

## Revisión

# Conjugated linoleic acid (CLA): effect modulation of body composition and lipid profile

A. Baddini Feitoza, A. Fernandes Pereira, N. Ferreira da Costa and B. Gonçalves Ribeiro

*Dietitian. Nutrition Institute Josue de Castro. Federal University of Rio de Janeiro. Rio de Janeiro. Brazil.*

### Abstract

Conjugated linoleic acid (CLA) refers to a family of polyunsaturated fatty acids, being represented by a group of isomers of linoleic acid called conjugated for having a double bound after a simple bound. Among its isomers, *trans-10,cis-12* and *cis-9, cis-12* CLA stand out. These isomers can lead to different effects on the body: anticarcinogenic, antidiabetogenic, antiatherogenesis and positive body composition alteration. The objective of this review is to describe their mechanisms of action, effects on body composition, on plasmatic lipoproteins and supplementation. Studies about CLA supplementation show its capacity of reducing fat percentage, body mass and of promoting an improvement in lipid metabolism. One of the adverse effects attributed to one of the isomers is insulin resistance by body fat redistribution. Limitations in the scientific models used in CLA researches make impossible to draw conclusions about the action of this fatty acid on human metabolism.

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Key words: *Conjugated linoleic acid. Body composition. Fat percentage. Lipid metabolism.*

### EL ÁCIDO LINOLEICO CONJUGADO (CLA): LOS EFECTOS EN LA MODULACIÓN DE LA COMPOSICIÓN CORPORAL Y EN EL PERFIL LIPÍDICO

### Resumen

El ácido linoleico conjugado (CLA) es un ácido graso que pertenece al grupo de los ácidos grasos poliinsaturados, representado por el conjunto de isómeros del ácido linoleico, que son denominados conjugados porque poseen una doble conexión tras una conexión simple. Entre sus isómeros se distinguen el *trans-10,cis-12* y *cis-9, cis-12* CLA. Estos isómeros son capaces de promover efectos distintos en el organismo: anticarcinogénesis, antidiabetogénesis, antiaterogénesis y cambios de composición corporal. El objetivo de esta revisión es describir sus mecanismos de acción, los efectos en las lipoproteínas plasmáticas, en la composición corporal y la suplementación. Los estudios acerca de la suplementación del CLA demuestran su capacidad de reducir el porcentaje de grasa, el peso corporal, y de mejorar el metabolismo lipídico. Sin embargo, unos de los efectos contrarios relacionados a uno de sus isómeros es la resistencia a la insulina a través de la redistribución de grasa corporal. Las limitaciones en los modelos científicos adotados en investigaciones acerca del CLA nos quitan la posibilidad de hacer conclusiones cuanto a la acción de este ácido graso en el metabolismo humano.

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Palabras clave: *Ácido linoleico conjugado. Composición corporal. Porcentaje de grasa. Metabolismo lipídico.*

### Introduction

Scientific researches suggest that the conjugated linoleic acid (CLA) may promote several physiological effects related to its different isomers. Models of study

in animals have indicated that CLA acts on lipid and glucose metabolisms promoting effects such as antidiabetogenic, antiatherogenesis, hypocholesterolemic, hypotryglyceridemic, improves in immunological system and decrease in adipose tissue, among others.<sup>1-15</sup>

Studies in humans confirmed the effects of CLA on the improvement in body composition and in the profile of plasmatic lipoproteins.<sup>16-19, 20-23</sup>

CLA supplementation has been proposed when the objective is to promote alterations in body composition, especially reduction of adipose mass. Among the set of CLA isomers, the *trans-10, cis-12* CLA isomer

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**Correspondence:** Adriana Baddini Feitoza.  
Avda. Delfim Moreira, 840 / apto. 210.  
CEP 25953-184 - Centro - Teresópolis - Rio de Janeiro.  
E-mail: abaddininutricao@gmail.com

