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## REPORT

## CLA

## Weight Loss and Other Benefits of Conjugated Linoleic Acid

By Dale Kiefer

Conjugated linoleic acid (CLA) is gaining the attention of a public grown ravenous for new weapons to wield in the never-ending “battle of the bulge.” You may have heard some of the hype, but what is the real story behind this relative newcomer to the weight-loss market? A growing body of research reveals that CLA is a potent nutrient responsible for a variety of important health benefits, from fighting cancer and diabetes to boosting fat loss and building lean muscle.

First hailed for its striking anti-cancer effects,<sup>1</sup> CLA is now the subject of intensive research by scores of scientists around the globe, all of them intrigued by this nutrient's multiple human health benefits. Accelerated fat loss is just one of several boons that have been ascribed to this fatty acid supplement. CLA's other reported benefits include combating diabetes, building lean muscle mass, and thwarting cancer at each major stage of its development.<sup>1-7</sup>

While it may be too soon to render the final verdict on all of CLA's purported benefits, the scientific evidence clearly supports some of its biological effects. In this article, we will examine the current state of CLA research, covering this important nutrient's demonstrated effects and examining others that remain to be fully elucidated.



## WHAT IS CLA?

CLA comprises several chemically similar compounds, or isomers, derived from the fatty acid known as linoleic acid. Present in dairy products and the meat of ruminant animals—livestock such as cattle and sheep that chew their cud—CLA is believed to play an important role in modulating immunity and regulating lipid metabolism.<sup>2,5,8</sup>

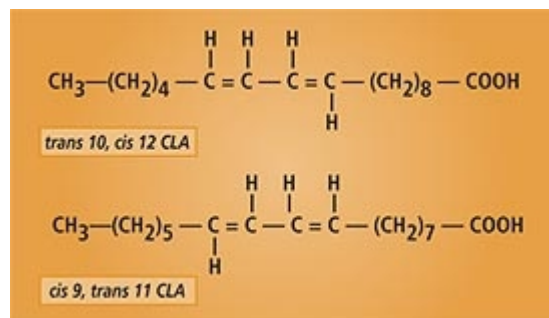
The “conjugated” portion of this nutrient's name refers to two double chemical bonds within its structure. The location of the bonds dictates a given isomer's specific designation. For example, the cis-9, trans-11 CLA isomer (also known as ruminic acid, or c9t11) is the most common isomer found in ruminant-derived foods, and is believed to be one of the most biologically active isomers. Trans-10, cis-12 CLA (t10c12) is present in far smaller concentrations, but may play an especially important role in modulating health.<sup>4</sup> These two isomers are considered the most biologically important forms of CLA for human health. Most commercially available CLA supplements include a roughly equal mixture of both.

## CLA AND WEIGHT LOSS

Early CLA experiments on laboratory rodents generated considerable surprise and excitement. Scientists discovered that CLA, when added to the diet, promotes dramatic and relatively rapid weight loss in a variety of lab animals. Perhaps more important, the animals lost body fat while increasing their lean muscle mass.

When researchers fed rabbits a diet that normally promotes atherosclerosis, the animals were considerably less likely to develop this artery-clogging disease when CLA was included in their diet. Their total cholesterol and LDL (low-density lipoprotein) levels dropped, as did their triglyceride values.<sup>9</sup> Furthermore, using a strain of rats bred for a tendency to develop obesity-related type II diabetes, scientists were able to significantly delay the onset of diabetes by adding CLA to the animals' diet.<sup>10</sup>

Needless to say, scientists were excited about CLA's potential to fight fat in humans. Obesity is epidemic in much of the developed world, and the federal Centers for Disease Control and Prevention reports that approximately two thirds of American adults are now overweight or obese. Even more alarming is that 13% of American children and adolescents are overweight.<sup>11,12</sup> All that excess tonnage takes a heavy toll, not only on individuals' health but also on our collective bottom line. In 2002, the



estimated total economic cost of obesity was about \$93 billion.<sup>13</sup>

It is understandable that hopes for CLA ran high in those early days of model-thin mice and shrinking rats. However, CLA may not be quite the magic bullet scientists had hoped it would be. Although CLA triggers dramatic fat loss in rodents, the effect is less pronounced in humans. Some human clinical trials have reported promising results,<sup>14</sup> while others have found little or no fat-loss effect.<sup>17</sup> A few studies have reported adverse effects of CLA on lipid profiles, markers of oxidative stress, and glucose handling,<sup>14</sup> while other long-term studies have not observed these negative effects.<sup>21</sup>

Thus, our understanding of CLA is in a state of flux. Much work remains to be done as we assess CLA's potential benefits or risks. With that caveat, let us shed some light on what is known about this important nutrient.

