In accordance with a specific aspect, the present invention relates to an insulinotropic peptide derivative comprising an amino acid of the following Formula 1.

R1-X-R2 <Formula 1>

wherein R1 is selected from the group consisting of desamino-histidyl, N-dimethyl-histidyl, beta-hydroxy imidazopropionyl, 4-imidazoacetyl and beta-carboxy imidazopropionyl;

CLAIMS

1. An insulinotropic peptide derivative, wherein N-terminal histidine residue of a native insulinotropic peptide is substituted with N-dimethyl-histidyl, wherein the insulinotropic peptide is exendin-4 or exendin-3.

2. The insulinotropic peptide derivative as set forth in claim 1, wherein the insulinotropic peptide is exendin-4.

3. The insulinotropic peptide derivative as set forth in claim 1 or 2, wherein the insulinotropic peptide derivative consists of an amino acid of the following Formula 1:
R1-X-R2 <Formula 1>
wherein R1 is N-dimethyl-histidyl;
R2 is selected from the group consisting of $-NH_2$ or -OH;
X is selected from the group consisting of Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Y-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Z-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser, Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Y-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Z-Asn-Gly-Gly and Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Y-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Z-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser;
Y is selected from the group consisting of Lys, Ser, and Arg; and
Z is selected from the group consisting of Lys, Ser, and Arg.

4. The insulinotropic peptide derivative as set forth in claim 3, wherein R1 is N-dimethyl-histidyl, Y is Lys or Ser, Z is Lys, and R2 is $-NH_2$.

5. A pharmaceutical composition comprising the insulinotropic peptide derivative of any one of claims 1 to 4.

6. The insulinotropic peptide derivative of any one of claims 1 to 4 or the pharmaceutical composition of claim 5 for use in the treatment of diabetes.

7. Use of the insulinotropic peptide derivative of any one of claims 1 to 4 in the preparation of a pharmaceutical composition for treating diabetes.