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was identified as the main isomer responsible for alterations in lipid metabolism and body composition.<sup>24-27</sup> Nonetheless, the main food sources of CLA are the dairy products where more than 90% of CLA are in the form of cis-9,trans-11 isomer.<sup>28</sup> According to Atkinson,<sup>22</sup> the amount of CLA obtained by foods is 200 mg/day. In this way, it is understood that for obtaining the beneficial effects of CLA on health it is necessary to include an additional supplementation of CLA in the habitual diet in view of the amount and type of isomer consumed habitually, especially those who have hipolipidic and/or hypercaloric diets as habit, and the vegetarians.

The objective of this review is to describe the conjugated linoleic acid, its mechanisms of action, effects on body composition and plasmatic lipoproteins, and supplementation.

### Definition

The conjugated linoleic acid (CLA) is a fatty acid belonging to the group of polyunsaturated fatty acids. It refers to a substance represented by the set of positional and geometric isomers of linoleic acid (cis-9, cis-12, octadecadienoic acid) which possess a double bound after a simple bound, being, therefore, named as conjugated. The double bounds of these isomers can be found at the positions of carbons 7 and 9, 9 and 11, 10 and 12 or 11 and 13, among others, taking the different cis and trans spatial configurations.<sup>29,30</sup>

CLA is formed at the animal rumen by the incomplete biohydrogenation of polyunsaturated fatty acids of the diet, but also endogenously through the desaturation of vaccenic acid (11-trans octadecanoic) by Delta-9-desaturase, an enzyme present in the mammary gland and adipose tissue.<sup>28</sup> As this vaccenic acid is also produced by means of biohydrogenation, this process is the greatest responsible for CLA existence and its predominance in ruminants explains the reason why their products are CLA main sources.<sup>31</sup>

CLA, in its natural composition, can be found in several foods. It is present in larger concentrations in phospholipids and triacylglycerols of milk and dairy products, such as cheeses and yogurts, beef and ruminant meat and vegetable oils. However, in fewer concentrations, it can also be found in lamb, chicken and turkey.<sup>29,32</sup> Sources from animal origin are richer in CLA than vegetable sources.<sup>33</sup> CLA concentration in dairy products varies from 2.9 to 8.2 mg/g of fat and in meats it is 4.3 mg/g of fat. Vegetable oils and the fat of non-ruminant animals only contain traces of CLA, normally in a proportion ranging from 0.6 to 0.9 g per gram of the total fat of the food.<sup>34-36</sup>

Chin et al.<sup>36</sup> estimated that the daily intake of CLA in humans is approximately 160 mg and Ritzenthaler et al.<sup>37</sup> estimated 212 mg in men and 151 mg in women, the latter being 60% originated from dairy products and 37% from meats.

Britton et al.<sup>38</sup> observed an increase in the incorporation of the cis-9,trans-11 CLA isomer in plasmatic phospholipids in human cells proportionally to the consumption of CLA source foods. In the same way, Huang et al.<sup>39</sup> verified an increase in this isomer related to the larger consumption of dairy products.

The most studied CLA isomers are cis-9,trans-11 CLA and trans-10, cis-12 CLA. The first seems to have an anticarcinogenic effect, whereas the second seems to modulate body composition mainly by the reduction of body weight and of fat percentage, besides promoting beneficial alterations in lipid metabolism.<sup>24-27</sup>

### Effects on body composition

The researches of West et al.<sup>7,12</sup> demonstrated that dietary supplementation with conjugated linoleic acid increase the energetic expenditure in animals. In one of those studies<sup>12</sup> CLA was added to the diet containing from 15% to 45% of lipids in relation to the total caloric offer for six weeks. At the end of this experiment CLA provided reductions ranging from 43 to 88% of adipose tissue, besides a decrease in the energetic uptake, and an increase in the basal metabolic rate and in the night respiratory quotient, independent from the composition of the administered diet – hypo or hyperlipidic.

