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BEEF FACTS: Nutrition

Conjugated Linoleic Acid and Dietary Beef – An Update

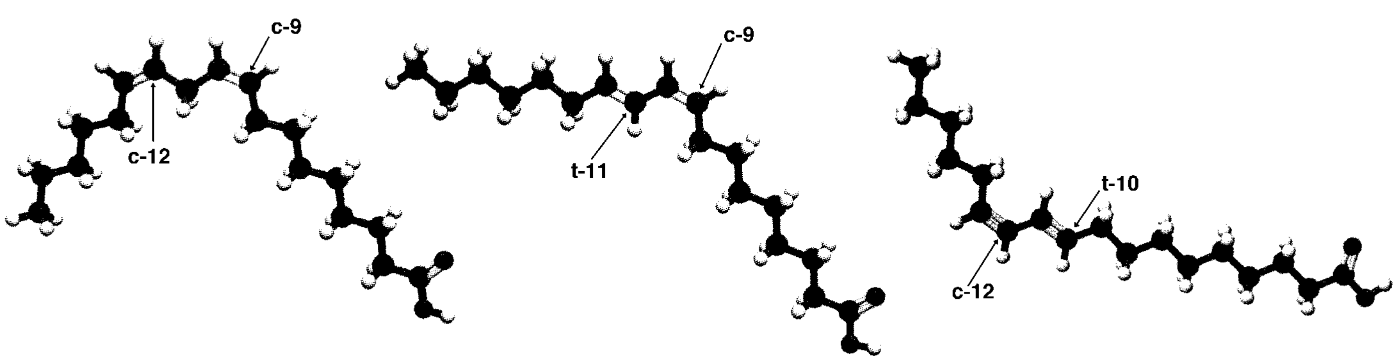
Conjugated linoleic acid (CLA), a natural derivative of the fatty acid linoleic acid, has received increasing attention in recent years. Starting with anticarcinogenic effects, the potential benefits of this unique fatty acid have extended to antiatherogenic properties, anti-diabetic properties, enhanced immune response and positive effects on energy partitioning and growth. These effects have been documented in numerous reviews (1-4) as well as in extensive scientific literature that has grown exponentially since the late 1980's (5).

As a naturally occurring compound in foods from ruminant animal sources, CLA's anticarcinogenic properties are unique. Of the vast number of naturally occurring substances, demonstrated to have anti-carcinogenic activity, all but a very few are of plant origin (1).

Chemistry/Structure

CLA is a collective term used to describe a mixture of positional and geometric isomers/forms of linoleic acid. Linoleic acid is an 18-carbon unsaturated fatty acid with two double bonds in positions 9 and 12, both in the "cis" (on same side) configuration. Thus, the "chemical name" of linoleic acid is cis-9, cis-12-octadecadienoic acid. In contrast, the two double bonds in CLA are primarily in positions 9 and 11, and 10 and 12 along the carbon chain with the designation of a conjugated diene. In addition to these "positional" changes of the double bonds, there can also be geometric changes (cis(c) or trans(t) [on opposite sides] configuration). Thus, at least eight different CLA isomers of linoleic acid have been identified. Of these isomers, the c9, t11 form is believed to be the most common natural form of CLA, with biological activity. However, in recent years, biological activity has been proposed for other forms, especially the t10, c12 isomer. Although not widely accepted, the name "rumenic acid" has been proposed as a "common name" for the major CLA isomer found in natural products (6). For a comparison of these CLA isomer "forms" with linoleic acid, see Figure 1. Additional potentially active isomers are also being identified and studied (2,7).

Figure 1. Chemical Structures of Linoleic Acid and Two Isomers of Conjugated Linoleic Acid (CLA). *



Linoleic acid (c-9, c-12) octadecadienoic acid | **Conjugated linoleic acid c-9, t-11 isomer** | **Conjugated linoleic acid t-10, c-12 isomer**

* Adapted from: Steinhart, C. Conjugated Linoleic Acid The Good News about Animal Fat. J.Chem.Educ. 73:A302; 1996.

