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Editor's note: Belury served as a consultant for Cognis from 2000-2001, and also received an unrestricted gift from the company to her research program from 2003 through 2006.

Previous stories pertaining to Professor Belury's research:

<u>"Fat That May Benefit</u> <u>Diabetics Reduces Weight,</u> <u>Blood Sugar,"</u> 1/24/03.

## WEIGHT-LOSS SUPPLEMENT SHOWS GOOD AND BAD TRAITS

COLUMBUS, Ohio – A supplement some people turn to in hopes of losing a few pounds may have some previously unknown, unsavory side effects, suggest two new studies.

Researchers studied how mice and rats responded to the supplement <u>conjugated linoleic acid (CLA)</u>, an essential amino acid found in trace amounts primarily in beef, lamb and milk. Synthetic forms of CLA are marketed as supplements that help reduce body fat, and some manufacturers also tout CLA for reducing the risk of diabetes and certain types of cancer.

The mice and rats responded in very different ways to CLA, said Martha Belury, the lead author of both studies and an associate professor of human nutrition at Ohio State University.

Mice fed a CLA-supplemented diet lost weight very fast, but also accumulated excessive amounts of fat in their livers – a common side effect of rapid weight loss. Excessive fat accumulation in the liver is linked to insulin resistance, a hallmark of T



Martha Belury

linked to insulin resistance, a hallmark of Type 2 diabetes.

Yet CLA didn't help rats lose weight they had gained prior to taking the supplement. But it effectively decreased the amount of fat that had accumulated in the animals' livers due to the weight gain. In turn, the rats were less resistant to insulin.

"Many people take CLA as a supplement in hopes of trimming body fat, and it seems to work," Belury said. "But we're not sure what else it does to the body. Studying CLA's effects in two different animal models may help us to better understand any additional effects in humans.

"It seems that these mice and rats represent a continuum of possible side effects induced by CLA," she continued. "The question is, are humans more like mice or rats? We're probably somewhere in between."

The current mouse study appears in a recent issue of the <u>Journal</u> <u>of Lipid Research</u>, while the rat study will appear in an upcoming issue of the <u>Journal of Nutritional Biochemistry</u>.

In a study from 2003, Belury found that CLA supplements lowered body mass and blood sugar levels of diabetics. The study participants took CLA supplements for two months.

Researchers fed two groups of mice different diets. The first group ate a diet containing CLA for four weeks, followed by four weeks of a diet without CLA.

The second group of animals ate a CLA-free diet for two weeks followed by two weeks of a diet that included CLA. During the latter two weeks, some of the mice received daily injections of the antidiabetes drug rosiglitazone. The researchers found that CLA supplementation significantly decreased body fat in the first group of mice, but at the same time excessive amounts of fat accumulated in the animals' livers. Belury linked this accumulation of fat in the liver to increased insulin resistance.

Rosiglitazone makes the body more sensitive to insulin. Mice serving as controls for both groups did not consume CLA.

The researchers monitored insulin sensitivity in all mice throughout the study. They also monitored levels of adiponectin, a hormone secreted by fat tissue and thought to play a role in insulin resistance.

"Adiponectin helps regulate insulin levels," Belury said.
"Lowered levels are associated with obesity and type 2 diabetes."

The researchers found that CLA supplementation significantly decreased body fat in the first group of mice, but at the same time excessive amounts of fat accumulated in the animals' livers. Belury and her colleagues linked this accumulation of fat in the liver to increased insulin resistance.

When CLA was removed from the diet, the animals gained weight but lost fat in the liver. The mice also became less resistant to insulin.

"When we took CLA away, we lost that suppressive effect on body fat, but we were actually able to restore insulin sensitivity," Belury said. But the group of mice given rosiglitazone injections while on a CLA-rich diet neither lost weight nor became insulin resistant.

"The drug kept adiponectin levels steady during the weeks the mice consumed CLA," Belury said. "We think that's what kept the animals from becoming resistant to insulin.

"While this is an interesting finding, it doesn't mean that someone taking CLA should also take an anti-diabetic drug," she continued. "It's too soon to tell if that would be the case in humans."

In the rat study, Belury and her colleagues studied a special kind of rat model bred to gain weight quickly. These rats were also less susceptible to CLA-induced weight loss. All rats ate a high-fat diet for four weeks. For the remaining four weeks of the study, half of the rats ate a low-fat diet supplemented with CLA, while the rest of the animals ate a low-fat diet without CLA.

The supplement didn't help the rats lose weight. But it seemed to keep fat from accumulating in the animals' livers, compared to the rats eating the diet without CLA.

Belury pointed out that up to 75 percent of people with obesity and diabetes develop an illness called non-alcoholic fatty liver disease in which fat accumulates in the liver and can ultimately make a person insulin resistant.

CLA may or may not have a similar effect on humans, and it will take time to determine how the human body responds to the supplement. But clinical trials are underway – Belury is currently working with researchers from Ohio State's medical center who are conducting a clinical trial of the effects of CLA on women with diabetes.

Belury conducted the studies with Aparna Purushotham and Angela Wendel, both graduate fellows in human nutrition; and Li-Fen Liu and Gayle Shrode, both graduate research associates in human nutrition.

Support for the work was provided by <u>Cognis North America</u>, a manufacturer of synthetic CLA headquartered in Cincinnati. Support also came from the Carol S. Kennedy research award and the Anita R. McCormick fellowship.

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