## CLA AND DIABETES

CLA appears to prevent the development of type II diabetes (often associated with obesity) in rats bred for their propensity to grow abnormally overweight. Some researchers have proposed that the t10c12 isomer is primarily responsible for this anti-diabetic and anti-obesity effect.<sup>14</sup>

Human studies confirm the efficacy of the t10c12 isomer in promoting weight loss. For example, in 2003, Swedish researchers published the results of a series of controlled experiments in which subjects received either a CLA mixture or purified t10c12 isomer. The results indicated that CLA does reduce body fat, though no overall weight loss was detected. Unexpectedly, the pure t10c12 isomer appeared to adversely affect glucose and lipid levels, and to impair insulin sensitivity.<sup>14</sup>

Other research, however, suggests that CLA may improve the insulin sensitivity of fat cells, and may work in combination with nutrients such as biotin and coenzyme Q10 to prevent diabetes.<sup>15</sup>

A recent study showed that eight weeks of CLA supplementation increased insulin sensitivity in young, sedentary humans. Ten participants took 4 grams of CLA daily. Six of the subjects experienced large increases in insulin sensitivity, while two showed no change and two demonstrated a decrease in insulin sensitivity. These results suggest that response to CLA varies among individuals, with many responding favorably.<sup>16</sup>



In 2000, researchers in California conducted an experiment on 17 women who were confined to a metabolic laboratory for three months. Their activity levels and food intakes were strictly controlled. After a month of baseline monitoring, the subjects were given a daily supplement of 3 grams of either a CLA mixture or an inactive placebo. After two months of supplementation, the scientists concluded that CLA had no effect on body composition.<sup>17</sup> The study's design did not, however, account for the possibility that CLA may reduce body fat or weight by suppressing appetite, since all of the subjects in this trial were required to adhere to a uniform diet. It is also possible that the subjects simply did not consume enough CLA or did not consume it long enough to generate significant changes in body composition.

## REDUCING BODY FAT

Other researchers have reported that CLA does indeed reduce body fat, if not overall weight. In a double-blind experiment, a leading researcher gave 21 patients with type II diabetes a daily dose of 8 grams of either a CLA mixture or placebo. After two months, the researchers correlated the subjects' CLA blood levels with changes in their weight. They discovered that the t10c12 isomer—but not the c9t11 isomer—was significantly associated with weight loss.<sup>10</sup> Intriguingly, the t10c12 isomer, which scientists believe may exert the most potent effects on body composition, is also associated with a decrease in leptin, a hormone associated with the body's hunger-satiety feedback mechanism. Interestingly, the amount of CLA used in this study, 8 grams per day, is more than twice the amount given to subjects in trials in which no significant fat loss was reported.<sup>10</sup>

Other research, however, indicates that 2-4 grams of CLA taken daily may be enough to trigger fat loss. Several Scandinavian studies over the last five years offer evidence that relatively low doses of CLA reduce body fat, if not overall weight. A Norwegian study documented significant body-fat loss with just 1.8 grams of CLA per day. This double-blind, placebo-controlled, randomized study of 20 healthy, normal-weight people lasted three months. Subjects performed standardized exercises for 90 minutes, three times a week. They consumed either a placebo or 1.8 grams of a commercially available CLA mixture, which featured the c9t11 and t10c12 isomers in equal amounts. Subjects taking CLA experienced significant reductions in body fat, as measured by near-infrared light, and the CLA was well tolerated. The placebo subjects, by contrast, showed no change in body fat.<sup>18</sup>

