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PROCEEDINGS

The effect of *trans*-10,*cis*-12 conjugated linoleic acid on lipogenesis is tissue dependent in hamsters

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Introduction

Conjugated linoleic acid (CLA) has been reported as a potent modulator of body composition, especially by reducing the accumulation of body fat into adipose tissue [1]. Moreover, CLA can also modify triacylglycerol metabolism in other organs and tissues that play an important role in lipid metabolism, such as the liver [1]. There is now strong evidence showing that the *trans*-10,*cis*-12 CLA isomer is mostly responsible for these effects [2]. The mechanisms by which *trans*-10,*cis*-12 CLA alters triacylglycerol metabolism have not been completely clarified.

The aim of the present work was to investigate the effects of *trans*-10,*cis*12 CLA intake on the expression of two lipogenic enzymes, acetyl-CoA carboxylase (ACC) and fatty acid synthase (FAS) and the transcriptional factors that regulate their activity, sterol regulatory element binding proteins SREBP-1a and SREBP-1c in adipose tissue and liver from hamsters fed an atherogenic diet.

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Materials and methods

The experiment was conducted with twenty 9-week-old (105 ± 1), male Syrian Golden hamsters, individually housed in metabolic cages. Hamsters were randomly divided into two dietary groups and fed a semi-purified atherogenic diet consisting of 200 g/kg of casein, 4 g/kg of L-methionine, 200 g/kg of wheat starch, 405 g/kg of sucrose, 100 g/kg of palm oil, 30 g/kg of cellulose, 4 g/kg of choline–HCl, 1 g/kg of cholesterol, vitamin mix 11 g/kg and mineral mix 40 g/kg, supplemented with 0.5% linoleic acid (control group) or 0.5% *trans*-10,*cis*-12 CLA, respectively. Animals had free access to food and water. Food intake and body weight were measured daily. At the end of the experimental period (6 weeks) animals were sacrificed under anaesthesia. Liver and adipose tissues from different anatomical locations (epididymal, perirenal and subcutaneous) were dissected, weighed, sliced and immediately frozen. Liver triacylglycerol content was determined spectophotometrically by using a commercial kit. ACC, FAS, SREBP-1a and SREBP-1c mRNA levels in epidydimal adipose tissue and liver were assessed by RT-PCR. Results are presented as means + SE of the means. Statistical analysis was performed using SPSS 11.0. Data were analysed by one-way ANOVA followed by Newman–Keuls post hoc test. Statistical significance was set-up at the $P < 0.05$ level.

Results

Differences neither in food intake nor in final body weight were found between both experimental groups. Hamsters fed the *trans*-10,*cis*-12 CLA isomer showed significantly reduced adipose tissue sizes and increased liver weight, but

Table 1 Final body weight, food intake, adipose tissue and liver weights, and hepatic triacylglycerol content of hamsters fed on the experimental diets for 6 weeks

Experimental groups	Control CLA		0.5% *trans*-10,*cis*-12 statistical significance	
	Mean	SEM	Mean	SEM
Final body weight (g)	121	3	119	1
Food intake (g/day)	6.0	0.14	5.7	0.08
Adipose tissue weight (g)				
Epididymal	2.48	0.18	1.96*	0.10
Perirenal	1.68	0.10	1.19**	0.09
Subcutaneous	3.78	0.25	2.67**	0.14
Liver				
Weight (g)	4.62	0.16	5.10*	0.11
Triacylglycerols (mg/g)	7.21	0.6	4.79**	0.48

* $P < 0.05$, ** $P < 0.01$

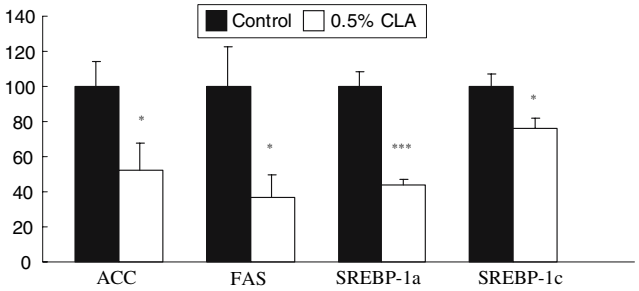

Fig. 1 Acetyl-CoA carboxylase, fatty acid synthase (*FAS*), SREBP-1a and SREBP-1c mRNA levels in edipidymal adipose tissue. * $P < 0.05$, *** $P < 0.001$

reduced hepatic triacylglycerol content (Table 1). ACC, FAS, SREBP-1a, SREBP-1c expression were significantly reduced in epididymal adipose tissue (Fig. 1). In contrast, no significant differences were observed in liver (Fig. 2).

Discussion

Conflicting results have been reported when the effects of CLA on lipogenic enzyme expression were assessed in adipose tissue. Kang et al. [3] found an increase in FAS mRNA induced by 0.2% *trans*-10,*cis*-12 CLA feeding for 4 weeks in mice. In contrast, Azain et al. [4] did not find changes in FAS activity induced by CLA feeding in rats. Other authors found reduced expression of FAS and ACC in mice [5, 6] . In the present work, *trans*-10,*cis*-12 CLA feeding significantly reduced the mRNA expression of the two specific lipogenic enzymes measured (ACC, FAS). SREBP-1a and SREBP-1c are potent activators of enzymes involved in fatty acid synthesis, and have been shown to be

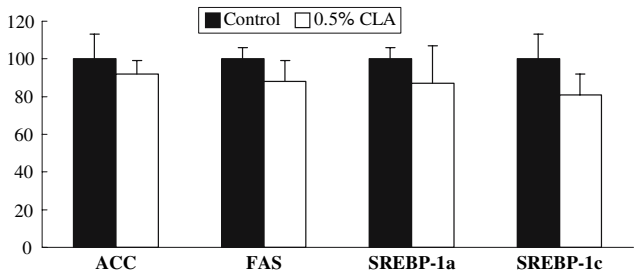

Fig. 2 Acetyl-CoA carboxylase, FAS, SREBP-1a and SREBP-1c mRNA levels in liver

affected by nutritional factors [7]. The reduction that we found in the mRNA expression of these transcriptional factors, induced by *trans*-10,*cis*-12, paralleled changes observed in ACC and FAS. Concerning the effects of CLA on liver, several studies in mice have shown that *trans*-10,*cis*-12 increased liver weight [8–13]. In some of these trials, hepatic triacylglycerol content was measured and it was concluded that hepatomegaly was due to lipid accumulation [5, 14–16]. In contrast, the studies performed on rats reported no effects on liver weight induced by CLA [4, 10, 17–20].

The present results show that feeding the *trans*-10,*cis*-12 CLA led to greater liver weight. This effect was similar to that found in mice, but in hamsters the effect was not due to increased fat accumulation; on the contrary, the triacylglycerol content in liver from animals fed this CLA isomer was significantly lower than that in the control group. With regard to the expression of lipogenic enzymes and their transcriptional factors, no significant changes were induced by *trans*-10,*cis*-12 CLA in liver.

All these results suggest that the effects of the *trans*-10,*cis*-12 CLA isomer on the expression of ACC and FAS, and the transcriptional factors that regulates these enzymes (SREBPs) are tissue-specific in hamsters. Decreased lipogenic enzyme expression in adipose tissue could contribute to reduced adipose tissue size. However, reduced liver triacylglcyerol content was not mediated by decreased lipogenesis.

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