Conjugated Linoleic Acid: A Fatty Acid With Health Benefits

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During the last few decades, conjugated linoleic acid has attracted interest from researchers and consumers for its potential health benefits. CLA is a polyunsaturated fatty acid with the same chemical formula as the omega-6, 18 carbon fatty acid linoleic acid. However, the word "conjugated" in its name refers to the fact that CLAs have a different structural arrangement from linoleic acid. CLA is composed of a group of 28 isomers, or forms of 18 carbon polyunsaturated fatty acids, that are defined by conjugated double bonds in two different geometric or positional locations of each molecule (fig. 1).

The CLA molecules can be derived from linoleic acid, also referred to as octadecadienoic acid. Small quantities of CLS can naturally be found in beef and dairy products. Of these isomers, the most studied and bioavailable isomers are *cis*-9,*trans*-11 (abbreviated c9,t11) CLA (80%-90% of the total CLA isomers) and *trans*-10,*cis*-12 (abbreviated t10,c12) CLA (3%-5% of the total CLA isomers) within the naturally occurring forms. The presence of one double bond in the trans configuration means that chemically, CLAs are considered trans fatty acids (Badawy et al. 2023; den Hartigh 2019). However, the presence of a cis double bond means that they are also considered cis fatty acids. Linoleic acid, on the other hand, is only a cis fatty acid (fig. 1). The FDA's ruling in 2008 did not result in designation of CLA as either a cis- or trans-fat (FDA 2008).

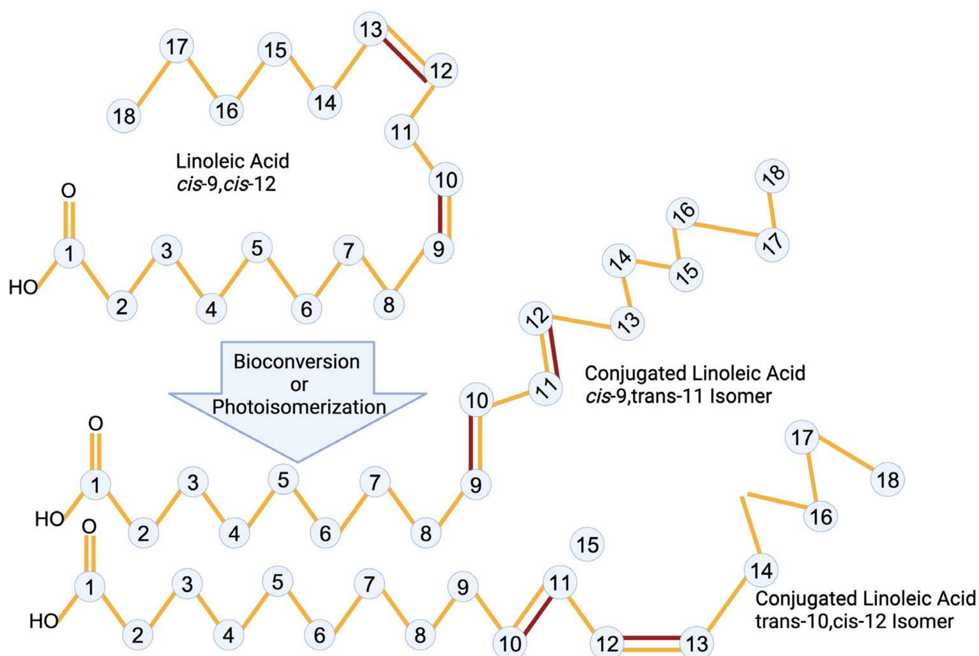

Figure 1. Linoleic and conjugated linoleic acid isomers. The cis and trans bonds for each are highlighted in red, and the carbon molecules connected by single chemical bonds are indicated by orange balls and lines. Note that linoleic acid is an omega-6 fatty acid when the carbons are counted using the omega method. Linoleic acid, 18:2 (omega 6) can also be called *cis*-9,*cis*-12-octadecadienoic acid. Conjugated linoleic acid, *cis*-9,*trans*-11-octadecadienoic acid and conjugated linoleic acid, *trans*-10,*cis*-12-octadecadienoic acid are shown. Created with BioRender, Good, D. (2025) https://BioRender.com/u39g820.