Another Norwegian controlled study enrolled 60 overweight or obese subjects who were randomly assigned to one of five groups and received daily doses of 1.7-6.8 grams of CLA or placebo. Body fat was measured by dual-energy X-ray absorptiometry at baseline and then at six and 12 weeks. Scientists found a significantly greater body-fat loss among the groups taking 3.4 grams or more of CLA compared to the control subjects. Intriguingly, the group receiving 1.7 grams of CLA experienced no significant body-fat loss, nor did the groups taking more than 3.4 grams of CLA see any additional body-fat loss.<sup>19</sup> Researchers concluded that a dose of 3.4 grams results in significant body-fat loss compared to placebo, but that greater amounts of CLA do not result in greater fat loss. The CLA was well tolerated and adverse events were no different among the placebo and various CLA groups. Forty-seven subjects completed the three-month study. Blood lipids and other blood-profile health parameters were unchanged among all groups.<sup>19</sup>



### SLIMMING NEWS FROM SWEDEN

A study in Sweden enrolled 53 healthy men and women who were randomly assigned to receive either 4.2 grams of CLA a day or an equal amount of placebo. Neither the subjects nor the researchers in this double-blind trial knew who was taking which substance. After three months, CLA subjects experienced a significant decrease in their proportion of body fat compared to control subjects. Weight, body mass index, blood glucose, and lipids remained unchanged for both groups. The researchers concluded that CLA reduces body fat without affecting other health parameters.<sup>20</sup>

A recent report from the University of Wisconsin confirmed CLA's safety. Obese people who were otherwise healthy received either 6 grams daily of CLA or a placebo for one year. General blood chemistries revealed no adverse effects on liver function, blood glucose, lipids, or insulin levels from long-term CLA supplementation.<sup>21</sup>

Although the research results remain somewhat mixed, CLA supplementation appears to be safe and potentially beneficial for people seeking to trim body fat.



### BATTLING CANCER AT EVERY TURN

Ironically, the potent cancer-fighter CLA was first identified in fried and grilled beef, foods that are better known for containing cancer-causing substances (such as heterocyclic amines) than for supplying beneficial anti-carcinogens.<sup>1,22,23</sup> Yet that is precisely where scientists at the University of Wisconsin first discovered the conjugated isomers they dubbed CLA.<sup>1</sup>

The Wisconsin scientists discovered that one or more of the isomers inhibit mutations in bacteria. Researchers believe that these mutations, which are generally damaging alterations to the genetic code, underlie the development of many cancers. They wondered whether CLA could offer protection against an experimentally induced laboratory model of skin cancer, and soon turned their attention to a rodent model of human cancer.<sup>1</sup>

The researchers enlisted the aid of rodents specially bred for their susceptibility to developing skin cancer when provoked with an appropriate toxin. One group of the cancer-prone mice was pre-treated with a synthetic mixture of four CLA isomers. Control groups of mice were pre-treated with either linoleic acid or an organic solvent. The researchers then applied a known carcinogenic chemical to the skin of all the test animals. It was soon apparent that CLA provides considerable protection against experimentally induced tumors, as the control subjects developed twice as many tumors as the CLA-treated mice.<sup>1</sup>

### SESAME LIGNANS ENHANCE CLA'S ACTION

Lignans, the fibrous compounds found in many plant-based foods, possess numerous health-promoting effects. Sesame seed lignans in particular are beneficial. Studies show that sesame lignans, including sesamin and sesaminol, enhance vitamin E's absorption and availability, improve lipid profiles, and help normalize blood pressure.<sup>40-42</sup> (See also "Do Your Antioxidants Suppress Enough Free Radicals?" in the February 2005 issue of *Life Extension*.)

Animal studies show that sesame lignans enhance the burning of fat. One study demonstrated that sesame increases the activity of several liver enzymes that break down fatty acids.<sup>43</sup> Optimizing the liver's fat-burning capacity may promote fat loss and may account for sesame's lipid-lowering effect.



