Peptide with anti-obesity action successfully tested in animal trial

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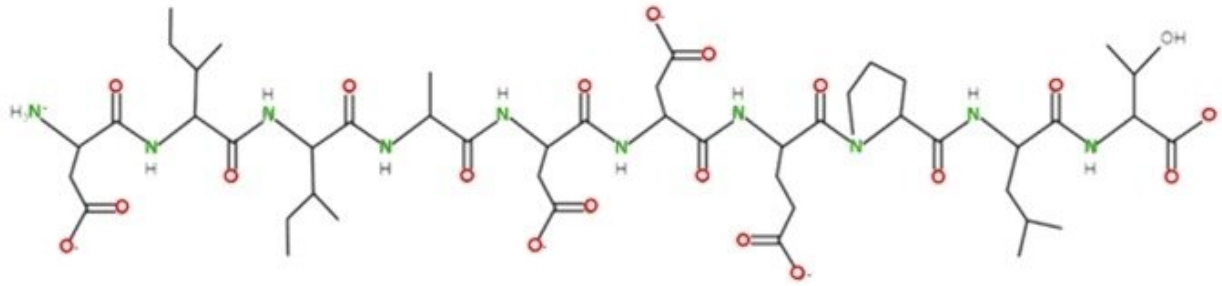

Chemical structure of Pep19. Credit: Researchers' archive

A study conducted at the University of São Paulo (USP) in Brazil shows that the synthetic molecule Pep19 acts on the endocannabinoid system, which helps regulate and balance key metabolic functions, such as appetite, fat breakdown (lipolysis), and energy release.

An article presenting the results of the study is published in the *International Journal of Molecular Sciences*. The study involved collaboration by researchers at the Federal University of Santa Catarina (Brazil), the University of Málaga and the Biomedical Center for Research on Diabetes and Associated Metabolic Diseases (Spain), and Israeli company Proteimax BioTechnology.

Scientists have long sought ways of influencing the functioning of the

endocannabinoid system to help people lose weight. Rimonabant, a drug that acted as a cannabinoid receptor antagonist, was launched in 2006 but banned in Brazil owing to severe adverse side effects, including anxiety and depression, with suicidal tendencies in some cases.

Studies have been performed since then to discover safer means to make the endocannabinoid system an ally of people who need to lose weight. Pep19 (DIIADDEPLT) is a novel peptide and one of the leading candidates in this field. It has obtained good results in animal trials without adverse effects on the central nervous system.

Promising performance

According to the recently published article, Pep19 is a synthetic version of a peptide naturally found in human cells. They are chemically identical, but Pep19 can be used in higher doses to achieve the desired effect. The researchers tested it on 50 mice divided into two groups, one fed a standard diet and the other a high-fat diet for 30 days. Pep19 diluted in saline was given to half of each group and saline only to the other half.

The results of the experiment were highly encouraging. The mice given the high-fat diet and Pep19 put on little weight and exhibited reduced insulin resistance, which can lead to type 2 diabetes and hypertension, among other problems. The molecule also reduced liver inflammation and fattiness, as well as inhibiting alanine-aminotransferase (ALT) activity. ALT increases with liver damage and is used as a marker to screen for liver disease.

Another benefit detected by the researchers was that the synthetic peptide converted part of the organism's white fat (its energy reserve) into brown fat, which is significant because brown fat is thermogenic, tending to assist weight loss by burning calories to generate energy and

heat.

"This process is associated with activation of a type of respiratory chain uncoupling protein known as UCP1. White fat doesn't normally produce the substance, but brown fat does," said Emer Suavinho Ferro, last author of the article. Ferro is a professor in the Pharmacology Department of the University of São Paulo's Biomedical Sciences Institute (ICB-USP) and heads the institution's Intracellular Peptide Pharmacology Laboratory. "We further confirmed the link in a visual analysis of the animals' fat. We saw that part of it had become beige, showing that Pep19 led to activation of UCP1."

According to Ferro, Pep19 benefited the animals without the adverse side effects caused by rimonabant. "Its action is peripheral and doesn't directly affect the central nervous system," he said.

The researchers plan to conduct more experiments, including clinical trials involving human patients, in an attempt to make the molecule a viable option for people who need to lose weight.

More information: Renata Silvério et al, Pep19 Has a Positive Effect on Insulin Sensitivity and Ameliorates Both Hepatic and Adipose Tissue Phenotype of Diet-Induced Obese Mice, *International Journal of Molecular Sciences* (2022). DOI: 10.3390/ijms23084082

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