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Conjugated Linoleic Acid (CLA) Supplementation for 8 Weeks Reduces Body Weight in Healthy Overweight/Obese Korean Subjects

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Abstract In the present study, a randomized, double-blind, placebo-controlled trial to determine the effect of conjugated linoleic acid (CLA) supplementation (50:50 ratio of *cis*-9, *trans*-11 and *trans*-10, *cis*-12 isomers) for 8 weeks on body composition and biochemical parameters in healthy overweight/obese (body mass index, BMI≥23 kg/m^2) Korean subjects was performed. Thirty participants (3 males and 27 females) were randomized to receive placebo (2.4 g olive oil/day) or 2.4 g/day CLA (mixture containing 36.9% of *cis*-9, *trans*-11 and 37.9% of *trans*-10, *cis*-12). Eight weeks of CLA supplementation significantly decreased body weight by −0.75 kg, BMI by −0.27 kg/m^2, and hip circumference by -1.11 cm. The reduction of body weight was ascribed to the reduction of body fat mass (−0.59 kg) and lean body mass (−0.18 kg), although these changes were not significant. No significant differences in serum lipid profiles, liver function enzyme activities, and protein concentration were observed in either the CLA or placebo groups. These results indicate that short term supplementation (8 weeks) with CLA (2.4 g/day) may decrease body weight in Korean overweight/obese subjects.

Key words: conjugated linoleic acid, overweight, obese, body composition

Introduction

Conjugated linoleic acid (CLA) is a collective term used to describe a mixture of positional and geometric isomers of linoleic acid with conjugated double bonds (i.e., the 2 double bonds are separated by 1 single bond). The double bonds, each of which may be in the *cis* or *trans* configuration, can be in any position on the carbon chain. They are, however, most frequently found in positions 8 and 10, 9 and 11, 10 and 12, or 11 and 13 (1).

CLA has been detected in milk fat, cheese, and ruminant meat (2). The *cis*-9, *trans*-11 (*c*9,*t*11)-CLA isomer is naturally produced through the biohydrogenation of unsaturated fatty acids by the rumenal bacterium *Butyrvibrio fibrisolvens* in ruminants, such as cows, sheep, goats, and camels (3,4). Most of the CLA products sold as dietary supplements for human consumption contain 60-90% CLA in the form of either free fatty acids or triglycerides, and they usually contain a mixture of isomers, predominantly *cis*-9, *trans*-11 (*c*9,*t*11), and *trans*-10, *cis*-12 (*t*10,*c*12) isomers (5).

CLA is known to have beneficial biologic effects such as inhibiting carcinogenesis, attenuating atherosclerosis, diabetes management, reducing inflammation, and positively influencing the immune response in animal models (6-10). The effect of CLA on body composition has been studied extensively not only in animals, but also in human clinical studies, specifically with regard to the reduction of body fat mass and a possible increase in lean body mass (11,12).

The scale of the obesity epidemic creates a pressing consumer need as well as an enormous business opportunity for the successful development and marketing of food products with added benefits for weight control (5,13,14). Among the various food products used for weight control, the market size of CLA has increased considerably year by year since it appeared on the market. According to experts, it is reported that the CLA market has increased from 35 million dollars in 2000 to 2 billion in 2004, especially in the USA, Europe, and Japan, and it is expected that the number will increase gradually in the future (15). In Korea, CLA is available over the counter in health food stores and via home shopping, and is getting much attention due to its potential health benefits since its admission as a functional health food for weight control by the Korea Food & Drug Administration in 2005 (16).

Although a number of controlled clinical studies in humans have been published investigating the effect of CLA on body composition, relatively little published data are available from Asia regarding Korean subjects.

In this study, therefore, we examined the effect of CLA supplementation for 8 weeks on body composition and biochemical parameters in healthy overweight (body mass index, BMI≥23 kg/m^2) Korean subjects.

Materials and Methods

Subjects Thirty apparently healthy subjects aged 19-65 years with a BMI of 23-38 were recruited from Y Fitness Center, Seoul, Korea. The procedures were explained in detail to all the volunteers in advance, and all gave their signed informed consent before participating in the study. The exclusion criteria included drug therapy, special diets, or the use of dietary substitutes for weight loss 2 weeks prior to the start of the study. Subjects with diabetes mellitus, renal, liver, pancreatic or chronic inflammatory or infectious diseases, cardiac failure or malignant tumors were excluded. The study was performed between October

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2007 and January 2008. Individual characteristics, health status, and smoking habits were obtained by questionnaire. This study was approved by the Hannam University Ethics Committee and conducted in agreement with the Declaration of Helsinki of 1975 as revised in 1983 and in accordance with the International Conference on Harmonization guidelines.

