MEDICINE

Anti-Obesity and Diabetes Drug Shows Promise in Early Experiments

An experimental drug that targets the enzymes thought to slow metabolism in fat cells yielded positive results in laboratory tests on mice.

By Kelsey Lindsey
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Ian Hooton via Getty Images

Stanley Watowich, an associate professor of biochemistry and molecular biology at the University of Texas Medical Branch at Galveston, was looking for something new.

After conducting drug discovery work for viruses like West Nile, he wanted to broaden his focus and work on a disease that impacts a wider swathe of the population. Obesity — a condition that affects 36.5 percent of American adults, according to the US Centers for Disease Control and Prevention, and may lead to serious diseases including Type 2 diabetes — seemed like a good bet.

In a new study published in the journal *Biochemical Pharmacology*, Watowich and his co-authors detail a new anti-obesity and anti-Type 2 diabetes drug tested on obese mice. The drug targets an enzyme found mainly in fat cells called nicotinamide-N-methytransferase (NNMT), which has been suspected of slowing down fat cell metabolism in obese persons, making it harder to lose weight. If the drug passes further testing on mice, it would then be tested for its viability for inhibiting NNMT in humans.

"Your body is making this because it's saying, 'You're putting on weight because there's a reason for it, and we're going to help you keep this weight on,'" Watowich said. "And you and I are thinking, 'My God, don't do that, don't let me keep this weight on.'"

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The researchers developed a molecule to prevent NNMT production. Blocking the NNMT enzyme can increase fat cell metabolism, which in turn reduces the size of fat cells in tissue.

"We're going to lose weight but we're going to lose weight where it really counts, which is these fat cells," Watowich said.

In experiments, the researchers first feed mice plenty of high-fat food to make them obese. They then separated them into two groups: One received an injection of the drug, and the other group was administered a placebo. Both sets of mice kept their high-fat diet during the 11-day treatment period and ate the same amount of food, after which they were examined.

The obese mice receiving the drug lost an average of two grams while mice receiving the placebo had an average weight gain of 0.6 grams. Cholesterol levels in the first group also returned to what would be deemed normal levels for non-obese mice.

The researchers also looked at the white fat tissue mass, which contains fat cells, in the two groups. In humans, white fat congregates primarily around the hips, buttocks, and stomach when we gain weight. An excess of white fat is associated with heart disease, diabetes, cancer, and other physical ailments like sleep apnea.

The researchers found that the fat tissue mass was 30 percent less in the mice receiving the drug than the tissue mass of the placebo group. This indicates that the fat cells shrunk when the mice lost weight.

The study was published in the journal *Biochemical Pharmacology* and funded by the Department of Defense, the University of Texas Medical Branch, and the National Institutes of Health.

Watowich bills the drug as both an anti-obesity and anti-Type 2 diabetes drug, given the high risk of developing the latter disease if one is obese. A 2006 study analyzing data from a secondary care diabetes clinic in the United Kingdom found that 86 percent of patients with Type 2 diabetes were overweight or obese.

Watowich said many anti-obesity and anti-diabetes drugs already on the market haven't gotten a lot of traction because of their unfavorable side e ects. Drugs that block fat absorption, for example, may cause gastrointestinal issues in patients. And a common side e ect for people taking insulin for Type 2 diabetes is weight gain.

"There is a large number of pharmaceuticals that are looking at Type 2 diabetes given the size of the market, and we said, 'What can we do di erently?'" Watowich said.

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While some people might cast obesity as a failure of proper nutrition and exercise, the full extent of the condition is more complicated.

Watowich brought up a popular study looking at 14 former contestants of the extreme weight-loss TV show "The Biggest Loser." The research found that most of the contestants had regained some of their weight after the show. Their resting metabolic rate had slowed after the competition and stayed low when they regained the weight.

"Obesity isn't a lifestyle or [lack of] willpower, it's a disease," Watowich said. "And we talked to a lot of doctors that treat obese patients and Type 2 diabetes and they're like, 'Yeah, it's a challenge.'"

This drug, currently known as RLT-001, might help obese people with Type 2 diabetes lower their blood sugar levels, although Watowich is clear about its implications for extreme weight loss.

"It's going to help your obesity, but it is not going to make you thin. It is not going to be, all of the sudden, the magical pill," Watowich said. "We're going to cut your weight back and we're hoping 10 or 15 percent. But that 10 or 15 percent is going to make a drastic improvement in your glucose level."

Watowich said that the drug will next be tested on obese mice that are also on a diet. There are years of research ahead until the drug may be tested in human clinical trials.

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