CONJUGATED LINOLEIC ACID AND THE ATHEROSCLEROSIS IN ANIMAL MODELS – REVIEW

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ABSTRACT

Conjugated linoleic acid (CLA) refers to a group of isomeric forms of linoleic acid (LA) containing two conjugated sites of unsaturation. During last 20 years, CLA has been the subject of investigations considered on its possible benefits on health. Both CLA isomers are found in products from ruminants because of the action of rumen micro-organisms in fatty acid biohydrogenation. The purpose of this review is to underline the potential for *cis-9*, *trans-11* and *trans-10*, *cis-12* CLA to modify atherosclerosis, with focus on the rabbit, hamster and the mouse examples.

INTRODUCTION

The development of many types of diseases is influenced by our lifestyle, including diet. In 1970s dr. Pariza's group from the University of Wisconsin - Madison investigated that the modified fatty acids derived from grilled beef have not only anti-cancer properties but also anti-atherogenic [12].

The fatty acid responsible for beneficial effects on health was identified as a conjugated linoleic acid (CLA). Further investigations show a wide range of CLA's biological positive effects on cancer, cardiovascular disease, diabetes, body composition, immune system and bone health [12, 17].

Many studies in animal models, have been carried out using products that contain individual isomers of CLA's. Some of them show the differences between *cis-9, trans-11* and *trans-10, cis-12* isomers on body compositional effects. Because the interest in CLA research still persists and there is many questions without answer, this review will highlight some positive health benefits in animal models.

STRUCTURE OF CLA

Conjugated linoleic acid (CLA) refers to a group of the polyunsaturated fatty acids (PUFA) and describes the positional and geometric isomers of the omega-6, octadecadienoic acid [2, 9]. The structure, shown in Figure 1, consist of 18 carbon fatty acid with two conjugated double bonds separated by a single bond, opposite to linoleic acid, which is non-conjugated diene [14]. The location of the double bonds identifies the *cis* or the *trans* isomeric configuration [21]. Instead, the *cis* or *trans* configuration are present predominantly in positions 8 and 10, 9 and 11, 10 and 12, or 11 and 13 [2].

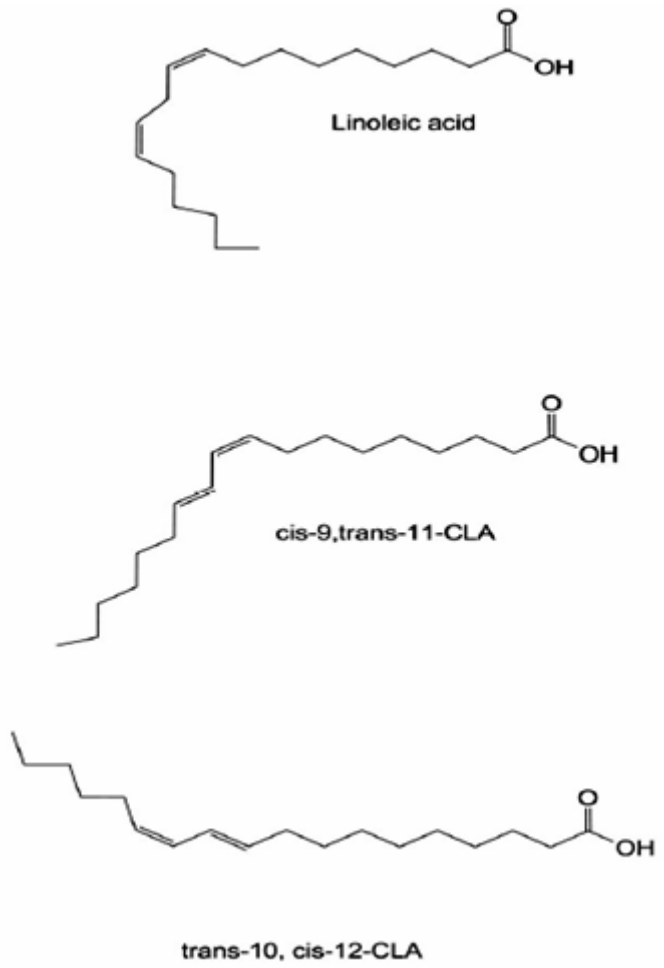


Fig. 1. Structures of linoleic acid and isomers of conjugated linoleic acid (CLA). Source: [15]

