A novel Dual Amylin and Calcitonin Receptor Agonist (DACRA), KBP-089, induces weight loss through a reduction in fat, but not lean mass, while improving food preference - DTU Orbit (20/06/2019)

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Background and Purpose
Obesity and associated co-morbidities, such as type 2 diabetes and non-alcoholic fatty liver disease, are major health challenges – hence, development of weight loss therapies with the ability to reduce the co-morbidities is key.

Experimental Approach
The effect of the dual amylin and calcitonin receptor agonist (DACRA), KBP-089, on bodyweight, glucose homeostasis, and fatty acid accumulation in liver and muscle tissue, food preference was investigated. Further, we elucidate weight-independent effects of KBP-089 using a weight-matched group.

Key Results
High fat diet fed rats were treated with KBP-089 s.c., at 0.625, 1.25, 2.5 µg·kg⁻¹ and vehicle resulting in a dose-dependent and sustained ~17% weight loss by the 2.5 µg·kg⁻¹ (p<0.001). Moreover, KBP-089 reduced fat depot size and reduced lipid accumulation in muscle and liver.

In Zucker Diabetic Fatty rats, KBP-089 improved glucose homeostasis through improved insulin action. To obtain a weight-matched group, significantly less food was offered (9% less than in the KBP-089 group). Weight-matching led to improved glucose homeostasis through lowered plasma insulin; however, these were inferior to the effect of KBP-089.

In the food preference test, normal diet rats obtained 74% of their calories from chocolate. KBP-089 administration reduced total caloric intake, and induced a relative increase in chow consumption while drastically lowering the chocolate compared to vehicle.

Conclusion
The novel DACRA, KBP-089 induces a sustained weight loss, leading to improved metabolic parameters including food preference, and these are beyond those observed simply by diet-induced weight loss.

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