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A meta-analysis of the effects of conjugated linoleic acid on fat-free mass in humans

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Abstract: Treatment of laboratory animals with a 50:50 mixture of c9,t11 and t10,c12 conjugated linoleic acid (CLA) results in fat loss and, to a smaller degree, fat-free mass (FFM) gain. In a previous meta-analysis, we found that CLA produced a fat loss, but that humans were not as responsive as mice. We performed a similar meta-analysis in the same 18 studies to test whether CLA increased FFM. Only placebo-controlled trials that measured body composition were included. We found that FFM increased during CLA treatment (0.3 ± 0.7 kg; $p = 0.05$), but that the change did not display an effect of length of treatment (0.001 ± 0.005 kg·week^{-1}; $p = 0.8$), or an effect of dosage (0.1 ± 0.1 kg·g CLA^{-1}·day^{-1}; $p = 0.3$). We conclude that FFM does increase in humans during CLA treatment, but the onset of the increase is rapid and the total increase is small (<1%).

Key words: body composition, dietary supplement, partitioning, fatty acid, biohydrogenation.

Résumé : Le traitement d'animaux de laboratoire au moyen d'un mélange (50:50) d'acides linoléiques conjugués (CLA) c9,t11 et t10,c12 suscite une perte de gras et, dans une moindre mesure, un gain de masse maigre (FFM). Dans une méta-analyse récente, nous avons observé que les CLA suscitent une perte de masse grasse, mais que les humains ne sont pas autant sensibles que les souris. Nous avons fait une méta-analyse similaire dans les mêmes 18 études pour vérifier si les CLA augmentent la FFM. Nous n'avons retenu que les essais comparatifs avec groupe placebo incluant l'évaluation de la composition corporelle. Nous avons observé que la FFM augmente au cours du traitement au moyen des CLA (0,3 ± 0,7 kg, $p = 0,05$), mais que la variation n'était pas reliée à la durée du traitement (0,001 ± 0,005 kg·semaine^{-1}, $p = 0,8$) ni à l'importance du dosage (0,1 ± 0,1 kg·g CLA^{-1}·jour^{-1}, $p = 0,3$). En conclusion, nous disons que la FFM des humains augmente au cours d'un traitement au moyen des CLA, mais que le début de l'augmentation est hâtif et l'augmentation totale, faible (<1 %).

Mots-clés : composition corporelle, supplément alimentaire, partitionnement, acides gras, biohydrogénation.

[Traduit par la Rédaction]

Introduction

Conjugated linoleic acid (CLA) is a series of geometric isomers of an 18 carbon, straight chain fatty acid with 2 conjugated double bonds. These fatty acids have been shown to have multiple biological effects beyond those of fatty acids in general, including alteration of body composition (Field and Schley 2004; Pariza 2004; Wang and Jones 2004). Of the various isomers investigated to date, Park et al. (1997) demonstrated that the most potent, with regard to alteration of body composition, is t10,c12 CLA. This isomer is usually administered along with c9,t11 CLA, because Riserus et al. (2002) found that when t10,c12 CLA was given alone, it was associated with an increase in insulin resistance that was mitigated when the 50:50 isomeric mixture was administered.

This mixture has been found to decrease fat mass and increase fat-free mass (FFM) in animals (Park et al. 1997). The effect on fat mass is dose and species dependent, with mice being the most responsive lab animal (Pariza 2004; Wang and Jones 2004). An increase in FFM has also been reported in animal studies, but the effect is considerably smaller than that for fat mass (Park et al. 1997). A recent meta-analysis by Whigham et al. (2007) of the effects of CLA on fat mass in humans found that the 50:50 CLA mixture also reduces fat mass in humans, but that humans were less responsive with regard to fat loss than mice. For that analysis, Whigham et al. (2007) combined the results from 18 human trials and found that, on average, CLA produced a slow decrease in fat mass that was relatively linear through 6 months of treatment and appeared to maximize between 1 and 2 years of treatment. The rate of fat loss was

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Table 1. Summary characteristics of the 18 studies included in the meta-analysis.

