Dietary Effect of Conjugated Linoleic Acid on Lipid Levels in White Adipose Tissue of Sprague-Dawley Rats

Masao Yamasaki¹, Keiko Mansho¹, Hiroko Mishima¹, Masaaki Kasai², Michihiro Sugano³, Hirofumi Tachibana¹, and Koji Yamada¹†

¹Laboratory of Food Science, Department of Food Science and Technology, Faculty of Agriculture, Kyushu University, Fukuoka 812-8581, Japan
²Nagoya Factory, Rinoru Oil Mills Co. Ltd., 37-15 Shiomi-cho, Minakoku, Nagoya 455-0028, Japan
³Faculty of Human Life Sciences, Prefectural University of Kumamoto, Kumamoto 862-8502, Japan

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We examined the effect of dietary conjugated linoleic acid (CLA) on lipid parameters in the liver, white adipose tissue (WAT) and brown adipose tissue (BAT) of Sprague-Dawley rats and found that it reduced the levels of triglycerides and non-esterified fatty acid in the liver and WAT without significant change in the BAT lipid levels. These results suggest that CLA has an obesity-preventing action. 

Key words: conjugated linoleic acid; white adipose tissue; brown adipose tissue; liver

Conjugated linoleic acid (CLA) is a geometric term for the positional and structural isomers of linoleic acid. CLA has been reported to have anti-carcinogenic, anti-atherosclerotic, anti-diabetic and anti-allergic activities. In addition, CLA has been reported to reduce body fats, and to decrease the weight of white adipose tissue (WAT) in rats. WAT stores the excess energy from the diet as neutral lipids and supplies this energy as free fatty acid and glycerol when there is an inadequate supply of energy. The WAT adipocytes usually contain 0.5-0.9 µg (the highest limit is 1.2 µg) of lipids per cell and their diameters are 10-200 µm. The number of adipocytes is usually around 300 billion while 400-600 billion cells per body are common with obesity. In addition, the weight of WAT can constitute 30-40% of body weight in obese persons against approximately 20% in normal person. In the present paper, we report the dietary effect of CLA on the lipid metabolism of Sprague-Dawley rats to clarify the mechanism for the fat-reducing activity of CLA.

CLA and safflower oil (SAF) were supplied by Rinoru Oil Mills Co. (Nagoya, Japan). CLA was composed of 34.7% (c-9, t-11 and t-9, c-11 isomers), 35.6% (t-10, c-12), 2.3% (c-9, c-11 and c-10, c-12) and 1.6% (t-9, t-11 and t-10, t-12) isomers of octadecadienoic acid. Four-week-old male Sprague-Dawley rats (Seiwa Experimental Animals, Fukuoka Japan) were acclimatized in an air-conditioned room for one week. The rats were then separated into three groups of six animals each who were given free access to an AIN-93G diet. This diet contained 7% SAF (control group), 6% SAF + 1% CLA (1% CLA group) or 5% SAF + 2% CLA (2% CLA group). The food intake and body weight were recorded every other day. After 3 weeks of feeding, the rats were killed by withdrawing blood from the abdominal aorta under light diethyl ether anesthesia. After the collected blood, WAT, BAT and the liver were excised. The sera and tissues were stored at −80°C before the analysis. Lipid extraction from these samples was performed by the method of Folch et al. The triglyceride (TG), phospholipid (PL) and non-esterified fatty acid (NEFA) levels in WAT, BAT, the liver and serum were analyzed by using enzymatic kits (Wako Pure Chemicals, Osaka, Japan).

There was no significant difference among the dietary groups in their food intake, body weight, weight gain during the feeding period, food efficiency, and tissue weights of WAT, BAT and the liver (data not shown). On the other hand, CLA significantly decreased the WAT TG level, as shown in Table 1. In the case of PL, CLA had no significant effect in WAT (Table 1), nor in BAT and the serum (data not shown). The liver TG level tended to be decreased by CLA administration. The serum TG level in the 1% group was significantly lower than that of the control group, while the level of the 2% CLA group was intermediate between the two other groups (Fig. 1). CLA markedly reduced the serum and liver NEFA levels in a dose-dependent manner as shown in Fig. 1. In the case of WAT, the NEFA level of the 1% CLA group was significantly lower than that of the control group.