CLA CONCENTRATION IN FOOD

In human and animal diet, the main source of CLA isomers are meat and dairy products like milk fat and cheese. CLA is synthesized in the rumen as a result of the biohydrogenation of linoleic acid to stearic acid. During this processes, over 90% of total CLA (primary *cis-9, trans-11* CLA) is formed by linoleic acid isomerase enzyme, which is express by the gram-negative bacteria *Butyrivibrio fibrosolvens.*

The CLA concentration in food is shown in Table 1. The highest level of conjugated linoleic acid we can find in lamb (4,3–19,0 mg/g lipid) and in beef (1,2–10,0mg/g lipid). Other meat products as pork or chicken are characterized by lower amount of CLA, usually less than 1 mg/g lipid. Very interested is the fact that the CLA content in turkey is relatively high (2,0–2,5 mg/g lipid) [17].

3,0 to 9,0 mg/g lipid is the typically range CLA concentration in dairy products. About 73–93 percent of the total CLA makes the *cis-9, trans-11* isomer. The level of CLA in cheese is dependent on the type, but typically it is from 3,59 to 7,96 mg/g lipid. Blue cheese, brie or Swiss cheese have significantly higher CLA amount than other cheeses [9].

Table 1. CLA content in some products [mg/g lipid]

Product	CLA content [mg/g]
Salami	4,2
Beef smoked sausage	3,8
Mince meat	3,5
Corned beef	6,6
Lamb muscle	4,3 – 19,0
Beef muscle	1,2 – 10,0
Pork meat	0,6
Chicken meat	0,7 – 1,5
Turkey meat	2,0 – 2,5
Cheese	3,59 – 7,96
Cultured dairy products etc.	3,82 – 4,66
Cow's milk	3,38 – 6, 39

Source [8, 9, 17]

Kramer et al. suggested that the dietary CLA accumulation in animal depends on the amount in diet and length of intake. He reported also that the conjugated linoleic acid isomers are absorbed and incorporated both in adipose and membrane phospholipids [10].

Moreover, Chin et al. [4] and Dhiman et al. [7] reported that the level of CLA isomer in milk fat is dependent upon the diet feds to cows. According to Chouinard et al. research the CLA content in milk could be significantly higher after the diet modification [5].

Eggs produced by hens fed diet enriched in 5% CLA could provide a substantial increase of CLA in human food. Research showed that after this diet, eggs can contain from 310 to 365 mg of CLA per egg [3].

Nakamura et al.[15] mentioned that the CLA we can find also in fish, monogastric animal products and plant products, but in much lower concentration. In his opinion, CLA isomers have been identified as a result of hydrogenation of fat. That is why we can find conjugated linoleic acid primarily in foods considered high in fat.

CLA EFFECTS ON ATHEROSCLEROSIS IN SELECT ANIMAL STUDIES

Cardiovascular disease, which is highly connected with atherosclerosis, is known as a complex of disease with a strong lipid metabolic and inflammatory component influenced on the vascular endothelium. The response, on the inflammatory, of the cells in the vascular wall is in consequences foam cell formation and atherosclerosis [21].

During last 20 years conjugated linoleic acid has received attention as a component, which might prevent the development of atherosclerotic lesions or reduced plasma lipoprotein levels. The possibility that the *cis-9*, *trans-11* and *trans-10*, *cis-12* CLA isomers can influence anti-atherogenic, has been tested in animal models.

The study in rabbits fed with a diet containing CLA isomers for 22 weeks showed that, the level of atherosclerotic lesions in rabbit's aortas, was lower [2].

There are also other studies that showed significantly lower aortic lipid deposition when the diet is enriched with CLA isomers. Lee et al. reported that rabbits fed with diet supplemented with conjugated linoleic acid, had significantly less aortic fatty lesions compared to control group. The diet enriched with 0,5% CLA resulted in less atherosclerosis in aortas of CLA's fed rabbis [12]. Similarly, 1% of CLA in New Zealand rabbits diet caused in inhibition of atherogenesis of 30 percent [11].

Valeille et al. [19] reported that the diet with *cis-9, trans-11* CLA isomer in Syrian Golden hamsters, had beneficial effects on reduction of aortic lipid accumulation by 30–35%.

Another study showed that when the hamster's diet is supplemented with *cis-9*, *trans-11* CLA, the aortic lipid deposition is lower [14]. What is more, in hamsters aortas, fed with 1% of CLA isomers in diet, was less number of atherosclerotic lesions, but these changes were not statistically significant [13].