Sesame lignans also boost the weight-loss effects of CLA. Japanese scientists studied whether dietary manipulations could enhance CLA's effects in reducing body fat. They found that sesamin helped stimulate the loss of adipose tissue. Researchers think that sesame lignans increase CLA's effects by stimulating a pathway of fatty acid breakdown called beta-oxidation.<sup>44</sup>

The combination of CLA with sesamin is also effective in lowering serum triglycerides, according to another research team. Triglycerides may increase the risk of heart disease and stroke. Enhanced fatty-acid oxidation in the liver may be responsible for the triglyceride-lowering effect of CLA and sesamin.<sup>45</sup>

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#### STRONG EVIDENCE OF ANTI-CANCER EFFECTS

Over the past 18 years, numerous medical and nutritional scientists have published research that validates and expands on the Wisconsin team's groundbreaking work. Thanks to their efforts, we now know that CLA isomers, when added to the diets of laboratory animals, protect the animals against experimentally induced breast cancer, colon tumors, and skin cancer. These effects occurred regardless of whether the CLA was given during or after tumor initiation.<sup>3,5,24,25</sup>

Mounting evidence suggests that CLA's anti-tumor activity comes primarily from the c9t11 isomer. The evidence for CLA's ability to decrease the incidence, progression, tumor burden, and number of metastases in models of breast, prostate, skin, and colon cancer had grown so convincing by the mid-1990s that the National Academy of Sciences published a statement in 1996 declaring, "[CLA] is the only fatty acid shown unequivocally to inhibit carcinogenesis in experimental animals."<sup>26</sup>

One of the animal models used in CLA research routinely serves as a model of a type of human breast cancer called ductal carcinoma in situ.<sup>5,24</sup> The finding that CLA inhibits the formation of new tumors in rodents suggests that it may also reduce breast cancer metastasis in women. Confirming this expectation is an important new goal for oncology researchers, as the growth of secondary tumors (metastasis) is the leading cause of death among cancer patients.<sup>5</sup>

CLA also inhibits the growth of transplanted breast and prostate cancer cell lines in laboratory rodents.<sup>27,28</sup> This effect was so dramatic that one research team was inspired to write, "Mice fed the CLA-supplemented diet displayed not only smaller local tumors than the regular diet-fed group, but also a drastic reduction in lung metastases."<sup>28</sup> Considerable evidence indicates that CLA inhibits the initiation stages of cancer, and research also shows that CLA inhibits the post-initiation and promotion phases of cancer growth.<sup>5</sup> At least one study found that CLA inhibits the formation of secondary tumors in mice, even after cancerous mammary cells are seeded into the mice.<sup>29</sup>

In fact, recent evidence suggests that CLA fights cancer at every step in its progression, beginning with its initial development. By blocking cell cycle proteins that regulate the creation of new cells, CLA has been shown to stop runaway cell proliferation before aberrant (but benign) tissue transforms into far-from-benign cancer.<sup>5,30,31</sup>



In one experiment, researchers fed mice CLA for two weeks before inoculating them with aggressive human breast adenocarcinoma cells. Although the mice used in the study were bred for their inability to resist immune challenges, the CLA-treated mice developed 73% fewer local tumors by nine weeks after inoculation than did the control mice, which had not been pre-treated with dietary CLA. Furthermore, CLA dramatically inhibited the spread of breast cancer cells to lungs, peripheral blood, and bone marrow. The researchers concluded, "These results indicate the ability of dietary CLA to block both the local growth and systemic spread of human breast cancer via mechanisms independent of the host immune system."<sup>27</sup>

Other research has shown that in a rodent model of human breast cancer, dietary exposure to CLA while mammary glands are maturing confers protection against the cancer. Even when CLA was withdrawn from the diet after mammary glands had matured, rats previously nourished with CLA continued to enjoy significant protection against mammary tumors. The mechanism by which CLA protects in this instance appears to be distinct from its anti-initiation activity.<sup>24,32</sup>

More recently, scientists in western New York gathered data from more than 1,100 women with confirmed breast cancer, as well as from about 2,000 cancer-free control patients. By assessing the subjects' self-reported dietary intake of CLA, the researchers were able to look for statistical relationships between CLA intake and health status. Although no clear correlation appeared to exist between dietary intake of CLA and overall breast cancer risk, "a marginally significant reduction in risk of having an [estrogen receptor-negative] tumor" was reported among women with the highest intake of CLA. Regarding CLA, the researchers noted, "There may be associations with tumor biology at least among premenopausal women."<sup>33</sup>