Study	BMI, kg·m^{-2}	Age, y	Dose,* g·d^{-1}	Duration, wk	Placebo, *n*	Treatment, *n*
Atkinson (1999)	27–40	20–50	2.7	26	55	36
Berven et al. (2000)	28–39	>18	3.4	12	22	25
Blankson et al. (2000)	25–35	>18		12	8	
	25–35	>18	1.7	12		11
	25–35	>18	3.4	12		7
	25–35	>18	5.1	12		11
	25–35	>18	6.8	12		10
Eyjolfson et al. (2004)	ca. 25–30	<25	3.0	8	6	8
Gaullier et al. (2004)	25–30	18–65	3.6	52	57	61
	25–30	18–65	3.6	52		60
Gaullier et al. (2005)	25–30	18–65	3.6	104	0	134
Gaullier et al. (2007)	28–32	18–65	3.4	24	52	52
Kreider et al. (2002)	healthy weight	18–29	5.8	4	12	12
Lambert et al. (2007)	<30	21–45	2.6	12	~31	~31
Malpuech-Brugere et al. (2004)	25–30	35–65	1.5†	18	15	18
		35–65	3.0†	18		18
Mougios et al. (2001)	19–24	<30	0.7 and 1.4	8	22	22
Petridou et al. (2003)	<30	19–24	2.1	7	16	16
Pinkoski et al. (2006)	20–30	20–30	5.0	7	39	38
Riserus et al. (2002)	27–39	35–65	2.7	12	19	19
	27–39	35–65	2.5†	12		19
Smedman and Vessby (2001)		23–63	4.2	12	24	26
Taylor et al. (2006)	>27	35–60	3.2	12	19	21
Watras et al. (2007)	25–30	18–44	3.4	26	18	22
Zambell et al. (2000)	25–41	20–30	1.3	9	7	12

Note: BMI, body mass index.
*Excludes weight oils other than 9c,11t and 10t,12c conjugated linoleic acid.
†t10,c12 isomer only.

dose dependent (0.02 kg fat·week^{-1}·g CLA^{-1}·day^{-1}), which, for the median dose of 3.2 g·day^{-1} of the 50:50 isomeric mixture, corresponds to a loss of fat of 0.05 kg·week^{-1}. The loss was slightly larger (0.09 kg·week^{-1}) than that in the placebo group, because fat mass tended to increase in the placebo groups.

Herein, we perform a parallel meta-analysis for change in FFM in humans during administration of CLA. We used the same studies identified in the previous meta-analysis, and investigated the effects of dose and time of CLA administration on FFM.

Materials and methods

The criteria used to identify studies for this meta-analysis were that the study be a placebo-controlled, double-blind, randomized study of CLA, and that body composition be measured by isotope dilution, dual-energy X-ray absorptiometry, densitometry, or bioelectrical impedance, so that change in fat mass and FFM, expressed as kilograms, could be obtained from the published results. Studies in which CLA was administered after weight loss to test the efficacy of weight maintenance were excluded. These criteria identified 18 studies published between 1999 and 2007. The methods for these studies were detailed in our previous meta-analysis (Whigham et al. 2007), and are summarized here in Table 1.

Statistical analysis

Results are expressed as means ± standard deviation, unless otherwise indicated. Regression analysis was performed using a least squares fit to a linear model. The criterion for statistical significance was $p < 0.05$.

Results

FFM did not change significantly in the placebo groups (–0.06 ± 0.8 kg or –0.002 ± 0.09 kg·week^{-1}) The change in FFM during CLA treatment was calculated (in kilograms) without adjustment for the nonsignificant change observed in the placebo groups. Results were plotted against the duration of the CLA treatment (in weeks) (Fig. 1). The FFM change was regressed against duration, and the change as a function of time was virtually 0 (0.001 ± 0.005 kg·week^{-1}; $p = 0.8$). Because we did not identify an effect of treatment length on change in FFM, we calculated the average change. This was 0.3 ± 0.7 kg ($p = 0.05$) in the CLA group alone and 0.3 ± 0.7 kg ($p = 0.04$) when the CLA group was compared with placebo.

To test whether there was a dose effect, the doses of CLA were calculated by multiplying CLA purity by the total dose of oil, and were expressed as grams per day of the 50:50 mixture of c9,t11 and t10,c12 CLA. The weight of the dose for the 2 groups (Riserus et al. 2002; Malpuech-Brugere et al. 2004) that were provided only the t10,c12 isomer was doubled to provide a dose weight equivalent to the more

commonly used 50:50 isomeric mixture. The change in FFM, regardless of duration of CLA treatment, was expressed as kilograms. The change in FFM did not display a dose effect (Fig. 2). The slope of the regression of increase in FFM against dose (0.01 ± 0. 1 kg·g CLA^{-1}·day^{-1} was not significant (p = 0.3).

Discussion

This meta-analysis demonstrated that treatment with a 50:50 c9,t11 and t10,c12 CLA mixture does result in a small increase in FFM in humans. Although only a few of the individual studies included in this meta-analysis reported a significant increase in FFM, the trend in FFM was positive in 19 of 28 subject groups that met the criteria for inclusion in this meta-analysis. The absence of statistical significance in most individual studies, however, is not surprising, in light of the fact that the 0.3 kg average increase in FFM reported in the current meta-analysis is generally less than the standard deviation of the techniques used for body composition analysis and, thus, type 2 errors are not uncommon. FFM increases with CLA treatment in humans and in laboratory animals. The increase, however, is small compared with the decrease in fat mass associated with CLA treatment, which we previously reported to be 0.05 kg·$week^{-1}$ for the first 6 months of treatment (Whingham et al. 2007). As such, fat loss predominates after about 6 weeks of CLA treatment. After 1 to 2 years of treatment, fat loss greatly exceeds FFM gain (2.0 kg vs. 0.3 kg).

