Effect On Food Intake And Body Weight Variation Of Leptin Fragments Intracerebroventricularly Administered In Rats And Normal And Ob/Ob Mice.

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All over the world a growing number of people suffer from obesity. Obesity is a disorder characterized by the increasing of adipose tissue mass as a result of systemic imbalance between energy intake and expenditure. Leptin, mainly produced by adipose tissue, plays a central role in the regulation of several 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, characteristic of the short-helix cytokines. In our previous studies employing leptin fragment, we found that the fragment Ac-hLEP$_{110-119}$-NH$_2$ induces a significantive reduction in both body weight and food intake [Martins et al. DOI: 0.1016/j.regpep.2008.11.013]. In this work, we described the effect caused by this fragment in comparison to its analogue, Ac-[Ser^{117}]-hLEP$_{110-119}$-NH$_2$, when intracerebroventricularly is administered in *Wistar* rats and *ob/ob* mice. These 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. From our results we found that in rats the fragment Ac-[Ser^{117}]-hLEP$_{110-119}$-NH$_2$ caused a big increasing on food intake (>42%) and practically no increasing on body weight. On the other hand, no significative changes on food intake and body weight were observed for Ac-hLEP$_{110-119}$-NH$_2$. In both normal and ob/ob mice both fragments caused a decreasing on food intake and body weight, but the effects were more drastic with fragment Ac-[Ser^{117}]-hLEP$_{110-119}$-NH$_2$ that caused 32 and 25% decreasing on body weight and food intake, respectively, when administered to normal mice. Our results clearly indicates that the replacement of the Cys residue by Ser improved the bioactivity, maybe due a no dimmer existence of Ac-hLEP$_{110-119}$-NH$_2$ caused by disulfide bridge formation.

Palavras Chave: leptin, leptin fragments, food intake, body weight, ob/ob mice
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