Further studies confirmed the alteration of the energetic expenditure in mice and in other animal models.<sup>1,3,5,6,10</sup> According to Atkinson,<sup>22</sup> this increase in the energetic expenditure is sufficient enough to justify reduction of the fat deposit in CLA-supplemented mice.

The body fat-lowering effect of CLA has also been reported in humans,<sup>16,18,20-23</sup> but it seems to be less prominent than in animals.

The effects of a mixture of CLA isomers on the body composition of 60 obese individuals, with body mass index (BMI) ranging from 25 to 35 kg/m<sup>2</sup> was evaluated by Blankson et al.<sup>21</sup> The sample was divided into five groups which received: 9 g/day of olive oil (placebo); 1.7 g/day; 3.4 g/day; 5.1 g/day and 6.8 g/day of CLA. At the end of 12 weeks all the groups which received CLA presented a significant reduction of fat percentage when compared with the placebo group. The reduction of body fat was higher as in the group which received 3.4 g/day as in the group which received 6.8 g/day of CLA, hence suggesting that the doses over 3.4 g of CLA are unnecessary. It was not possible to observe alterations in lean body mass and blood lipids. Diet and non controlled physical activities were a few of the limitations of this study.

In a controlled-placebo study Thom et al.<sup>20</sup> confirmed the decrease in body fat in a sample of 20 individuals supplemented with CLA who were practitioners of physical activity and presented less than 25 kg/m<sup>2</sup> BMI. Volunteers were divided into two groups of five females and two groups of five males. Control

groups received placebo (hydrogel) and CLA groups received 1.8 g of a mixture of CLA isomers. Volunteers carried out a standardized training of 90 min of intense physical exercises three times a week, and were oriented not to modify food habits and lifestyle during all the time of the study. At the end of the 12 weeks of supplementation, body fat was significantly reduced in CLA groups. No significant decrease in BMI and body weight, no difference between genders, and no adverse effects were reported in any of the groups.

Gaullier et al.<sup>16</sup> evaluated the effect of CLA supplementation on the body composition of overweight and physically active adults over a period of 12 months. The 180 volunteers were distributed in three groups which received: 1) 45 g of CLA, being 80% in the form of free fatty acids; 2) 4.5 g of CLA, being 76% in the form of triacylglycerols and; 3) 4.5 g olive oil (placebo). No restriction as regards lifestyle and diet was implemented. At the end of the 12 months of supplementation, body fat and BMI decreased significantly in the CLA groups; the mean of body fat in CLA groups was lower than in the placebo group, and in group 1 the mean of lean body mass was higher than in the placebo group. These results suggest a decrease in body fat in both forms of CLA supplementation and an increase in lean body mass related to the use of CLA in the form of free fatty acids.

Atkinson et al.<sup>22</sup> verified that CLA significantly reduced body fat in obese and overweight individuals, Blankson et al.<sup>21</sup> in physically active individuals and Smedman & Vessby<sup>23</sup> in women with adequate weight. Later, Risérus et al.<sup>18</sup> proved that CLA reduced the abdominal perimeter in men with central obesity.

On the other hand, other studies did not verify any effects of CLA on body composition. Zambell et al.<sup>40</sup> did not find any alterations in body composition, energetic expenditure, respiratory quotient and rate of fat oxidation in obese women supplemented with 3g of CLA for 64 days. Risérus et al.<sup>41</sup> did not find any differences in body composition when the cis-9,trans-11 CLA isomer was supplemented in men with android obesity.