Natural and Enhanced Sources of CLA

CLA can be obtained in the human diet using natural food sources or food sources that are enhanced with added CLA. In addition, CLA is found in supplements in the form of pills, powders, and emulsions. The average human diet contains 15-174 mg of CLA from natural food sources per day without supplementation. As diets vary across countries, the estimated average daily intake of CLA also varies from one country to another: 36 mg in Brazil, 37 mg in Japan, 35-43 mg in Germany, 97.5 mg in the UK, and 151-212 mg in the U.S. (Putera et al. 2023).

Natural Sources of CLA

Naturally occurring CLA is a byproduct of the conversion of unsaturated fatty acids to saturated fatty acids by rumen bacteria in ruminant (or grazing) animals. The fatty acids are then absorbed into the bloodstream and deposited in fat and other tissues. Dairy products are the major natural food source (3.5-6.0 mg/g fat, 70% of natural sources), but CLAs are also found in ruminant meat (lamb, beef, deer, and goat making up <25% of natural intake), poultry, and fish (Ritzenthaler et al. 2001) (table 1).

Table 1. Food products containing natural CLA. This table lists sources where the CLA is a natural part of the food and not added after food production.

Product	CLA (mg/g fat)
Cow milk	0.7-10.1
Sheep milk	10.8-20.7
Butter	4.7-8.11
Plain yogurt	4.8-9.01
Cheese	3.6-5.86
Lamb	5.6
Beef	2.9-4.3
Ground turkey	2.5
Chicken	0.9
Shrimp	0.6
Salmon	0.3
Safflower oil	0.7
Canola oil	0.5
Sunflower oil	0.4

Source: Table was created with information from Acosta Balcazar et al. (2022).

As the overall fat content of milk can be influenced by feed type, the CLA levels in cow milk can be modulated by feed type as well. For example, feeds containing flax seed and fresh forage have higher levels of alpha-linolenic acid, which can be a direct precursor to CLA in the rumen. A review reported that the milk of grass-fed cows contains a higher amount of CLA than grain-fed cows (Acosta Balcazar et al. 2022). Supplementing the diet of feedlot lambs with cracked safflower seeds tripled the level of CLA level in muscle meat and doubled the amount of CLA in adipose tissue compared to their normal diet of beet pulp, oat, and soybeans alone, although both were still less than 1 mg/g of tissue (Bolte et al. 2002).

Similar results were found when comparing safflower- or sunflower-oil-supplemented beef and dairy cattle (Bottger et al. 2002; Kelly et al. 1998). A small human study with just six participants found no change in plasma CLA levels after safflower oil intake, and this study did not measure CLA levels in adipose tissues (Herbel et al. 1998). It is possible that humans can convert linoleic acid to CLA in their owns guts, as both *Lactobacillus* and *Bifidobacterium* bacterial species found in the gut microbiomes of humans have been shown to convert linoleic acid to CLA (Wu et al. 2024).

Enhanced Sources of CLA

CLA can be chemically synthesized from linoleic acid in vegetable oils such as safflower, sunflower, corn, and soybean. Safflower oil is known for its high concentration of linoleic acid (71%-75%) (Khalid et al. 2017) compared to other vegetable oils; however, as discussed above, there is only about 50-80 mg CLA/g of fat in the natural oil. This seed-derived oil can be used as a substrate to synthesize CLA (c9,t11/t10,c12) by various synthesis and extraction techniques, including microbial culture preparation (Iorizzo et al. 2024; Yang et al. 2017; Zhang et al. 2017) and exposing the oil to ultraviolet light in a photoisomerization reaction (Gammill, Proctor, and Jain 2010; Gangidi and Lokesh 2014).