Study design The design adopted was a randomized double-blind placebo-controlled design. The subjects were assigned at random to the placebo group (2.4 g olive oil/4 capsules, n=15) or CLA supplement group (2.4 g CLA/4 capsules, n=15). The active soft gel capsule contained 750 mg olive oil of which 78.8% was CLA (Lipozen, Inc., Pyontaek, Korea) containing 36.9% of *cis*-9, *trans*-11 isomer and 37.9% of *trans*-10, *cis*-12 isomer and produced by chemical isomerization of linoleic acid from safflower oil. All subjects were on an *ad libitum* diet and participated in a standard training program offered by local training center 3 days/week.

Clinical assessment Individual characteristics (including smoking, drinking, and exercise habits) and demographic data were recorded when subjects entered the study (at week 0). Weight, BMI, waist and hip circumferences, and body composition were recorded before and after the study (week 0 and 8). Body composition was measured with the bioimpedence analyzer SlimManager N40 (Uhealthpia, Inc., Los Angelis, CA, USA). Waist and hip circumferences were measured by standard protocols. The measurements were then used for calculating the BMI and waist/hip ratio. Blood was drawn from the volunteers after overnight fasting and centrifuged (450×g for 30 min) to obtain plasma or serum, which was then stored at −80°C until further analysis. Serum lipid profiles [total cholesterol, high density lipoprotein (HDL)-cholesterol, and triglycerides], albumin concentration, alanine aminotransferase (AST), and aspartate aminotransferase (ALT) activities were measured using assay kits (Bioclinical Systems, Anyang, Korea), and a photometric autoanalyzer (CH-100 Plus; SEAC, Calenzano, Italy). Plasma low density lipoprotein (LDL)-cholesterol levels were calculated using the formula developed by Friedewald *et al.* (17), and the atherogenic index was calculated according to the following formula: (total cholesterol-HDL cholesterol)/HDL cholesterol.

Statistical analysis Data were analyzed using the SPSS 14.0 package for Windows. Values were expressed as mean ±standard error (SE) unless stated otherwise. Statistical differences between groups and within groups were considered significant at $p<0.05$ by Student's *t*-test and paired *t*-test. Categorical variables were analyzed by using the χ^2 test.

Results and Discussion

Study subjects No significant differences were found between the 2 groups in demographic variables such as gender, age, smoking, alcohol, and exercise habits, and in baseline registrations of height, weight, BMI, waist and hip circumference, body composition, and serum biochemical parameters (Table 1-3).

Effect of CLA on weight, BMI, and body composition Eight weeks of CLA supplementation significantly decreased body weight by −0.75 kg ($p=0.006$), BMI by −0.27 kg/m^2 ($p=0.007$), and hip circumference by −1.11 cm ($p=0.037$), whereas there was no change in the placebo group (Table 2). The reduction of body weight in the CLA group was ascribed to the reduction of body fat mass (−0.59 kg) and lean body mass (−0.18 kg), although these changes were not significant (Fig. 1). CLA has been studied extensively in various animal species and, in general, it is now widely recognized that feeding CLA to animals such as mice,

Table 1. Characteristics of the study subjects

	CLA	Placebo	*p*
Sex			
Male/Female (n)	2/13	1/14	0.82
Age (yrs)[1)]	38.7±4.2	40.7±4.0	0.72
Height (cm)[1)]	161.7±2.0	158.8±1.0	0.20
Tobacco use (%)[2)]	11.1	0	0.43
Alcohol use (%)[3)]	40.0	58.3	0.77
Exercise (%)[3)]	88.9	83.3	0.61

[1)]Values for age and height are given as mean±SE.
[2)]Tobacco and alcohol use are expressed as the % subjects who answered positively to these questions (% yes).
[3)]Exercise is expressed as the % subjects who answered 'do exercise regularly'.