Recent reports indicate that CLA may also protect against breast and other types of cancer by inhibiting angiogenesis, the process by which tumors create a new blood supply network to obtain nutrients needed for growth. Halting or reversing angiogenesis is an anti-cancer strategy that has received intense attention by researchers from a variety of disciplines in recent



CLA also promotes apoptosis (programmed cell death, or cellular suicide) of cancer cells.<sup>36-38</sup> Cancer cells are adept at evading apoptosis, which accounts for much of their insidious nature. Apoptosis allows the body to remove damaged or potentially harmful cells in a way that minimizes waste and ameliorates damage to surrounding tissues. CLA evidently affects the functioning of immune system components involved in apoptosis.<sup>38</sup>

Recently, a research team in Argentina published a report on diet and the incidence of colon cancer among the local population. Argentineans consume a great deal of beef that is rich in saturated fat and cholesterol, while eating relatively little fish or dietary fiber. Fiber is generally recognized as protective against colon cancer, while heart-healthy omega-3 fatty acids, which are present primarily in seafood, may also help prevent cancer. Despite the Argentineans' seemingly unhealthy eating habits, they do not succumb to colon cancer as commonly as might be expected.<sup>39</sup>

An analysis of epidemiological data revealed that high consumption of lean meats (less than 15% fat content) is actually associated with a significant reduction in the incidence of colon cancer among the populace. By contrast, high consumption of fatty meats, such as cold cuts and sausages, was associated with an increased risk of developing colon cancer. Because lean beef is a primary source of CLA, the researchers reasoned that CLA's protective effects outweigh any presumed negative effects associated with the saturated fats and cholesterol in lean beef.<sup>39</sup>

Intentionally consuming more beef in order to obtain CLA is not a practical method of protecting one's health. Most beef comes from cattle that are commercially fed and therefore have relatively little CLA. Numerous scientific studies indicate that those who over-consume beef have higher risks of common diseases.<sup>46-49</sup> Those seeking to obtain CLA should consider supplements that provide standardized CLA concentrations.

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## References

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1. Ha YL, Grimm NK, Pariza MW. Anticarcinogens from fried ground beef: heat-altered derivatives of linoleic acid. *Carcinogenesis*. 1987 Dec;8(12):1881-7.
2. Pariza MW, Park Y, Cook ME. Conjugated linoleic acid and the control of cancer and obesity. *Toxicol Sci*. 1999 Dec;52(2 Suppl):107-10.
3. Liew C, Schut HA, Chin SF, Pariza MW, Dashwood RH. Protection of conjugated linoleic acids against 2-amino-3-methylimidazo[4,5-f]quinoline-induced colon carcinogenesis in the F344 rat: a study of inhibitory mechanisms. *Carcinogenesis*. 1995 Dec;16(12):3037-43.
4. Belury MA. Dietary conjugated linoleic acid in health: physiological effects and mechanisms of action. *Annu Rev Nutr*. 2002;22:505-31.
5. Belury MA. Inhibition of carcinogenesis by conjugated linoleic acid: potential mechanisms of action. *J Nutr*. 2002 Oct;132(10):2995-8.
6. Belury MA, Vanden Heuvel JP. Protection against cancer and heart disease by CLA: potential mechanisms of action. *Nutr Disease Update*. 1997;1:58-63.
7. Scimeca JA. Cancer inhibition in animals. In: Yurawecz MP, Mossobo MM, Kramer JKG, Pariza MW, Nelson GJ, eds. *Advances in Conjugated Linoleic Acid Research*, Vol. 1. Champaign, IL: AOCS Press; 1999:420-43.
8. Pariza MW, Park Y, Cook ME. Mechanisms of action of conjugated linoleic acid: evidence and speculation. *Proc Soc Exp Biol Med*. 2000 Jan;223(1):8-13.
9. Lee KN, Kritchevsky D, Pariza MW. Conjugated linoleic acid and atherosclerosis in rabbits. *Atherosclerosis*. 1994 Jul;108(1):19-25.
10. Belury MA, Mahon A, Banni S. 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*. 2003 Jan;133(1):257S-60S.
11. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002

