has potent insulinotropic activity and promotes weight loss such that it can be used for the treatment of non-insulin dependent diabetes and/or obesity.

OXM peptides with amino acid substitutions to improve stability and with additional modifications to slow clearance, such as PEGylation or lipidation are disclosed in WO 2008101017, WO2006134340, WO2007100535, and Pocai et al. *Diabetes* 58:2258-2266, 2009. While these OXM-derived peptides may represent a potential improvement over the wild type peptide, the doses required to achieve a sizable weight reduction in a diet-induced obese (DIO) mouse model are typically higher than may be considered feasible for pharmaceutical commercialization. For example, Pocai *et al* (2009) reported an average 11 g (~25 %) weight loss after 13 days of dosing with 1900 nmol/kg (~8 mg/kg) every other day (QOD).

Despite the availability of various OXM peptides and analogues thereof, there is still a need for more potent, stable, long-acting, and well-tolerated OXM peptide analogues having a ratio of GcgR/GLP-1R activity which has been optimized such that the potency and insulinotropic activity of the peptide provides effective treatments for diabetes, preferably type 2 diabetes and related disorders. It is also desirable to provide OXM peptide analogues thereof which provide effective treatments to reduce body weight. Accordingly, the present invention seeks to provide effective treatments for diabetes and/or obesity.

Summary

In a first aspect of the present disclosure, there is provided an Oxyntomodulin peptide analogue comprising the amino acid sequence:
His-(Aib)-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Lys-Lys-Ala-Gln-Glu-Phe-Val-Gln-Trp-Leu-Leu-Asn-(Aib)-Gly-Arg-Asn-Arg-Asn-Asn-Ile-Ala-Xaa_{38}-Xaa_{39} (SEQ ID NO: 5) wherein Xaa_{38} is Cys, Cys-PEG, or is absent; Xaa_{39} is Cys, Cys-PEG, or is absent; and wherein the C-terminal amino acid is optionally amidated.

In a second aspect of the present disclosure, there is provided a pharmaceutical composition comprising the Oxyntomodulin peptide analogue as defined herein, and a pharmaceutically acceptable carrier, diluent, or excipient.

In a third aspect of the present disclosure, there is provided a pharmaceutical composition comprising the Oxyntomodulin peptide analogue as defined herein, together with a pharmaceutically acceptable carrier, diluent, or excipient and optionally other therapeutic ingredients.

In a fourth aspect of the present disclosure, there is provided the use of an Oxyntomodulin peptide analogue as defined herein in the manufacture of a medicament for treating non-insulin-dependent diabetes.

In a fifth aspect of the present disclosure, there is provided the use of an Oxyntomodulin peptide analogue as defined herein in the manufacture of a medicament for treating obesity.

In a sixth aspect of the present disclosure, there is provided the use of an Oxyntomodulin peptide analogue as defined herein in the manufacture of a medicament for treating non-insulin-dependent diabetes or obesity.

In a seventh aspect of the present disclosure, there is provided the Oxyntomodulin peptide analogue as defined herein for use as a medicament.

In an eighth aspect of the present disclosure, there is provided the Oxyntomodulin peptide analogue as defined herein for use in the treatment of non-insulin-dependent diabetes.

In a ninth aspect of the present disclosure, there is provided the Oxyntomodulin peptide analogue as defined herein for use in the treatment of obesity.

In a tenth aspect of the present disclosure, there is provided the Oxyntomodulin peptide analogue as defined herein for use in the treatment of non-insulin-dependent diabetes or obesity.

Description

The present invention comprises an OXM peptide analogue with amino acid substitutions introduced to optimize metabolic stability and modulate the relative GcgR/GLP-1R activities while optimizing overall potency. In addition, the OXM peptide analogue of the present invention is PEGylated at selected positions for enhancement of time action thereby allowing for less frequent dosing.

The present invention provides an Oxyntomodulin peptide analogue comprising the amino acid sequence:

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1                   5                   10
His-(Aib)-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-
     15                  20                  25
Leu-Asp-Ser-Lys-Lys-Ala-Gln-Glu-Phe-Val-Gln-Trp-Leu-Leu-Asn-
       30                  35
(Aib)-Gly-Arg-Asn-Arg-Asn-Asn-Ile-Ala-Xaa38-Xaa39 (SEQ ID NO: 5)
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