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History/Identification/Sources

CLA is a naturally occurring fatty acid found in food products from ruminants (cattle and sheep). Although identified much earlier, increased interest in CLA occurred when it was isolated and identified by Pariza and coworkers as an anticarcinogenic substance from grilled ground beef (8-10). It was also found to be present in a variety of dairy products (11).

The total CLA content in foods may vary widely. Representative and relative concentrations of CLA in a variety of foods are summarized in Table 1. CLA concentrations are highest in foods from ruminants (including beef, lamb and dairy products). Seafoods, pork, most poultry products and vegetable oils are not notable sources of CLA (12).

CLA has been found in triglycerides, lipoproteins and cell membrane phospholipids in various tissues of rodents, rabbits and humans (2). As a normal isomerization product of linoleic acid metabolism by rumen bacteria, CLA is synthesized from free linoleic acid through biohydrogenation pathways and enzymatic isomerization. Early studies suggested that CLA content could be increased in foods that are heat processed (dairy pasteurization, pan frying of meats, etc.) (11). However, later studies (13) suggest that CLA is not increased by cooking, but rather with water loss, CLA remains constant on a per gram of fat basis. Additionally, CLA is stable and not destroyed by cooking or storage.

Foods from ruminant sources (beef and dairy) generally have CLA levels in the range of 3-7 mg/g fat; although, recent studies have shown it may be possible to increase these "naturally" occurring levels (4,14-16).

Table 1. Representative/Relative Concentrations of CLA in Uncooked Foods [adapted from Chin et al. (12)].

Food	Total CLA (mg/g fat)	c9, tll-isomer (%)
Meat		
Fresh ground beef	4.3	85
Beef round	2.9	79
Beef frank	3.3	83
Beef smoked sausage	3.8	84
Veal	2.7	84
Lamb	5.6	92
Pork	0.6	82
Poultry		
Chicken	0.9	84
Fresh ground turkey	2.5	76
Seafood		
Salmon	0.3	n.d.*
Lake trout	0.5	n.d.
Shrimp	0.6	n.d.
Dairy Products		
Homogenized milk	5.5	92
Butter	4.7	88
Sour cream	4.6	90
Plain yogurt	4.8	84
Ice cream	3.6	86
Sharp cheddar cheese	3.6	93
Mozzarella cheese	4.9	95
Colby cheese	6.1	92
Cottage cheese	4.5	83
Reduced fat swiss	6.7	90
Am. Processed cheese	5.0	93
Cheez whiz™	5.0	92
Vegetable Oils		
Safflower	0.7	44
Sunflower	0.4	38
Canola	0.5	44
Corn	0.2	39

* n.d. => not detectable

Multisite Anticarcinogen – Cell and Animal Studies

Following the initial identification of CLA as a modulator of mutagenensis and carcinogenesis, research interest accelerated. Additional studies confirmed this anticarcinogen effect in a variety of tissues, especially skin and forestomach. Continuing work with a wide variety of cell cultures and cancer cell lines (including malignant melanoma, colorectal cancer, breast/mammary cancer, lung adenocarcinoma, prostate cancer, leukemia, ovarian and liver cancers) have demonstrated inhibition by CLA (3,17-20). In contrast, linoleic acid did not inhibit the growth of any cell line and in some cases stimulated tumor growth and metastasis (18,21).

Perhaps the most significant early anticarcinogenic effects of CLA were described by Ip and co-workers (22,23) where CLA prevented mammary cancer in rodents given CLA in the diet, prior to administration of a carcinogen. This contrasted with earlier studies that used acute dosing by direct contact, gavage, or via cell culture additions. These dietary studies found a dose-dependent protection at levels of 1% CLA and below, but no further beneficial effect was evident at levels above 1%. In studies with dietary CLA at 0.05, 0.1, 0.25 and 0.5%, as little as 0.1% CLA was sufficient to cause a significant reduction in mammary tumors. This confirmed CLA as a powerful anticarcinogen, which could be administered safely via the diet to achieve cancer protection, in an animal model.