Table 2. Effect of CLA supplementation on body composition

	CLA (n=15)			Placebo (n=15)		
	Week 0	Week 8	Δ8-0	Week 0	Week 8	Δ8-0
Body weight (kg)	67.1±2.9[1)]	66.3±2.8**	-0.75±0.23	65.5±2.6	65.4±2.6	-0.12±0.25
Body mass index (kg/m^2)	25.5±0.8	25.3±0.8**	-0.27±0.09	26.3±1.0	25.9±1.0	-0.39±0.36
Body fat mass (kg)	21.3±1.3	20.7±1.3	-0.59±0.35	20.3±1.6	20.2±1.5	-0.16±0.31
% Body fat	31.6±0.9	31.1±1.1	-0.52±0.44	31.5±1.3	31.4±1.2	-0.14±0.35
Lean body mass (kg)	45.8±2.0	45.6±2.0	-0.18±0.33	44.1±1.1	44.1±1.1	0.04±0.18
Muscle weight (kg)	40.4±2.7	42.3±1.8	1.89±2.02	40.9±1.0	40.9±1.0	0.03±0.16
Waist circumference (cm)	83.5±2.2	83.3±2.1	-0.25±0.89	83.9±2.6	83.1±2.2	-0.82±0.83
Hip circumference (cm)	99.6±1.3	98.5±1.4*	-1.11±0.48	99.4±1.7	98.9±1.6	-0.57±0.56
Waist-hip ration	0.84±0.02	0.84±0.02	0.007±0.010	0.84±0.02	0.84±0.01	-0.003±0.007

[1)]Mean±SE; *,**statistically significant at $p<0.05$, $p<0.01$ by paired *t*-test in the CLA supplemented group, respectively.

Table 3. Effect of conjugated linoleic acid (CLA) supplementation on serum lipid profiles, AST, ALT activity, and albumin concentration

	CLA (n=15)			Placebo (n=15)		
	Week 0	Week 8	Δ8-0	Week 0	Week 8	Δ8-0
Total cholesterol (mg/dL)	204.0±7.3[1)]	213.2±10.1	9.23±6.17	184.9±7.8	189.5±5.6	4.58±7.10
HDL-cholesterol (mg/dL)	47.6±2.4	47.7±2.8	0.11±1.87	50.7±3.7	48.2±2.7	-2.58±4.42
Triglycerides (mg/dL)	98.5±5.5	93.7±6.9	-4.85±8.22	90.7±7.4	80.2±6.4	-10.50±4.98
LDL-cholesterol (mg/dL)	136.8±7.7	146.7±10.7	10.01±6.09	113.5±7.4	125.1±6.0	9.75±7.12
Atherogenic index	3.5±0.3	3.7±0.3	0.21±0.20	2.9±0.3	3.1±0.3	0.21±0.43
AST[2)] (U/L)	24.4±1.2	27.8±4.4	-1.29±1.15	28.2±2.9	24.9±2.4	-3.35±2.11
ALT[3)] (U/L)	24.9±3.0	24.7±3.0	-1.58±1.62	28.0±3.1	23.5±2.9	-4.50±2.58
Albumin (g/dL)	5.1±0.1	5.0±0.1	-0.15±0.08	5.1±0.1	5.0±0.1	-0.13±0.06

[1)]Mean±SE.
[2)]Alanine aminotransferase.
[3)]Aspartate aminotransferase.

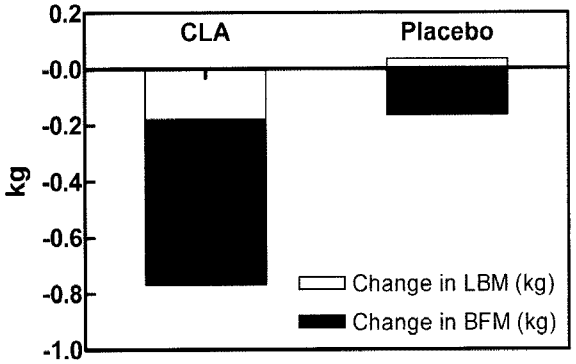

Fig. 1. Changes in body fat mass (BFM) and lean body mass (LBM) of subjects given conjugated linoleic acid (CLA) or placebo for 8 weeks.