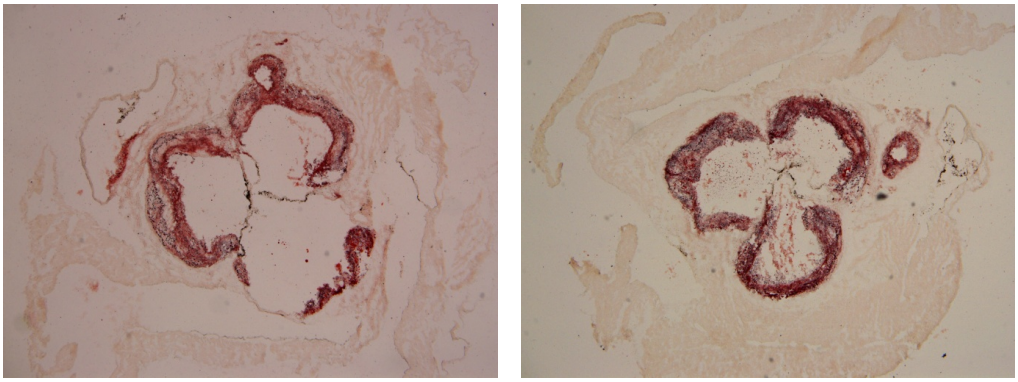
Wilson et al. demonstrated the differences in health benefits of *cis-9, trans-11* and *trans-10, cis-12* CLA isomers. In their study, only hamsters fed with diet enriched with *cis-9*, *trans-11* isomer, had the amount of atherosclerotic lesions reduced [22].

Toomey et al. used in the investigation the CLA mixture, in which was 80% of *cis-9*, *trans-11* CLA. They reported that CLA isomers in mouse diet markedly reduced the lesion area compared to mouse fed with control group (saturated fat diet). The most important thing in this report is the fact that author noticed decreases in macrophage accumulation in lesion area and other facts, which can suggest a role for CLA in modification of the immune response [18].

In Cooper's et al. study after 12 weeks supplementation of 50:50 mix CLA isomers in mouse diet, there was no significant increase in atherosclerotic lesion area in either *en face* or in *cross section* preparation [6].

There are also some researches which suggest opposing effects of the cis-9, trans-11 and *cis-9*, *trans-11* isomer on atherosclerosis in the apoE-/- mouse. Arbones-Mainar et al. investigation revealed that the *cis-9*, *trans-11* isomer, in mouse diet, significantly reduced lesion area in the *cross section* analyses of the aortic root. On the other hand, *trans-10, cis-12* isomer significantly increased lesion area in *en fac*e examination of the vessel, compared to control group [1].

The last research describes the influence of 0,5% supplementation in apoE/LDLR-/- mouse diet. Franczyk – Żarów et al. reported, that compared to the control group fed with semi-purified diet, diet enriched in *cis-9*, *trans-11* isomer after 2 months, reduced the atherosclerosis lesion area in both *en face* and *cross section* preparation. Picture 1 presents the comparison of *cross sectional* examination of the aortic root in control mouse group and in CLA-fed mouse group [8].



Picture 1. Comparison of the cross section atherosclerosis lesion area in control mouse group (left side) and in *cis-9, trans-11* CLA-fed group

CONCLUSION

Atherosclerosis is serious problem which may be associated with dietary and lifestyle choices. The diet may have a strong influence on conjugated linoleic acid level. Both isomers *cis-9, trans-11* and *trans-10, cis-12* are shown to have distinct biological effect. A wide range of literature indicates that CLA and individual isomers may have a lot of health benefits. Most of researches are reported with animal models and a very limited amount with human effects. Multiple health effects in animal studies cannot be a complete picture representative of the human disease. This is for example because of the differences in dosage of conjugated linoleic acid in animal diet or differences in source of CLA. On the other hand, animal models are very useful to assess the effects of conjugated linoleic acid supplementation, with the most probably knowledge of the potential of interactions between CLA and atherosclerosis factors.

This review shows that, research using three different species: rabbit, hamster and mouse, was considered to separate or synergistic actions of the two CLA isomers. In almost all reports, there was shown a positive health effect of mix isomers supplemented diet. Moreover, the *cis-9, trans-11* CLA seems to be more effective diet ingredient, which can reduce incidence of atherosclerotic lesions. In conclusion, CLA has potentially anti-atherosclerotic and cardio protective effect.

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