To put in perspective, the effect of CLA (an animal fat) in cancer prevention is specific and is more powerful than for any other fatty acid in modulating tumor development (1). For instance, unlike linoleic acid (a close relative of CLA) which sometimes stimulates carcinogenesis (21), CLA is inhibitory. Also, the n-3 fatty acids of fish oil, which generally are responsible for tumor suppression, require in excess of 10% in the diet to elicit the same tumor suppression responses. In contrast, CLA at levels as low as 0.1% in the diet produce a significant reduction in mammary tumor yield in animal studies.

Further work by Ip and co-workers has shown that the timing of CLA feeding can be critical. For instance, when CLA is given during the time the mammary tissue is actively developing, you see a lasting protective effect. If CLA is given after carcinogen administration, a continual supply of CLA is needed for a preventive effect. CLA appears to have a major impact on the mammary gland, making the tissue less susceptible to tumor formation (4,23,24).

Work continues to determine the exact mechanism by which CLA may effect carcinogen metabolism, activation or detoxification (2,3,25). Studies with mice given CLA, prior to administration of the heterocyclic amine IQ, have shown varying reductions in IQ-DNA adducts in the liver, lung, large and small intestine, kidneys and colon (26,27). CLA at levels equivalent to 0.5% of the diet, exerted inhibitory effects on the process of colon carcinogenesis (27).

Other Beneficial Effects of CLA

Antiatherogenic and Hypocholesterolemic

Based on the possibility that CLA would exhibit antioxidant activity, both in vivo and in vitro (22,28), studies were initiated to examine the effect of CLA on experimental atherogenesis in rabbits (29). When CLA, was added at 0.5% to an atherogenic diet, for 12 weeks, the aortas of the CLA fed rabbits exhibited less atherosclerosis. Also, LDL (low-density lipoprotein) cholesterol and triglycerides (TG) were lower in the CLA fed group (29). This observation was later supported by studies in hamsters where CLA feeding resulted in lower plasma total and LDL cholesterol and TG levels (30). The CLA fed animals also had less aortic streak formation.

Fat Partitioning and Metabolism

One of the most interesting effects of CLA appears to be its influence on body fat levels and the proportion of lean to fat, especially in young growing animals. CLA induces a relative decrease in body fat levels and an increase in lean muscle. This observation has been noted in several studies with mice, rats, chicks and pigs (4,31-33). In a study with growing pigs, the results were quite dramatic. Backfat thickness was reduced up to 27% in CLA fed pigs and there was a 6.8% increase in percent lean (33). Such results have generated considerable interest as to whether humans will experience similar fat reductions and increases in proportion of muscle mass if CLA is consumed in the diet. Studies in humans are currently underway (4).

Effects on Immune Response and Bone Formation

The effects of CLA on fat partitioning may be at least partially the result of modulation of the immune system. Ordinarily, stimulation of the immune system produces cytokines (proteins released by a cell, upon contact with an antigen, acts as a mediator) which can cause breakdown of muscle cells. CLA can modulate (decrease) the production of cytokines and thus prevent muscle degradation. Experiments in chicks, rats, and mice show that CLA increases feed efficiency and counteracts immune-induced cachexia or malnutrition (4,31,34). Through this effect on cytokines, CLA may also have positive effects on bone health (4,35,36). Diets rich in fats containing CLA, compared to soybean oil, caused a greater rate of bone formation (4).

Anti-diabetic Effects

CLA has been found to help normalize or reduce blood glucose levels and possibly prevent diabetes (37). Using a laboratory animal model for diabetes, CLA was found to prevent the onset of diabetes. CLA appears to work as well as a new class of diabetes-fighting drugs (thiazolidinediones) and may provide the added advantage of weight reduction, as drug treatments often result in weight gain. These initial findings with diabetic rats are very encouraging and are the basis for continuing studies in human diabetics.

Other Human Studies – Epidemiology

Epidemiological studies support the hypothesis that there is some factor in whole milk that exerts a protective effect against breast cancer and coronary heart disease (4,38,39). Lower incidences of these diseases were related to greater consumption of whole milk but not to intakes of low fat milk. The presence of CLA in milkfat may be a protective factor. In a recent report the incidence of breast cancer was significantly lower in women with higher breast tissue levels of CLA (40).