12. Hedley AA, Ogden CL, Johnson CL, et al. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *JAMA*. 2004 Jun 16;291(23):2847-50.
13. Finkelstein EA, Fiebelkorn IC, Wang G. National medical spending attributable to overweight and obesity: how much, and who's paying? *Health Aff (Millwood)*. 2003 Jan;Suppl Web ExclusivesW3-26.
14. Riserus U, Smedman A, Basu S, Vessby B. CLA and body weight regulation in humans. *Lipids*. 2003 Feb;38(2):133-7.
15. McCarty MF. Toward a wholly nutritional therapy for type 2 diabetes. *Med Hypotheses*. 2000 Mar;54(3):483-7.
16. Eyjolfson V, Spriet LL, Dyck DJ. Conjugated linoleic acid improves insulin sensitivity in young, sedentary humans. *Med Sci Sports Exerc*. 2004 May;36(5):814-20.
17. Zambell KL, Keim NL, Van Loan MD, et al. Conjugated linoleic acid supplementation in humans: effects on body composition and energy expenditure. *Lipids*. 2000 Jul;35(7):777-82.
18. Thom E, Wadstein J, Gudmundsen O. Conjugated linoleic acid reduces body fat in healthy exercising humans. *J Int Med Res*. 2001 Sep;29(5):392-6.
19. Blankson H, Stakkestad JA, Fagertun H, et al. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J Nutr*. 2000 Dec;130(12):2943-8.
20. Smedman A, Vessby B. Conjugated linoleic acid supplementation in humans—metabolic effects. *Lipids*. 2001 Aug;36(8):773-81.
21. Whigham LD, O'Shea M, Mohede IC, Walaski HP, Atkinson RL. Safety profile of conjugated linoleic acid in a 12-month trial in obese humans. *Food Chem Toxicol*. 2004 Oct;42(10):1701-9.
22. Rohrmann S, Linseisen J, Becker N, et al. Cooking of meat and fish in Europe—results from the European Prospective Investigation into Cancer and Nutrition (EPIC). *Eur J Clin Nutr*. 2002 Dec;56(12):1216-30.
23. Felton JS, Knize MG, Salmon CP, Malfatti MA, Kulp KS. Human exposure to heterocyclic amine food mutagens/carcinogens: relevance to breast cancer. *Environ Mol Mutagen*. 2002;39(2-3):112-8.
24. Ip C, Chin SF, Scimeca JA, Pariza MW. Mammary cancer prevention by conjugated dienoic derivative of linoleic acid. *Cancer Res*. 1991 Nov 15;51(22):6118-24.
25. Belury MA, Nickel KP, Bird CE, Wu Y. Dietary conjugated linoleic acid modulation of phorbol ester skin tumor promotion. *Nutr Cancer*. 1996;26(2):149-57.
26. Available at: <http://www.asas.org/JAS/symposia/proceedings/0938.pdf>. Accessed February 16, 2005.
27. Visonneau S, Cesano A, Tepper SA, et al. Conjugated linoleic acid suppresses the growth of human breast adenocarcinoma cells in SCID mice. *Anticancer Res*. 1997 Mar;17(2A):969-73.
28. Cesano A, Visonneau S, Scimeca JA, Kritchevsky D, Santoli D. Opposite effects of linoleic acid and conjugated linoleic acid on human prostatic cancer in SCID mice. *Anticancer Res*. 1998 May;18(3A):1429-34.
29. Hubbard NE, Lim D, Summers L, Erickson KL. Reduction of murine mammary tumor metastasis by conjugated linoleic acid. *Cancer Lett*. 2000 Mar 13;150(1):93-100.
30. Ip C, Dong Y, Thompson HJ, Bauman DE, Ip MM. Control of rat mammary epithelium proliferation by conjugated linoleic acid. *Nutr Cancer*. 2001;39(2):233-8.
31. Futakuchi M, Cheng JL, Hirose M, et al. Inhibition of conjugated fatty acids derived from safflower or perilla oil of induction and development of mammary tumors in rats induced by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP). *Cancer Lett*. 2002 Apr 25;178(2):131-9.

