CLA significantly reduced total body fat gain and regionally reduced the percentage of abdominal fat and peripheral fat as a percentage of total body weight. (21)

Long-Term Studies

CLA may be useful for long-term weight management and support of a healthy body composition by helping reduce or prevent the common gain of weight that occurs during the holiday season—an issue for many people who struggle with weight management. (20) To investigate the long-term effects of CLA on body fat mass and lean body mass, Gudmundsen and colleagues evaluated the effects of one year of CLA supplementation in healthy overweight adults consuming an ad libitum (unrestricted) diet with no specific lifestyle restrictions. Compared to placebo, CLA supplementation (4.5 g/day for 12 months) significantly reduced body fat mass and increased lean body mass. (22) In an extension of this study, 134 of the 157 patients who concluded the 12-month study were included in an open study (all groups received CLA) for an additional 12 months (total of 24 months). There was a significant reduction in body weight and body fat in the individuals who were formerly part of the placebo group. No body fat, body weight, or lean body mass changes occurred in individuals who responded during the initial 12-month study. The long-term maintenance of body fat mass, body weight, and lean body mass suggests that CLA may be beneficial in preventing the weight regain commonly associated with the “yo-yo” effect observed with most diet plans. (23)

Potential Mechanisms

Despite the positive effects of CLA on body fat and lean body mass, the mechanism of action has yet to be elucidated. There have been some proposed mechanisms, tested mainly in animals and cell culture. The activity of several enzymes involved in lipogenesis lipoprotein lipase (LPL), acetyl-CoA carboxylase (ACC), and stearoyl-CoA desaturase (SCD) is decreased by 50:50 mixture c9,t11:t10,c12 isomers of CLA (found in most CLA supplements) or by t10,c12 alone. (24-26) Other potential mechanisms include increased fat oxidation, decreased adipocyte size, and decreased energy intake. (27-29) Short- and long-term studies in healthy, overweight, obese, sedentary, and active individuals have demonstrated beneficial effects of CLA in reducing body fat and increasing lean body mass. Results seen in human studies have not been as dramatic as those of animal studies. One explanation for
this is that the dosage used in animals is much higher than that used in human studies. More long-term studies, possibly using higher doses of CLA, and combined with exercise and dietary changes, might provide even more substantial results. The mechanisms of action still need to be worked out, and in time, further research should help provide a greater understanding of the true versatility of this compound.

Conclusions

The results with regard to changes in body fat and lean body mass are even more impressive in that these results were achieved without any changes in diet and level of physical activity. Despite the extensive amount of research on CLA, more long-term human trials are needed to determine the overall safety and efficacy of CLA as a tool to help support the fight against obesity. More studies, especially those combined with a healthy eating and exercise plan, will help us determine with greater accuracy the true value as well as the specific mechanisms whereby CLA exerts its effects on body fat and lean body mass.

Many scientists believe that the current epidemic of obesity and type 2 diabetes will continue to get worse. Currently, one in three Americans are obese, and by the year 2050, one in three will be diagnosed with type 2 diabetes. With the lack of safe and effective pharmaceutical agents for weight management, we need to more rigorously investigate natural therapies that can be used in conjunction with lifestyle changes.

More human studies are also needed to help us fully understand the potential of CLA as a chemopreventive agent. These studies will allow scientists to elucidate mechanisms of action, effective dose, efficacy, and safety in specific types of cancer. Overall, the future of CLA looks bright.

References


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