Malpuech-Brugere et al.<sup>42</sup> evaluated the effect of the two main CLA isomers on body composition in obese individuals. The sample was composed of 81 individuals of both genders, adults, healthy, and overweight. For a period of six weeks all volunteers consumed dairy beverage containing 3 g of sunflower oil with high concentration of oleic acid. At the end of these six weeks, volunteers were divided into five groups which daily received, for a period of 18 weeks, dairy beverage containing: group 1) 3 g of sunflower oil with high concentration of oleic acid; group 2) 1.5 g of cis-9,trans-11 CLA; group 3) 3 g of cis-9,trans-11 CLA; group 4) 1.5g of trans-10,cis-12 CLA and; group 5) 3 g of trans-10, cis-12 CLA, all in the form of triacylglycerols. At the end of the 24 weeks the authors did not find any significant differences in body composition and energetic uptake among the groups. The decrease in body fat, although not signifi-

cant, was higher in groups 3 ( $-0.8 \pm 2.1$  kg) and 5 ( $-0.9 \pm 1.7$  kg), both supplemented with 3 g of CLA.

In agreement with these findings, Tricon et al.<sup>43</sup> did not find any significant alteration caused by any of those two isomers in the body composition of healthy adults. As well as Kreider et al.<sup>44</sup> when they did not obtain improvement in body composition when evaluated the effect of CLA on trained practitioners of resistance exercises. In this study, 23 individuals were evaluated and were divided into a placebo group, supplemented with 9 g/day of olive oil, and a CLA group, supplemented with 6g/day of CLA, for 28 days. The authors found that the group supplemented with CLA did not present alterations in total body mass, fat-free mass, and body fat percentage.

Although several studies have verified favorable changes in body composition,<sup>16,18,20-23</sup> others point at possible side effects related to the trans-10, cis-12 CLA isomer in lipid metabolism, and tolerance to glucose and sensitivity to insulin.<sup>45</sup>

### Mechanisms of action on body composition

Despite the many investigations concerning the alterations in body composition, the exact mechanisms through which CLA acts on the adipose tissue are still unknown.

In vivo and in vitro experimental models evaluated the physiologic modifications promoted by CLA in relation to the gene expression and specific proteins. The results suggest that CLA exerts an effect of decrease in adipose tissue through modulation of the energetic expenditure, apoptosis mechanisms, oxidation process of fatty acids, lipolysis, cellular differentiation and lipogenesis.<sup>46</sup> According to Azain et al.,<sup>3</sup> CLA presents different physiologic actions depending on the animal species.

In vitro models for study<sup>47,48</sup> demonstrated that CLA promotes modifications in the membrane of the adipose tissue, altering the gene expression of the adipocyte, leading to the decrease in the concentration and consequently to the activity of the Delta-9 desaturase enzyme.

Houseknecht et al.<sup>49</sup> drew the conclusion that CLA improves the sensitivity to insulin and tolerance to glucose in animals. This effect explains one of the mechanisms through which CLA reduces adiposity. The increase in sensitivity to insulin allows a higher amount of fatty acids and glucose to overpass the membrane of the muscle cells and to be used as source of energy. In this way, they prevent the deposition of these fatty acids in the adipose cells in the form of triacylglycerols. This confirms what Park et al.<sup>14</sup> suggested when they stated that the effect of CLA on body composition was due in part to the increase in lipolysis and beta oxidation, with a consequent reduction in the deposit of fatty acids in the adipose tissue on account of their less availability for triacylglycerol synthesis.

According to the review of Wang & Jones,<sup>50</sup> the anti-obesity mechanisms proposed as regards CLA include: decrease in the energetic intake and in the process of lipogenesis, increase in energetic expenditure, lipolysis and oxidation of fatty acids. Thus, it is understood that the effects of CLA on body composition are related to reduction of the adipose tissue and increase in lipolysis,<sup>21,46</sup> reduction of the activity of the lipoprotein lipase enzyme and of the intracellular concentration of triacylglycerols,<sup>9</sup> and increase in basal metabolism due to the increase in muscle mass.<sup>14,51</sup>

According to a recent review of Park & Pariza<sup>52</sup> the effects of CLA on body composition occur on account of the increase in energetic expenditure through the increase in the synthesis of uncoupling proteins-UCPs; reduction of body fat mass through decrease in the number and size of adipocytes on account of the inhibition of lipoprotein lipase enzyme (LPL); stimulation of the apoptosis process of pre-adipocytes; increase in lipolysis and beta oxidation in muscle tissue evidenced by the increase in carnitine acyltransferase I and II (CAT I and II).

