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# Conjugated Linoleic Acid Metabolism and Body Fat Loss in Mice

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## Summary

Mice were fed conjugated linoleic acid (CLA) with or without fish oil or aspirin, which deplete tissue arachidonic acid and block arachidonic acid metabolism, respectively. Mice fed fish oil did not lose body fat when supplemented with CLA but mice fed soy oil did. Aspirin did not alter CLA-induced body fat loss. CLA may be metabolized to an isomer of arachidonic acid to induce a loss of body fat. However, this body fat loss is apparently not mediated via alteration of prostaglandin synthesis. Understanding the regulation of body fat by CLA may offer insight into the mechanisms of body fat regulation in cattle.

## Introduction

Conjugated linoleic acid (CLA) refers to a group of isomers of linoleic acid which have multiple health benefits. The *cis*-9,*trans*-11 isomer is produced naturally and deposited in the fat of ruminant animals. The CLA isomers can be metabolized like linoleic acid to longer-chain conjugated fatty acids including isomers of arachidonic acid. We previously reported (2002 Nebraska Beef Report, pp 92-93) that mice consuming a diet deficient in essential fatty acids (linoleic and linolenic acids) lost more body fat when supplemented with CLA than did control mice. While the *cis*-9,*trans*-11 isomer has no effect on body fatness, it does have other health benefits includ-

ing prevention and treatment of certain cancers. Since this isomer can be metabolized similarly to the *trans*-10,*cis*-12 isomer responsible for the loss of body fat, understanding the metabolism of one isomer may contribute to our knowledge of how several of the isomers induce biological effects. In addition, the regulation of body fat deposition is largely not understood but essential to our ability to alter that deposition. Therefore, our first objective was to determine the effect of modulating the dietary concentration of essential fatty acids (linoleic, linolenic, and arachidonic acids) on CLA-induced body fat loss.

Arachidonic acid is a precursor to the series 2 prostaglandins via metabolism by cyclooxygenase and the series 4 leukotrienes via metabolism by lipoxygenase. It is unknown if CLA, metabolized to a conjugated isomer of arachidonic acid, interferes with the normal conversion of arachidonic acid to prostaglandins or leukotrienes, or if conjugated eicosanoids are formed. Aspirin is a known inhibitor of cyclooxygenase. Our second objective was to determine if altering arachidonic acid metabolism by inhibiting cyclooxygenase would alter CLA-induced body fat loss.

## Procedure

### Experiment 1

Eighty newly weaned male mice were fed either a control diet (20% soy oil) or a fish oil diet (20% menhaden fish oil) for 6 weeks. Half of each group was subsequently supplemented with 0.5% CLA, replacing either soy or fish oil, for an additional 2 weeks. The mice then were killed and the retroperito-

neal fat pads, epididymal fat pads and livers were weighed and collected. Body fat and lean mass were determined by dual x-ray densitometry.

### Experiment 2

Eighty male mice (9 weeks of age) were fed either a control (7% soy oil), CLA (6% soy oil + 1% CLA), aspirin (control + 400 mg/kg diet aspirin), or aspirin+CLA (CLA diet + 400 mg/kg diet aspirin) diet for 2 weeks. Mice were killed and tissues were collected as in Experiment 1.

## Results

### Experiment 1

Adipose tissue from mice fed fish oil had a greater concentration of long-chain n-3 polyunsaturated fatty acids and arachidonic acid and less linoleic and linolenic acids than those fed soy oil (Table 1). Neither fish oil feeding nor the addition of CLA affected feed intake or body weight. Feeding either fish oil or CLA reduced ( $P < 0.05$ ) body fat compared to control (Figure 1). However, fat source by CLA interaction was observed ( $P < 0.01$ ); mice fed fish oil + CLA were not leaner than mice fed fish oil or CLA alone. Similar results were observed in fat pad weights. Fish oil-fed mice also had heavier ( $P < 0.001$ ) livers and greater ( $P < 0.05$ ) lean mass than soy oil-fed mice.

We hypothesized that feeding a basal fat source with altered essential fatty acid concentrations would alter the sensitivity to CLA-induced body fat loss. We previously reported support of this hypothesis, in that a greater loss of body fat was

**Table 1. Effect of fish oil and/or conjugated linoleic acid (CLA) on fatty acid concentrations in retroperitoneal fat pads, Experiment 1.**