Functional foods containing enhanced CLA include beverages, bars, grain products, dairy products, margarines, and processed fruits and fruit juices, but most of these were used in research-based studies, and the products themselves are not currently available on the market. Thus, consumers who want to add CLA to their diets usually use CLA dietary supplements.

Dietary supplements containing CLA are available in a variety of forms such as pills, powders, emulsions, and gummies, with varying serving sizes and levels of supplemental CLA (800-5,000 mg). Even when commercially available products are labeled as containing CLA, the products usually only contain 56.6%-82% of the bioactive isomers (c9,t11 and t10,c12), with the rest of the product being linoleic acid and other less prevalent isomers.

Dietary supplements containing CLA are labeled with the CLA isomers and total content of oil, but the labeling is not always clear. For example, compared to safflower oil alone, proprietary blends of CLA contain up to 80% of the bioactive isomers (fig. 2). This means that taking a 1-gram pill will provide up to 800 mg of CLA, which is a significantly higher amount than found in any naturally occurring food source. Consumer confusion can happen as safflower oil pills are also sold with labeling such as "CLA safflower oil." While safflower oil supplements do contain up to 0.7% CLA, 2 grams of safflower oil pills will only give 100-140 mg of CLA, along with 1400 grams of linoleic acid (fig. 2A). This level of CLA is significantly lower than supplements derived from the enhanced products that have undergone photoisomerization to enhance the bioactive isomers (figs. 2B and 2C). Additionally, the product in fig. 2B does not provide information on the ratio or levels of the bioactive isomers, (c9,t11 and t10,c12) such that consumers do not know what isomers they are getting from those preparations. In one article, vastly different effects of safflower oil versus a commercial CLA blend (in this case for Cognis Nutrition and Health, Tonalin®) were seen with body weight reduction in postmenopausal women who were obese (Norris et al. 2009). Specifically, safflower oil containing only the 0.7% level of CLA had no effect on overall BMI or total adipose mass, but it did lower glucose and trunk fat levels as well as increase lean muscle mass levels, while CLA lowered overall BMI and total adipose mass.

When and if functional foods containing CLA enter the market, there is no FDA requirement to list CLA on the label under *trans* fats or to clarify isomer levels. However, it is likely that companies will want to highlight known higher contents of CLA and specific isomer percentages. Consumer education of the benefits and possible harms of CLA functional foods should occur before or concurrently with commercial-scale production of these products (Shinn, Ruan, and Proctor 2017).

Potential Health Benefits

Observational studies have found that CLA intake from foods is associated with a lower risk of various health problems (table 2). Experimental studies in both animals and humans have tried to confirm the findings from observational studies and reported that CLA exhibits numerous health benefits including anti-obesity, anti-carcinogenic, hypotensive, hypoglycemic, and immunomodulatory effects (table 2). Research indicates that the two main CLA isomers play both independent and synergistic roles. When supplemented alone in some animal studies, the t10,c12-CLA may contribute to anti-obesity (Park et al. 1999) and anti-diabetic effects, whereas c9,t11-CLA to anti-inflammatory effects. But the effects in humans are less clear. In a clinical trial, t10,c12-CLA supplementation induced insulin resistance and increased blood glucose level (Riserus et al. 2002). Most of the published studies have used a mixture of CLA isomers with two major forms, c9,t11-CLA and t10, c12-CLA, and a number of minor isomers (e.g., t7, t9-CLA; c9, c11-CLA; t9, t11-CLA; c10, c12-CLA; t10, t12-CLA; t11, t13-CLA; and c11, c13-CLA). These mixed isomers have been shown to have anti-carcinogenic effects (Kelley, Hubbard, and Erickson 2007), the human findings, such as for breast cancer are mixed (Fuke and Nornberg 2017; McGowan et al. 2013). In general, CLA intervention in human trials has been fraught with mixed results (Asbaghi et al. 2024;