32. Ip C, Scimeca JA, Thompson H. Effect of timing and duration of dietary conjugated linoleic acid on mammary cancer prevention. *Nutr Cancer*. 1995;24(3):241-7.
33. McCann SE, Ip C, Ip MM, et al. Dietary intake of conjugated linoleic acids and risk of premenopausal and postmenopausal breast cancer, Western New York Exposures and Breast Cancer Study (WEB Study). *Cancer Epidemiol Biomarkers Prev*. 2004 Sep;13(9):1480-4.
34. Augustin HG. Translating angiogenesis research into the clinic: the challenges ahead. *Br J Radiol*. 2003;76 Spec No 1S3-10.
35. Masso-Welch PA, Zangani D, Ip C, et al. Inhibition of angiogenesis by the cancer chemopreventive agent conjugated linoleic acid. *Cancer Res*. 2002 Aug 1;62(15):4383-9.
36. Song HJ, Sneddon AA, Barker PA, et al. Conjugated linoleic acid inhibits proliferation and modulates protein kinase C isoforms in human prostate cancer cells. *Nutr Cancer*. 2004;49(1):100-8.
37. Liu J, Chen B, Yang Y, Wang X. Effect of apoptosis in human mammary cancer (MCF-7) cells induced by cis9, t11-conjugated linoleic acid. *Wei Sheng Yan Jiu*. 2004 Jan;33(1):58-62.
38. Maggiora M, Bologna M, Ceru MP, et al. An overview of the effect of linoleic and conjugated-linoleic acids on the growth of several human tumor cell lines. *Int J Cancer*. 2004 Dec 20;112(6):909-19.
39. Eynard AR, Lopez CB. Conjugated linoleic acid (CLA) versus saturated fats/cholesterol: their proportion in fatty and lean meats may affect the risk of developing colon cancer. *Lipids Health Dis*. 2003 Aug 29;2(1):6.
40. Yamashita K, Iizuka Y, Imai T, Namiki M. Sesame seed and its lignans produce marked enhancement of vitamin E activity in rats fed a low alpha-tocopherol diet. *Lipids*. 1995 Dec;30(11):1019-28.
41. Sankar D, Sambandam G, Rao MR, Pugalendi KV. Impact of sesame oil on nifedipine in modulating oxidative stress and electrolytes in hypertensive patients. *Asia Pac J Clin Nutr*. 2004;13(Suppl);S107.
42. Kang MH, Kawai Y, Naito M, Osawa T. Dietary defatted sesame flour decreases susceptibility to oxidative stress in hypercholesterolemic rabbits. *J Nutr*. 1999 Nov;129(10):1885-90.
43. Ashakumary L, Rouyer I, Takahashi Y, et al. Sesamin, a sesame lignan, is a potent inducer of hepatic fatty acid oxidation in the rat. *Metabolism*. 1999 Oct;48(10):1303-13.
44. Sugano M, Akahoshi A, Koba K, et al. Dietary manipulation of body fat-reducing potential of conjugated linoleic acid in rats. *Biosci Biotechnol Biochem*. 2001 Nov;65(11):2535-41.
45. Sakono M, Yuji K, Miyanaga F, et al. Combined effect of dietary conjugated linoleic acid and sesamin triacylglycerol and ketone body production in rat liver. *J Nutr Sci Vitaminol*. 2002 Oct;48(5):405-9.
46. Chao A, Thun MJ, Connell CJ, et al. Meat consumption and risk of colorectal cancer. *JAMA*. 2005 Jan 12;293(2):172-82.
47. Larsson SC, Rafter J, Holmberg L, Bergkvist L, Wolk A. Red meat consumption and risk of cancers of the proximal colon, distal colon, and rectum: the Swedish Mammography Cohort. *Int J Cancer*. 2005 Feb 20;113(5):829-34.
48. Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study in major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr*. 2000 Oct;72(4):912-21.
49. Pattison DJ, Symmons DP, Lunt M, et al. Dietary risk factors for the development of inflammatory polyarthritis: evidence for a role of high level of red meat consumption. *Arthritis Rheum*. 2004 Dec;50(12):3804-12.

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