### Effects on plasmatic lipoproteins

Studies on animals evidenced that CLA acts on the metabolism of plasmatic lipoproteins significantly reducing plasmatic cholesterol<sup>4,9</sup> and preventing the atherosclerosis induced by feeding.<sup>13,15</sup>

Lee et al.<sup>15</sup> showed that CLA significantly reduced the plasmatic concentration of triacylglycerols and LDL-cholesterol and that the deposition of cholesterol in the aorta was 30% less in CLA-fed rabbits. Later, Nicolosi et al.<sup>13</sup> also proved that CLA supplementation reduced the plasmatic concentration of triacylglycerols and total cholesterol, and further that this CLA effect resulted in fewer incidences of atheroma plaques in hypercholesterolemic rats fed an atherogenic diet. This effect was confirmed by Kritchevsky et al.<sup>53</sup> when they showed that CLA promoted a substantial regression of the previously developed atherosclerosis in rabbits.

In humans, a few studies evaluated the result of CLA supplementation in the metabolism of plasmatic lipoproteins. In a placebo-controlled study, Noone et al.<sup>17</sup> supplemented normolipidemic individuals with 3 g of CLA or placebo during eight weeks. At the end of study, they verified that the supplement of CLA led to a significant reduction of the concentration of VLDL-cholesterol and plasmatic triacylglycerols without altering the content of HDL-cholesterol. Other two studies demonstrated that there was no improvement in the concentration of plasmatic lipids through supplementation of 3.9 g/day of CLA, for a period of 63 days<sup>54</sup> and of 4.2 g/day of CLA for a total of 12 weeks.<sup>19</sup> As Riséus et al.,<sup>55</sup> besides having not verified any CLA positive effect on the content of plasmatic lipoproteins, they reported that CLA supplementation reduced the concentration of HDL-cholesterol in obese men with metabolic syndrome.

### Effects of different isomers on plasmatic lipoproteins

Yotsumoto et al.<sup>56</sup> affirmed that only the trans-10, cis-12 CLA isomer was capable of inhibiting apolipoprotein B (ApoB) and the synthesis of triacylglycerols in Hep G2 liver cells. This hypotriacylglycerolemic propriety associated with the trans-10,cis-12 CLA isomer was confirmed by Gavino et al.<sup>4</sup> when they showed that rats supplemented with a mixture of CLA isomers which had a larger proportion of trans-10,cis-12 reduced the plasmatic concentration of triacylglycerols, while the cis-9, trans-11 CLA isomer did not present this effect, and later by Lin et al.<sup>57</sup> when they stated that this isomer was the most effective in inhibiting triacylglycerol secretion by Hep G2 liver cells. These results suggest that the trans-10, cis-12 CLA isomer is the isomer responsible for the hypotriacylglycerolemic effect of CLA.

Yotsumoto et al.<sup>56</sup> also demonstrated that both isomers, cis-9, trans-11 and trans-10, cis-12 CLA, were equally effective in decreasing the synthesis of the cholesteryl ester enzymes in Hep G2 cells, although Noone et al.<sup>17</sup> suggested that the cis-9, trans-11 isomer would be more potent in reducing the synthesis of this enzyme in vivo when they verified that the mixture of CLA containing a larger proportion of the cis-9, trans-11 CLA isomers led to the reduction of the concentration of VLDL-cholesterol. On the other hand, Terpstra et al.<sup>58</sup> did not find a decrease in the plasmatic lipids through supplementation of the cis-9,trans-11 CLA isomer in an isolated way, whereas Tricon et al.<sup>43</sup> verified that both isomers promoted modifications in the concentration of total plasmatic cholesterol and of LDL-cholesterol in healthy adults. However, in this particular study, the trans-10, cis-12 CLA isomer increased the LDL:HDL-cholesterol and total cholesterol: HDL-cholesterol relation, while cis-9, trans-11 CLA isomer presented a beneficial effect, decreasing these relations.

