

Effect Of New Leptin Fragments On Food Intake And Body Weight Of Rats

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Leptin plays an important role in the regulation of a variety of physiological functions, including food intake, body temperature and body weight maintenance. Tertiary structure of the leptin molecule reveals the existence of a four-helix bundle that is characteristic of the short-helix cytokines. In order to identify regions of the leptin molecule responsible for its bioactivity, a new series of decapeptides encompassing the region of fragments 98-122 [Oliveira, V. X. et al., *Regulatory Peptides*, 127, 123, 2005] were synthesized and their effects on body weight and food intake were assessed when administered into the lateral cerebroventricle of normal rats. Peptides were synthesized by SPPS, purified by RP-HPLC and characterized by LC/ESI-MS. We also performed a conformational study of the peptides by circular dichroism in order to correlate the biological activity and secondary structure of the leptin fragments. Among the fragments tested, we found that Ac-hLEP₁₁₀₋₁₁₉-NH₂ was able to induce a significantly reduction in both body weight and food intake. Interestingly, with fragment Ac-hLEP₁₁₃₋₁₂₂-NH₂ we observed a significant increase in the food consumption (>25%) but without any change in the body weight. The use of synthetic leptin-derivate fragments may offer the basis for the development of compounds with potential application in human obesity or to its related metabolic dysfunctions.

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