hamster, rats, chickens, and dogs, results in changes in body composition through the lowering of body weight and fat mass and a relative increase in lean body mass (18). However, research on the effects of CLA in humans has produced inconsistent results. According to a recent meta-analysis, 7 studies reported decreases in body fat and 10 reported no statistical effect among 17 placebo based studies looking at the effect of CLA on weight loss in humans (12). In the present study, 2.4 g/day CLA supplementation for 8 weeks significantly lowered body weight and BMI in overweight/obese subjects. These results are consistent with a previous human study demonstrating that supplementation with 0.7 g CLA (33.8% *c*9,*t*11 and 35.2% *t*10,*c*12 isomers)/day for 4 weeks followed by 1.4 g CLA/day for 4 weeks significantly reduced body fat mass (–0.7 kg) during the second period in Greek subjects aged 19-24 (baseline BMI: 23.8±2.7 kg/m^2). This study also showed reductions of body weight and BMI by –1.0 kg and –0.4 kg/m^2 during 8 weeks in the CLA group, which were not statistically significant, although the differences were relatively higher than those from our study (19). Risérus *et al.* (20) reported that 4 weeks of CLA supplementation (4.2 g/day, 36.9% *c*9,*t*11 and 37% *t*10,*c*12 isomers) significantly decreased abdominal fat measured by sagittal abdominal diameter in Swedish obese men aged 39-64 (baseline BMI: 32±2.7 kg/m^2). On the contrary, lean women supplemented with 3 g of CLA/day for 64 days were reported to have no significant changes in body composition compared to those given the placebo, although % body fat decreased by 0.67 with CLA vs. an increase of 0.05 with the placebo (21). The discrepancies between studies might be ascribed to CLA isomer composition and dosage, subject characteristics, study duration, and measurement methods. Therefore, Larsen *et al.* (1) suggested that the studies should be interpreted individually and differences between study groups (CLA vs. placebo) might be considered as significant whenever the *p* values are below 0.05 for the treatment. The mechanisms of apparent weight loss due to CLA are thought to be mediated by increased energy expenditure and the enhancement of fatty acid oxidation, in both adipocytes and skeletal muscle cells, and increased lipolysis in adipocytes based on animal studies (22,23)

Effects of CLA on laboratory blood analysis Table 3 shows the changes in laboratory blood parameters measured at the baseline and after 8 weeks of supplementation. No significant differences in serum lipid profiles, liver function enzyme activities, and albumin concentration were observed in either the CLA or placebo groups. Previous clinical studies in humans have reported various effects of CLA supplementation on blood lipid profiles, including a reduction of very low density lipoprotein (VLDL) without any effect on HDL or LDL, a reduction of HDL, and no effects on lipid profiles (24-26). The results obtained to date from clinical studies indicate that the 3.4-6.0 g/day of CLA supplementation induces no significant changes in serum AST and ALT activities in humans (26,27). In accordance with previous studies, there were no adverse effects of CLA supplementation for 8 weeks on blood biochemical parameters examined in healthy overweight/obese subjects in this study.

In conclusion, we found that supplementation with 2.4 g/day CLA for 8 weeks decreases body weight, BMI, and hip circumferences in Korean overweight/obese subjects without any adverse effects.

