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Dietary Oil May Need Help in Avoiding Any Side Effects of Weight Loss

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COLUMBUS, Ohio -- An oil made of natural fatty acids that is sometimes used as a weight-loss supplement may need to be paired with hormones or other substances to prevent health problems that can follow rapid weight loss, a new study suggests.

Conjugated linoleic acid (CLA), a compound naturally found in some meat and dairy products, can reduce body fat in some studies in humans. But a recent study in mice found that the hormone leptin adds an element of protection against side effects that can accompany fat loss with CLA.

Without leptin, fat loss occurs in mice eating a diet containing CLA, but the mice also become insulin resistant. When mice are fed CLA and given leptin, the same fat loss occurs but insulin resistance does not develop.

So though leptin is not essential to the fat loss, it has important protective effects to maintain insulin sensitivity, said Martha Belury, lead author of the study and associate professor of human nutrition at Ohio State University.

"Fat loss is not dependent on leptin but if we didn't have leptin, CLA could have some short-term effects on insulin resistance," said Belury, who also has a research appointment with the university's Ohio Agricultural Research and Development Center.

The study appears in a recent issue of the *Journal of Lipid Research*.

CLA is an essential fatty acid found naturally in trace amounts primarily in beef, lamb and milk. Synthetic forms of CLA are marketed as supplements that help reduce body fat.

But continuing research shows that there are consequences associated with the loss of fat. Because fat in the body is energy, it has to go somewhere if it is not burned away by metabolism. When CLA is driving fat out of fat tissue, the fat tends to end up in the liver or in muscles. If that fat can't be used, insulin resistance results. So Belury and colleagues are trying to find out precisely how CLA works to reduce body fat and how to prevent any associated side effects.

"You can reduce body fat, which is a good thing for a person trying to avoid diabetes. But if that body fat is lost too rapidly, the fat has to go somewhere else and in mice, it creates insulin resistance," Belury said. Sometimes, insulin resistance can lead to Type 2 diabetes.

In the animal study, Belury and colleagues tested the effects of leptin by using mice genetically engineered so they have no leptin in their bodies. These mice consume a lot of food and their metabolism is disrupted, so they tend to be quite overweight and are called fatty mice.

"Our thinking was that if you lower body fat, you also lower leptin levels. So if we have a mouse that has no leptin, what does CLA do then?" Belury said.

To create controls for comparison, the researchers gave leptin back to some of the fatty mice. Then they fed regular diets or diets containing CLA to all of the mice to observe the effects of CLA and regular diets with and without leptin present.

Finding that CLA diets can result in weight loss with or without leptin was a new finding. But more significant to understanding the mechanism, the study showed that insulin sensitivity was restored when CLA was fed with leptin present.

That finding answers just one of many questions about possible side effects associated with CLA-induced loss of body fat. The role of fat tissue in regulating metabolism is complex. It stores energy in the form of fat and also produces hormones essential to the metabolism, or burning, of the fat tissue.

In addition to continuing animal studies on CLA's interaction with hormones and other conditions associated with metabolism, Belury is leading parallel human clinical trials on the effects of CLA. So far, the research has shown that CLA can reduce body fat in postmenopausal women with Type 2 diabetes. Another trial is investigating whether CLA can suppress weight gain in people who are gaining weight because of a drug they take for diabetes management.

"People can safely take CLA, but we don't know the most effective dose for weight loss and how long people should take it. We think there are probably some subpopulations that shouldn't take it, but we don't know for sure yet," she said.

Belury conducted the study with former Ohio State nutrition graduate students Angela Wendel, now a postdoctoral researcher at the University of North Carolina; Aparna Purushotham, now with the National Institute of Environmental Health Sciences; and Li-Fen Liu, now a postdoc at Stanford University.

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