Considering that an average overweight adult human body includes 50 to 70 kg of FFM, an increase of 0.3 kg FFM following CLA treatment is small (<1%). This effect, therefore, should probably not be classified as body building, but rather as a protective effect in light of the small loss in FFM that would typically accompany a 1 to 2 kg loss in fat mass by energy restriction (Stiegler and Cunliffe 2006).

The increase in FFM for these human studies was also small, compared with that observed in growing pigs by Ostrowska et al. (1999). In that study, the increases in lean body mass were comparable in fractional body composition to the decreases in fat. It is not clear if this difference is due to the use of a CLA mixture that contains multiple other CLA isomers, a difference in maturity, or a difference in species. More studies are needed to understand these differences and to elucidate the mechanism of CLA's effect on FFM.

Interestingly, the increase in FFM did not display an effect of time. This temporal pattern is different from the change in fat mass, which, in the previous meta-analysis of these same studies, displayed a linear increase for up to 6 months before slowing and then approaching an asymptote at about 1 year of treatment (Whigham et al. 2007).

This meta-analysis does not allow for a determination of the composition of the FFM. Only one of the included studies involved a 4-compartment body composition model, and the change in FFM was not significant in that study (Watras et al. 2007). Laboratory animal studies, however, have documented an increase in whole body protein, indicating that the FFM is not simply water (Field and Schley 2004). Further research is needed to confirm that the increase in FFM is accompanied by an increase in protein mass in humans.

Fig. 1. The change in fat-free mass (FFM) during treatment with the 50:50 mixture of c9,t11 and t10,c12 conjugated linoleic acid (CLA) did not increase with the duration of treatment (0.001 ± 0.004 kg·$week^{-1}$; p = 0.8), but did display a positive intercept (0.3 ± 0.1 kg·g^{-1}; p = 0.05), indicating that treatment produced a small average increase in FFM. Changes in FFM in the placebo groups were not significant and were numerically small (see text); therefore, the data weres plotted for CLA treatment groups without adjustment for the placebo groups.

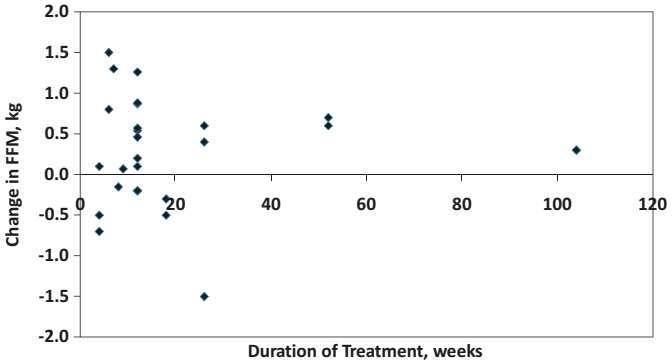
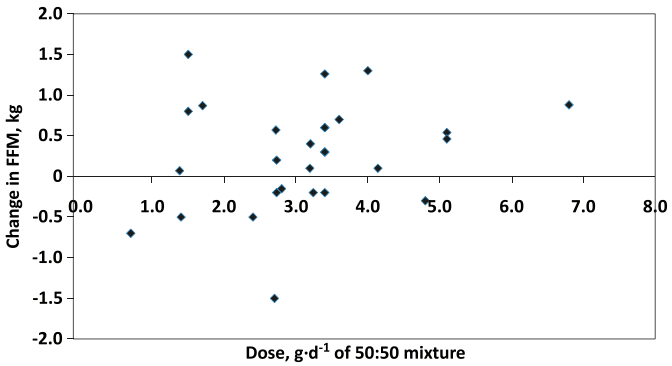


Fig. 2. The change in FFM did not significantly increase with dose of c9,t11 and t10,c12 CLA, but did trend upward (0.09 ± 0.08 kg·g^{-1}·d^{-1}; p = 0.3).



Although the increase in FFM did not display a dose effect, it did trend upward. Given the small average change in FFM, the absence of statistical significance in the current meta-analysis is not surprising, and even with this many data points, our power was insufficient to detect the effect. In conclusion, the meta-analysis did demonstrate that treatment of generally overweight but otherwise healthy adults with CLA does result in a small (<1%) increase in FFM.

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