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References

1. Larsen TM, Toubro S, Astrup A. Efficacy and safety of dietary supplements containing CLA for the treatment of obesity: Evidence from animal and human studies. J. Lipid Res. 44: 2234-2241 (2003)
2. Sehat N, Yurawecz MP, Roach JAG, Mossoba MM, Kramer JKG, Ku Y. Silver-ion high-performance liquid chromatographic separation and identification of conjugated linoleic acid isomers. Lipids 33: 217-221 (1998)
3. Kepler CR, Hirons KP, McNeill JJ, Tove SB. Intermediates and products of the biohydrogenation of linoleic acid by *Butyrinvibrio fibrisolvens*. J. Biol. Chem. 25: 1350-1354 (1966)
4. Chin SF, Liu W, Storkson JMS, Ha YL, Pariza MW. Dietary sources of conjugated dienoic isomers of linoleic acid, a newly recognized class of anticarcinogens. J. Food Compos. Anal. 5: 185-197 (1992)
5. Kovacs EMR, Mela DJ. Metabolically active functional food ingredients for weight control. Obes. Rev. 7: 59-78 (2006)
6. 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 16: 3037-3043 (1995)
7. Lee KN, Kritchevsky D, Pariza MW. Conjugated linoleic acid and atherosclerosis in rabbits. Atherosclerosis 108: 19-25 (1994)
8. Houseknecht KL, Vanden Heuvel JP, Moya-Camarena SY, Portocarrero CP, Peck LW, Nickel KP, Belury MA. Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty *fa/fa* rat. Biochem. Bioph. Res. Co. 244: 678-682 (1998)
9. Bassaganya-Riera J, Reynolds K, Martino-Catt S, Cui YZ, Hennighausen L, Gonzalez F, Rohrer J, Benninghoff AU, Hontecillas R. Activation of PPAR gamma and delta by conjugated linoleic acid mediates protection from experimental inflammatory bowel disease. Gastroenterology 127: 777-791 (2004)
10. Miller CC, Park Y, Pariza MW, Cook ME. Feeding conjugated linoleic acid. Biochem. Bioph. Res. Co. 198: 1107-1112 (1994)
11. Larsen TM, Toubro S, Astrup A. Efficacy and safety of dietary supplements containing CLA for the treatment of obesity: Evidence from animal and human studies. J. Lipid Res. 44: 2234-2241 (2003)
12. Whigham LD, Watras AC, Schoeller DA. Efficacy of conjugated linoleic acid for reducing fat mass: A meta-analysis in humans. Am. J. Clin. Nutr. 85: 1203-1211 (2007)
13. Lee CH. Functional food of interest to ASEAN: From traditional experience to modern production and trading. Food Sci. Biotechnol. 13: 390-395 (2004)
14. Han DS, Kwon EK, Kim DW, Kim YE, Lee CH, Kim IH. Biocellulose reduces body weight gain of rats fed high-fat diet. Food Sci. Biotechnol. 15: 70-76 (2006)
15. Arthi V. CLA-The Market Shaping Up! Available from http://www.frost.com/ prod/ servlet/market-insight-top.pag?docid=86833605. Accessed Apr. 22, 2008.
16. Food and Drug Administration. Approved healthy functional food in Korea. Available from http://www.kfda.go.kr. Accessed Apr. 22, 2008.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem. 18: 499-502 (1972)
18. Nagao K, Yanagita T. Conjugated fatty acids in food and their health benefits. J. Biosci. Bioeng. 100: 152-157 (2005)
19. Mougios V, Matsakas A, Petridou A, Ring S, Sagredos A, Melissopoulou A, Tsigilis N, Nikolaidis M. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. J. Nutr. Biochem. 12: 585-594 (2001)
20. Risérus U, Berglund L, Vessby B. Conjugated linoleic acid (CLA) reduced abdominal adipose tissue in obese middle-aged men with signs of the metabolic syndrome: A randomised controlled trial. Int. J. Obes. Relat. Metab. Disord. 25: 1129-1135 (2001)
21. Zambell KL, Keim NL, Van Loan MD, Gale B, Benito P, Kelley DS, Nelson GJ. Conjugated linoleic acid supplementation in humans: Effects on body composition and energy expenditure. Lipids 35: 777-782 (2000)
22. West DB, Blohm FY, Truett AA, DeLany JP. Conjugated linoleic acid persistently increases total energy expenditure in AKR/J mice without increasing uncoupling protein gene expression. J. Nutr. 130: 2471-2477 (2000)
23. Park Y, Storkson JM, Albright KJ, Liu W, Pariza MW. Evidence that the trans-10,*cis*-12 isomer of conjugated linoleic acid induces body composition changes in mice. Lipids 34: 235-241 (1999)
24. Risérus U, Arner P, Brismar K, Vessby B. Treatment with dietary *trans*10*cis*12 conjugated linoleic acid causes isomer-specific insulin resistance in obese men with the metabolic syndrome. Diabetes Care 25: 1516-1521 (2002)
25. Noone EJ, Roche HM, Nugent AP, Gibney MJ. The effect of dietary supplementation using isomeric blends of conjugated linoleic acid on lipid metabolism in healthy human subjects. Brit. J. Nutr. 88: 243-251 (2002)
26. Iwata T, Kamegai T, Yamauchi-Sato Y, Ogawa A, Kasai M, Aoyama T, Kondo K. Safety of dietary conjugated linoleic acid (CLA) in a 12-weeks trial in healthy overweight Japanese male volunteers. J. Oleo Sci. 56: 517-525 (2007)
27. 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. 42: 1701-1709 (2004)