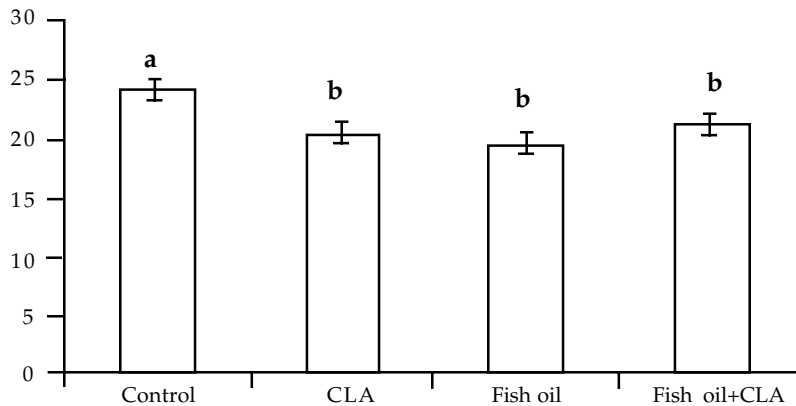
Fatty Acid, % <sup>a</sup>	Control <sup>b</sup>	CLA <sup>b</sup>	Fish Oil <sup>b</sup>	Fish Oil+CLA <sup>b</sup>	SEM <sup>c</sup>
C18:2 n-6	50.67 <sup>d</sup>	48.30 <sup>d</sup>	8.94 <sup>e</sup>	10.98 <sup>e</sup>	1.701
C18:3 n-3	3.43 <sup>d</sup>	2.48 <sup>e</sup>	1.67 <sup>f</sup>	1.78 <sup>f</sup>	0.107
C20:4 n-6	0.08 <sup>e</sup>	0.06 <sup>e</sup>	0.29 <sup>d</sup>	0.28 <sup>d</sup>	0.021
C20:5 n-3	0.02 <sup>e</sup>	0.10 <sup>e</sup>	1.22 <sup>d</sup>	1.13 <sup>d</sup>	0.121
C22:6 n-3	0.01 <sup>e</sup>	0.02 <sup>e</sup>	0.38 <sup>d</sup>	0.38 <sup>d</sup>	0.040
cis-9,trans-11 CLA	0.02 <sup>e</sup>	0.34 <sup>d</sup>	0.07 <sup>e</sup>	0.48 <sup>d</sup>	0.061
trans-10,cis-12 CLA	0.00 <sup>e</sup>	0.30 <sup>e</sup>	0.96 <sup>d</sup>	0.89 <sup>d</sup>	0.110

<sup>a</sup>Fatty acids were analyzed by gas chromatography and expressed as a percentage of total fatty acids.

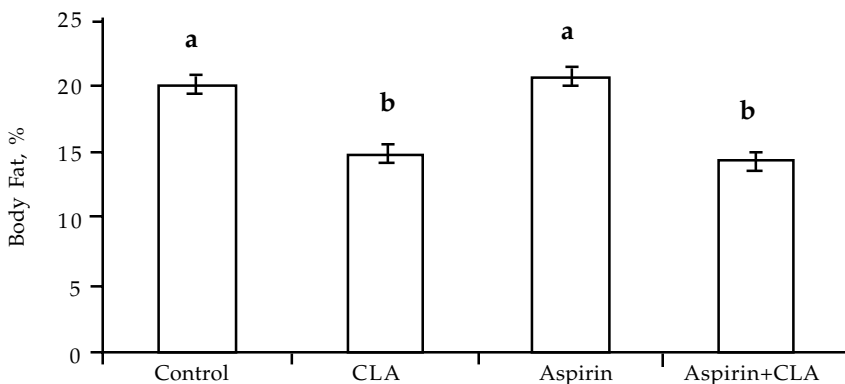
<sup>b</sup>Control (20% soy oil); CLA (19.5% soy oil + 0.5% CLA); Fish oil (20% menhaden fish oil); Fish oil+CLA (19.5% menhaden fish oil + 0.5% CLA).

<sup>c</sup>SEM = Standard error of the means.

<sup>d,e,f</sup>Different letters within a row indicate differences,  $P < 0.05$ .



**Figure 1. Effect of fish oil and (or) conjugated linoleic acid (CLA) on body fat, Experiment 1. Control (20% soy oil), CLA (19.5% soy oil + 0.5% CLA), Fish oil (20% menhaden fish oil), and Fish oil+CLA (19.5% menhaden fish oil + 0.5% CLA). <sup>ab</sup>Means with different superscripts differ,  $P < 0.01$ .**



**Figure 2. Effect of aspirin and (or) conjugated linoleic acid (CLA) on body fat, Experiment 2. Control (7% soy oil), CLA (6% soy oil + 1% CLA), Aspirin (control diet + 400 mg/kg aspirin), Aspirin+CLA (CLA diet + 400 mg/kg aspirin). <sup>ab</sup>Means with different superscripts differ,  $P < 0.001$ .**

observed in mice when both linoleic and arachidonic acids were reduced by feeding coconut oil (2002 Nebraska Beef Report, pp. 92-93). However in this experiment, no CLA-induced loss of body fat was

observed when arachidonic acid concentration was increased by feeding fish oil, although this diet also reduced linoleic acid concentration. Therefore, CLA may be metabolized to a conjugated isomer

of arachidonic acid that then results in the body fat loss observed in mice.

### Experiment 2

The addition of CLA to the diet of mice resulted in reduced feed intake ( $P < 0.05$ ) during both weeks and reduced body weight following week 2 ( $P < 0.01$ ). Aspirin feeding increased week 2-body weight ( $P < 0.01$ ). CLA supplementation reduced body fat by 26% ( $P < 0.001$ ) while aspirin had no effect (Figure 2). Similar results were observed in fat pad weights. CLA also increased liver weight ( $P < 0.001$ ) and lean mass ( $P < 0.01$ ) regardless of aspirin supplementation.

In our previous report and with Experiment 1 in this report, we indicated adipose tissue arachidonic acid concentration may be negatively correlated with the CLA-induced loss of body fat in mice. However, inhibition of arachidonic acid metabolism to the series 2 prostaglandins via cyclooxygenase did not affect CLA-induced body fat loss. Arachidonic acid is also metabolized to leukotrienes via lipoxygenase. Therefore a conjugated isomer of arachidonic acid may still interfere with arachidonic acid metabolism, but not at the level of cyclooxygenase.

Although the CLA isomer present in ruminant products, cis-9,trans-11, does not result in altered body fatness it does block cancer growth. This isomer can also be metabolized similarly to linoleic acid and the trans-10,cis-12 isomer that is responsible for the loss of body fat. Therefore, determining the pathway through which one CLA isomer induces a biological effect will give insight into the mechanism by which other isomers function.

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