A. Safflower Oil (linoleic acid)

Supplement Facts
Serving Size 3 Capsules
Servings Per Container 30

Amount Per Serving		% Daily Value
Calories	20	
Total Fat	2 g	3%**
Polyunsaturated Fat	1.5 g	†
Monounsaturated Fat	0 g	†
Vitamin B-6 (as pyridoxine HCl)	25 mg	1471%
Safflower oil (flower) [providing 70% high linoleic acid (1400 mg)]	2 g	†

** Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

B. Safflower-derived enhanced CLA

Supplement Facts
Serving Size: 1 Softgel
Servings per Container: 90

	Amount Per Serving	% Daily Value
Calories	10	
Calories from Fat	10	
Total Fat	1 g	1.5%
Safflower Oil (Carthamus tinctorius) (seed) (75% conjugated linoleic acid 750 mg)	1000 mg	*

*Daily value not established.

C. Proprietary CLA isomer blend (from safflower oil)

Supplement Facts
Serving Size 1 Softgel

Amount Per Serving		% Daily Value
Calories	10	
Calories from Fat	10	
Total Fat	1 g	1%
Tonalin® Proprietary Fatty Acid Blend (from safflower oil) [containing minimum 78% conjugated linoleic acid (CLA)]	1 g	*

Percent Daily Values are based on a 2,000 calorie diet.

*Daily Value not established.

Figure 2. Labeling of safflower oil and CLA supplements. A. Safflower oil supplement. B. CLA-enhanced supplement from safflower oil. C. Proprietary blend CLA supplement.

Benjamin and Spener 2009; Benjamin et al. 2015; den Hartigh 2019; Dilzer and Park 2012; Kim et al. 2016; Kulczynski, Sidor, and Gramza-Michalowska 2019; Putera et al. 2023). This appears to be due to the level of intake or supplements given in the various studies (ranging from natural foods only, to supplements of up to 9 grams per day) (Dilzer and Park 2012). Most researchers now agree that functional benefits of CLA for humans must meet a minimum intake level of 3 grams per day, and that 3-6 grams per day or more are needed to see weight loss and other benefits (Dilzer and Park 2012). This level of CLA would only be achievable in a functional food product or by using CLA pills and powders.

Table 2. Biological activities of CLA. This table lists potential activities of CLA observed in research studies (cited).

Activity	Effects	References
Anti-obesity activity	• CLA reduced body fat mass, body mass index, and body fat percentage; it increased lean body mass and muscle mass. • CLA improved body composition in adults, including reduced body mass and fat-free mass. • CLA in combination with calorie restriction and moderate physical activity reduced body weight more effectively compared to CLA alone.	Asbaghi et al. 2024; Basak and Duttaroy 2020; den Hartigh 2019; Fuke and Nornberg 2017; Kim et al. 2016; Li et al. 2023; Vyas, Kadegowda, and Erdman 2012
Immunomodulatory activity	• CLA improved immunity by reducing the production of pro-inflammatory cytokines. • CLA improved innate and adaptive immune responses.	Basak and Duttaroy 2020; Benjamin et al. 2015; den Hartigh 2019; Fuke and Nornberg 2017; Kim et al. 2016; Putera et al. 2023; Vyas, Kadegowda, and Erdman 2012
Anti-cardiovascular diseases	• CLA reduced atherosclerosis. • CLA improved blood lipid profile and decreased LDL ("bad") cholesterol levels.	Basak and Duttaroy 2020; Benjamin et al. 2015; den Hartigh 2019; Fuke and Nornberg 2017; Kim et al. 2016; Vyas, Kadegowda, and Erdman 2012
Anti-diabetes activity	• CLA enhanced insulin sensitivity. • CLA improved glucose management in prediabetes and diabetes.	Benjamin et al. 2015; den Hartigh 2019; Fuke and Nornberg 2017; Li et al. 2023
Anti-cancer activity	• CLA reduced the risks of colorectal, testicular, and breast cancers. • CLA altered cancer cell cycle and apoptosis.	Benjamin et al. 2015; Basak and Duttaroy 2020; den Hartigh 2019; Fuke and Nornberg 2017; Kim et al. 2016; Li et al. 2023
Improving physical performance	• CLA improved physical performance by modulating body composition, decreasing glycogen breakdown, increasing oxygen consumption rate. • CLA increased testosterone levels in men who were exercising.	Benjamin et al. 2015; Putera et al. 2023
Anti-osteoporotic effect	• CLA improved mineralization of bone.	Falahatzadeh, Najafi, and Bashti 2024; Li et al. 2023