Although still controversial, other researches confirmed a specific effect of the trans-10, cis-12 CLA isomer on lipid metabolism in humans,<sup>24,27</sup> suggesting that cardioprotector effects of CLA in animals also seem to be relevant in humans.

Other specific effects of these isomers were reported by Riséus et al.<sup>55</sup> when they found out that the trans-10, cis-12 CLA isomer caused insulin resistance in obese men and that the cis-9, trans-11 CLA isomer, besides promoting the increase in insulin resistance, intensified the process of lipid peroxidation.<sup>41</sup>

Moloney et al.<sup>59</sup> suggested that the cis-9, trans-11 CLA fatty acid was a mediator of the effects of sensitivity to insulin reducing the infiltration of macrophages and the inflammatory profile of adipose tissue in obese rats. This study demonstrated that the intervention with a diet enriched with cis-9, trans-11 CLA significantly reduced the concentrations of plasmatic insulin and glucose, decreased the HOMA-IR index of insulin

resistance and improved the QUICKI marker of sensitivity to insulin in an ob/ob mouse model which exposed an insulin-resistant phenotype. Alterations in metabolic profile, according to the authors, might be in part attributed to increase in the expression of GLUT4 (insulin-regulated glucose transporter) in the adipose tissue after the cis-9,trans-11 CLA diet.

### Mechanisms of action on plasmatic lipoproteins

Despite the few researches on the mechanism of action of CLA in the metabolism of plasmatic lipoproteins, it is probable that it exerts its function by modulating the metabolism of fatty acids in the liver.<sup>60</sup> These alterations are possibly mediated by the effects of the trans-10, cis-12 CLA isomer and/or by its metabolites in the biochemical regulation and activity of “key” adipocytes and enzymes of the skeletal muscle, as well as in the differentiation of adipocytes.<sup>61</sup> Therefore, it is probable that the trans-10, cis-12 CLA isomer might actually be the functional isomer as regards the alterations in the profile of plasmatic lipoproteins.

### Adverse effects of CLA supplementation

Although CLA seems to be a promising substance as regards reduction of body fat, it is important to consider the possibility of adverse effects found in animal models<sup>7,62</sup> and more recently in specific groups of humans.<sup>21,55,63,64</sup> Nonetheless, it is worthy to consider the limitation of these preliminary and controversial results which are also specific of the evaluated population.

The effects of CLA on the control of adiposity and on sensitivity to insulin mainly relate to the trans-10, cis-12 CLA isomer. There are evidences, as much from studies on rats as on humans, that this isomer probably promotes liver hypertrophy and insulin resistance through redistribution of body fat.<sup>49,55,65</sup>

West et al.<sup>7</sup> observed in animals two negative effects associated with the treatment with CLA. The first was the increase in liver weight which according to the authors may be due to the accumulation of lipids in the liver, since such occurrence has been demonstrated in a diversity of dietary manipulations, including a fast weight loss.<sup>66</sup> Histopathologic exams of the liver and pancreas of animals treated with or without CLA showed a light accumulation of lipids in the CLA group without clinical signs. The other negative effect of CLA supplementation observed in this study, particularly related to high doses of CLA, was the increase in the concentration of plasmatic insulin, inducing insulin resistance, possibly on account of the increase in the concentration of free fatty acids.<sup>62</sup>

Risérus et al.,<sup>55</sup> when verifying the effect of CLA supplementation of different isomers in obese individuals with metabolic syndrome, observed that specifi-

cally the trans-10, cis-12 CLA isomer was capable of increasing the oxidative stress and also some inflammatory markers such as C-reactive protein. Hence, a much narrow relationship seems to exist between the increase in oxidative stress (lipid peroxidation) and the induction of insulin resistance observed in these individuals.