Table 1. Effect of Conjugated Linoleic Acid on Lipid Parameters in the White Adipose Tissue of Sprague-Dawley Rats

<table>
<thead>
<tr>
<th></th>
<th>Total lipids (mg of tissue)</th>
<th>TG</th>
<th>PL (µEq/g of tissue)</th>
<th>NEFA (µEq/g of tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>596±18</td>
<td>21.7±4.6</td>
<td>13.7±1.3³</td>
<td></td>
</tr>
<tr>
<td>1% CLA</td>
<td>636±19</td>
<td>281±31 µ²</td>
<td>20.3±3.4</td>
<td>8.2±0.5³</td>
</tr>
<tr>
<td>2% CLA</td>
<td>652±4</td>
<td>219±30³</td>
<td>19.5±2.9</td>
<td>10.9±0.8³</td>
</tr>
</tbody>
</table>

Each value is the mean±SE for 6 rats.

Abbreviations: CLA, conjugated linoleic acid; WAT, white adipose tissue; BAT, brown adipose tissue; TG, triglyceride; PL, phospholipid; NEFA, non-esterified fatty acid; SAF, safflower oil; PPAR, peroxisome proliferator-activated receptor; TZD, thiazolidinedione

† To whom correspondence should be addressed. Tel/Fax: +81-92-642-3007; E-mail: yamadako@agr.kyushu-u.ac.jp

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control group, while the level of the 2% CLA group was intermediate between the two other groups.

In obesity, the lipid content of each adipocyte is increased and the cells become hypertrophic and cause hyperplasty. Thus, excess storage of TG in adipocytes is a feature of obesity. The results in this report suggest that dietary CLA would reduce the risk of hypertrophy and/or hyperplasty. NEFA serves as lipid fuel released from adipocytes by lipolysis into the circulation system. The stimulators of NEFA release are insulin, catecholamines, the growth hormone and cortisol. The release of NEFA from upper-body subcutaneous fat has been related to the level of the upper-body fat mass. An excess NEFA level could be a risk factor of obesity because it induced a reduction in insulin sensitivity by lowering the potential for glycogen synthesis, hypertriglyceridemia and reduction of insulin clearance by hepatocytes. The reduction of the serum TG and WAT NEFA levels was more marked in the 1% CLA group than in the 2% CLA group. It is thus considered that the optimum dose would be that to exert an effect on particular lipid parameter. In the present study, dietary CLA reduced NEFA levels in the serum and liver, so dietary CLA could lighten the risk of obesity and related disease. BAT has thermogenic activity resulting from uncoupling protein, and its dysfunction or reduction of its function could cause obesity and hypertriglyceridemia. It has been reported that fasting also caused a reduced BAT function and, as a result, the PL and TG levels were increased and the weight was decreased. In this present study, CLA did not affect BAT lipid levels and weight, so it is considered that CLA did not affect the BAT function.

It is believed that peroxisome proliferator-activated receptor (PPAR) γ is a key factor for adipocytes differentiation. Thiazolidinedione (TZD) is an insulin sensitizers and could induce the differentiation of preadipocytes to mature adipocytes. TZD has been reported to be a ligand of PPARγ and it has been considered that TZD functioned via PPARγ activation. On the other hand, it has been reported that CLA normalized impaired glucose tolerance like TZD and that CLA also elevated the levels of mRNA belonging to PPARγ-responsive genes. Consequently, CLA could regulate adipocyte differentiation via PPARγ regulation and exert a preventive effect on obesity.

In conclusion, CLA reduced the accumulated lipid levels in WAT and reduced the level of NEFA. Thus, dietary CLA could be an anti-obesity food component which would regulate diverse effects via PPAR activation.

References
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