It is clear that the CLA content of blood serum and breast milk can be modified by diet (41-43). In earlier studies in Australia, it had been found that breast milk from women of the Hare Krishna religious sect contained twice as much CLA as milk from Australian mothers on conventional diets (11.2 vs. 5.8 mg/g) (44). This

Table 2. Estimates of CLA Intake in Humans.

Reference	Population Studied		Males	Females	All
			mg/day		
10	Not specified		—	—	"several hundred mg/day"
45	Australian (not specified)			—	500-1500
46	German men		310	—	—
47	German men & women		430	350	—
		(from meat)	110	80	—
		(from dairy)	286	240	—
48	CSFII 94-96	(beef users)	265	172	221
	Men & women	(non-beef users)	123	88	102
49	Adults 18-60 yr.	3-day record	137	79	—
	(mean 31 yr.)	3-day duplicate	148	132	—
		FFQ	197	93	—

was attributed to the large amount of butter and ghee (a clarified butter) consumed by the Hare Krishna. Park and coworkers (43) have also confirmed that CLA levels in human milk can be enhanced by increasing the CLA content of the maternal diet.

Effective Intake/Dose Levels

For any compound that produces the dramatic effects noted for CLA, an immediate question concerns the minimally effective dose level. Does it vary for different health and disease conditions, tissue sites and response levels? Is a "chronic" dose level required, or can an "acute" dose be effective and if so, when should it be consumed? Are food sources adequate or are supplemental sources required? If only some of the isomers of CLA are biologically effective, which ones are they? If so, dose levels of CLA should be "corrected" for the active isomer. Whether from food sources or supplements, any comparisons of effects should be sure to equate levels of the active isomer. These are just some of the many questions about CLA which require further research.

Usual Dietary Intakes

Current measures of usual or actual dietary intakes of CLA are very limited, most being only estimates. A listing of published reports based on estimates and data analysis is presented in Table 2. (10,45-49).

A variety of factors can influence estimates of CLA intake. Food composition and frequency of intake of particular foods affect dietary intake of any food component. For CLA, there may be the added variable of level of the biologically active form/isomer of CLA consumed. Also, men usually consume more meat than women do; dairy foods generally provide a higher percentage of dietary CLA than beef; and individuals may be beef or dairy users or non-users. In addition, intake estimates may be based on assumptions of dietary proportions, such as in the German studies of meat/meat products (40/60) and pork/beef (80/20) (47).

In another study (48), available data on CLA content of foods has been applied to consumption data from the USDA CSFII 94-96 (Continuing Survey of Food Intake of Individuals). Based on intake data from this large dataset it is estimated that approximately 36% of total CLA intake is from beef and approximately 52% from dairy products.

Dietary Beef as a Source

Can a reasonable diet, containing beef, provide beneficial levels of CLA, considering that the minimal effective dose response is still unknown? At present, the answer would be "probably", but more studies are needed to determine minimally effective levels of CLA. Animal studies have shown benefits at dietary levels as low as 0.1-0.5%. Also, the potential for CLA enhanced, (but still "natural"), dietary sources of beef and dairy products is just now being explored (4). It has been shown that a number of dietary components for cattle can increase CLA levels in milk and beef. These include: plants consumed in pasture, forage in feeds, and unsaturated plant oils (with sunflower oil resulting in the most CLA). CLA concentrations in milk have been increased up to four fold by various dietary manipulations (4,14). Increases in the CLA content of beef tissue is currently being explored, with preliminary indications that elevations in CLA content are possible via feeding practices (16).

Summary

CLA is a very unique fatty acid from ruminant animal sources that exhibits powerful anticarcinogenic effects at relatively low dietary levels. In addition, CLA has been shown to be anti-atherogenic, anti-diabetic and to provide beneficial effects on growth, health and body-fat levels and proportion of lean to fat. Much remains to be learned about the exact mechanisms by which CLA exerts its effects (25). In addition, the exciting findings from animal studies need to be replicated, as appropriate, in humans. Dietary beef represents one of the primary "natural" sources of this intriguing compound which some have called a "previously unrecognized nutrient" (50).

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