Brown & McIntosh<sup>63</sup> also observed a reduction of the sensitivity to insulin with a consequent increase in glycemia in individuals supplemented with 3.4 g/day of the trans-10, cis-12 CLA isomer. This increase in glycemia was also observed in the CLA group in the study of Smedman & Vessby<sup>19</sup> when compared to the control group.

Smedman & Vessby,<sup>19</sup> when they evaluated the supplementation with a mixture of CLA isomers in healthy males and females, demonstrated that there is an increase in the plasmatic concentration of HDL-cholesterol, although this increase has been less than that found in the control group. They also reported an increase in the ApoB. Alterations in lipid profile were also observed by Risérus et al.<sup>55</sup> in obese men, indicating a specific tendency of the trans-10, cis-12 CLA isomer in reducing the concentration of HDL-cholesterol and in increasing the concentration of VLDL-cholesterol. Moreover, other studies also evidenced reduction of the HDL-cholesterol through CLA supplementation<sup>21,64</sup> although these studies are still controversial since Zambell et al.<sup>40</sup> reported that adults supplemented with CLA did not present any modifications in the profile of plasmatic lipids.

In the study of Medina et al.,<sup>67</sup> the CLA group was compared to the control group during the seven weeks which followed supplementation and there was a reduction of the plasmatic concentration of leptin secreted by the adipocytes according to the amount of adipose tissue in the system.<sup>68</sup> But this effect disappeared after the ninth week, suggesting that the loss of adipose tissue was not continuous after the end of supplementation.

In spite of the studies reported above, Whigham et al.<sup>69</sup> demonstrated in that CLA may be used safely in healthy obese individuals over a period of 12 months without causing side effects. This research consisted of three phases where the individuals received 6 g/day of CLA or placebo. The first phase consisted of hypocaloric diet (13 calories/day for ideal weight kilo) for 12 weeks or until there was a reduction from 10 to 20% of the initial weight. In the second phase, from the 12<sup>th</sup> to the 28<sup>th</sup> week, the individuals were re-fed a diet ranging from 25 to 30 calories/day for ideal weight kilo. The third phase was free, where the individuals of both groups took CLA from the 28<sup>th</sup> week up to the 52<sup>nd</sup> week. Blood samples were utilized for evaluation of liver function, glucose, insulin, plasmatic lipids and hemogram. The adverse effects reported, such as cutaneous rash, depression, irritability/aggressiveness, alopecia and infection, occurred in less frequency in the CLA group. There was no significant difference among the groups

as regards the concentration of plasmatic insulin, and only in the second week of supplementation it was observed a significant increase in plasmatic glucose in the CLA group ( $93.1 \pm 1.5$  mg/dL) was observed, compared to the placebo group ( $87.2 \pm 1.6$  mg/dL). At the end of the 12 months of supplementation it was evidenced that no one of the participants developed intolerance to glucose.

## Conclusion

In spite of having already been demonstrated that CLA prevents the development of obesity in specific animal models, these metabolic effects of CLA in humans seem really complex, and not much clarified yet. The propriety of CLA of controlling obesity in humans is still much controversial, taking into account that most of the conducted clinical studies present considerable methodological differences as regards the studied population, dose and types of supplement isomers, duration of the study, and the use of different techniques for evaluation of body composition. This lack of standardization as regards the methodology of studies implies in the limitation of conclusions.

In this way, it is understood that additional studies on CLA in humans are necessary having as objective an in-depth evaluation of its main effects to health, its mechanisms of action, identification of the active isomers and their particularities, side effects and damages to health, with a well defined methodology as regards the sample, type of isomer, time of supplementation, control of physical activity and dieting.

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