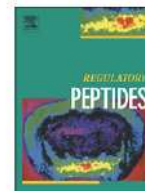




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Intranasal administration of mouse [D-Leu-4]OB3, a synthetic peptide amide with leptin-like activity, enhances total uptake and bioavailability in Swiss Webster mice when compared to intraperitoneal, subcutaneous, and intramuscular delivery systems

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ABSTRACT

Using a synthetic peptide strategy, we localized an active domain in mouse leptin to a sequence between amino acids 106 and 140. Intraperitoneal (ip) administration of a number of synthetic peptide amides encompassed by this domain reduced body weight gain, food and water intake, blood glucose levels, and increased insulin sensitivity in genetically obese mice. In the present study, we examined the pharmacokinetics of mouse [D-Leu-4]OB3, our most potent peptide, in male Swiss Webster mice following ip, subcutaneous (sc), and intramuscular (im) injection, and after intranasal administration with Intravail®, a new class of patented transmucosal delivery enhancement agents. Total uptake (1,072,270, 1,182,498; 1,481,060; ng/ml/min), serum half-life (48.8; 34.0; 30.0 min) and relative bioavailability (1.0, 1.1; 1.4;) of mouse [D-Leu-4]OB3 were similar when the peptide was given by ip, sc, or im injection, respectively. Total uptake and relative bioavailability were enhanced following intranasal delivery (4,336,963 ng/ml/min and 4.0, respectively), and serum half-life was 41.1 min. These results indicate that intranasal delivery of mouse [D-Leu-4]OB3 with Intravail® is a more effective method of peptide administration than injection methods, and suggest that it may have potential as a novel, non-invasive approach to the treatment of obesity and its associated metabolic dysfunctions in humans.

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