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Treatment of Obesity and Type 2 Diabetes

https://www.iocbtech.cz/project/treatment-obesity-type-2-diabetes-2-2/

LIPIDIZED ANALOGS OF ANOREXIGENIC NEUROPEPTIDES FOR THE TREATMENT OF OBESITY AND TYPE 2 DIABETES

Scientists

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CHALLENGE

Prevalence of obesity and type 2 diabetes is increasing at an alarming rate with an estimation of more than 350 million patients by 2030. Currently, several treatments are available, however, none of them addresses the underlying pathophysiology and therefore, efficacy is progressively lost over time. This leads to loss of effective blood-glucose-levels and body-weight control and results in need of insulin parental application resulting in dangerous adverse effects of the therapy in the longer horizon. Furthermore, an intensive focus of the Pharma industry demonstrates that there is an urgent need to develop effective drugs with innovative mechanisms of action (MOA) to slow down the obesity and diabetes epidemics.

TECHNOLOGY

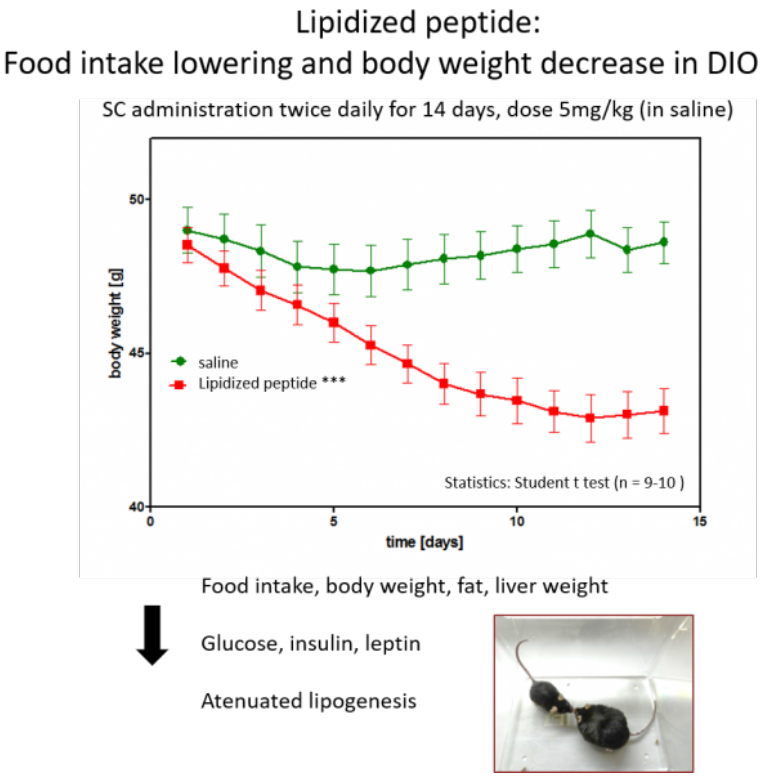
We have discovered one innovative neuropeptide drug candidate with unique and verified MOA – a modified version of the natural hormone with the following indications: treatment of obesity and type 2 diabetes.

The drug candidate is an anorexigenic neuropeptide that inhibits food intake. The corresponding receptor is expressed in the brain and plays an important role in the regulation of body weight and energy expenditure. We have modified the native hormone by lipidization and produced a stable analog with good biopharmaceutical properties. The drug candidate can be applied in the periphery and efficiently act centrally. The modified

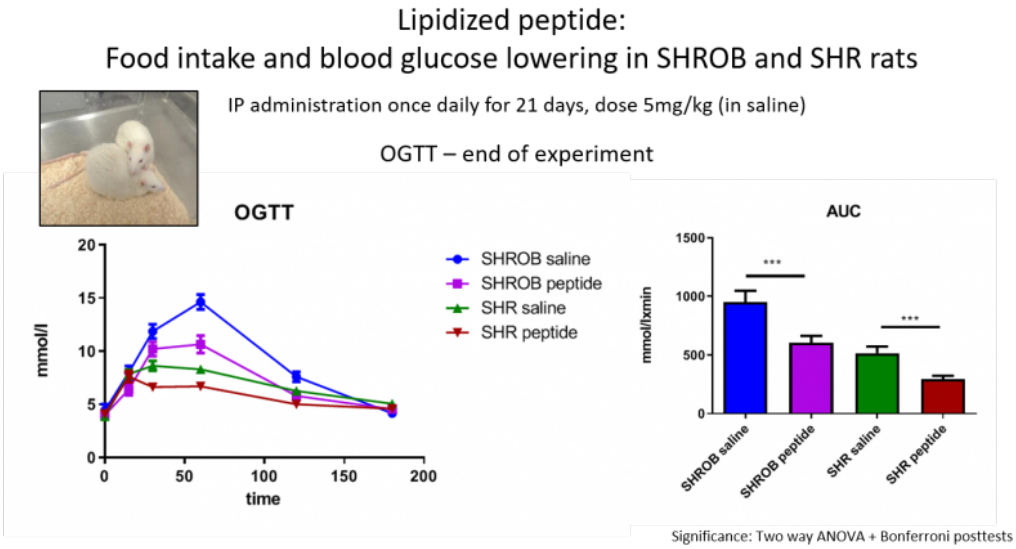
peptide safely promotes fat loss and improves glycemic control. We have demonstrated that a low dose subcutaneous injection of lipidized peptide translates into an effective suppression of appetite, subsequent weight loss and improved glycemic control in a range of preclinical obesity and diabetic models. We have used several models: diet-induced obesity (DIO) mouse and rat, the ZDF rat diabetic model, the MSG mouse obesity model, Koletsky rat obesity/diabetes model, and others.

To date, no evidence of toxicity has been observed in a number of exploratory non-GLP rodent studies after single and multiple dosing or during the increased duration of dosing (> 1 month and up to 100 mg/kg per day). Furthermore, ongoing exploratory non-GLP studies in non-human primates (Macaques) showed favorable preliminary results. Manufacturing of lipidized neuropeptide has been recently outsourced to Polypeptide Laboratories Inc (Torrance, CA) who has significant expertise and experience in the commercial manufacture of peptide APIs.

RESULT PREVIEW



The candidate drug efficacy has been verified in various preclinical obesity and diabetic models. Among other results, the lipidized peptide showed clear effect on body weight lowering (Fig. 1) in the diet-induced obesity (DIO) mouse model within two weeks of the experiment. Blood glucose levels (OGTT test) were significantly decreased after the administration of tested modified peptide using the Koletsky (SHROB) genetic rat model for diabetes/obesity (Fig. 2) and control SHR rats.



COMMERCIAL OPPORTUNITY

This technology was successfully licensed to Novo Nordisk.

PATENT SITUATION

- Patent applications or granted patents in EP, US, CA, JP, AU, IL in following indications
- Lipidated peptides as anti-obesity agents (priority date 2012)
- Lipidated peptides lowering blood glucose (priority date 2014)
- Lipidated peptides as neuroprotective agents (priority date 2014)

IP OWNER

- Institute of Organic Chemistry and Biochemistry of the CAS