Dosage

A daily recommended intake (DRI) level of CLA has not been established, but most studies have established that 3-6 grams per day is safe for daily consumption (Badawy et al. 2023). The European Food Safety Authority Panel on Dietetic Products, Nutrition, and Allergies recognized CLA as a safe food ingredient up to 3.5 grams per day (EFSA 2010). The U.S. Food and Drug Administration regulates CLA as a dietary supplement, and CLA was given GRAS (Generally Recognized as Safe) status in 2008 (FDA 2008). The FDA's GRAS status for CLA is limited to certain food types, including beverages and grain products, milk products, and processed fruit juices at a level of no more than 1.5 grams per serving (FDA 2014). A CLA mixture (c9,t11:t10,c12=1:1) was also recognized as a GRAS food ingredient (Kim et al. 2016) at a level of 3.2 grams per day.

Adverse Effects and Interactions of CLA

When CLA is consumed at low levels in foods, it is generally safe. CLA supplementation at higher levels has been determined to be safe by the FDA (FDA 2008; den Hartigh 2019; Iwata et al. 2007; Whigham et al. 2004). Despite the numerous health benefits of CLA, several adverse effects when supplements are taken in high amount (≥3.5 grams per day over a six-month period) have been reported (table 3). It appears that t10,c12-CLA may cause mild to moderate adverse effects, whereas the c9,t11-CLA is not related to adverse effects, but more human studies are needed to understand these effects in more detail.

The impact of CLA supplementation on liver enzyme levels has been investigated, and inconsistent results have been reported. One systematic review did not find that CLA supplementation elevated liver enzyme levels except for an increase in one liver enzyme called aspartate aminotransferase, which can signal liver damage (Mirzaii et al. 2016). Due to these adverse effects, some individuals should be cautious when taking CLA supplements until more studies can be done. These include individuals who have underlying diabetes or metabolic syndrome, heart disease, and liver disease. Consumption of CLA by children and pregnant or lactating women has not been studied extensively, and more work is needed in this area.

Table 3. Adverse effects of CLA. (This table was created with information from review articles cited, where the studies used levels of at least 3 grams of CLA per day.)

Adverse Effects	References
Gastrointestinal discomfort: • Upset stomach. • Constipation. • Diarrhea. • Indigestion.	Benjamin et al. 2015; NIH 2022; Putera et al. 2023
General malaise: • Fatigue. • Headache.	Benjamin et al. 2015; NIH 2022
Altered metabolism: • Increased total cholesterol levels. • Lowered HDL ("good") cholesterol. • Fatty liver. • Mixed results on glucose metabolism and insulin sensitivity.	Benjamin et al. 2015; Kim et al. 2016; NIH 2022; Riserus et al. 2002
Inflammation: • Increased inflammation. • Increased oxidative stress. • Hepatitis (3 cases, no cause-effect determined).	Benjamin et al. 2015; Kim et al. 2016; Nortadas and Barata 2012; Ramos et al. 2009

Conclusion

CLA is a naturally occurring component of ruminant milk fat and meat with potential health benefits. Synthetic CLA is processed from high linoleic acid containing plant oils and used in processed foods and supplements. Despite the consistent effects of CLA on potential health benefits from animal studies, recent reviews of human studies have shown mixed results except for modest anti-obesity effects. This discrepancy may be due to many factors including the dose, isomer types, the duration of CLA intervention, and participants' physical activity status and health conditions. More studies are required to gather more evidence to determine the efficacy of CLA intake on chronic health conditions.

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