[6] The present inventors have found that insulin and the dual agonist are inconvenient in that administration must be made daily to the patient due to a short half-life, and have suggested, as a technique of maintaining the activity of protein drug and achieving improved stability at the same time in order to solve the abovementioned problems, a long-acting protein conjugate in which a conventional physiologically active polypeptide and an immunoglobulin Fc region are covalently combined with each other by a non-peptidyl polymer linker (Korean Patent No. 10-0725315). In particular, the inventors have confirmed that the sustainability of the *in vivo* effects of both the long-acting insulin conjugate and long-acting dual agonist conjugate is dramatically increased (Korean Patent No. 10-1058290, Korean Patent Application No. 10-2014-0022909 and Korean Patent Application Publication No. 10-2012-0139579).

[7] However, there are problems in that side-effects such as weight gain occur upon administration of GLP-1/glucagon dual agonist. Therefore, there still remains a need for the development of a therapeutic agent for diabetes having reduced side-effects, frequency and dosage

[8]

Disclosure of Invention

Technical Problem

[9] The present inventors have made many efforts to develop a therapeutic agent for diabetes which can reduce high blood glucose levels, suppress weight gain, and reduce the risk of hypoglycemia, which are required to treat diabetes. As a result, the present inventors have attempted a combined administration which simultaneously administers an insulin receptor and GLP-1/glucagon dual agonist, and specifically discovered that when a combined administration of a long-acting insulin and long-acting GLP-1/glucagon can maximize compliance of the patient, reduce the dosage of the insulin drug, reduce the risk of hypoglycemia, and help to reduce blood glucose level and body weight, thereby completing the present invention.

[10]

Solution to Problem

[11] An objective of the present disclosure is to provide a composition for

treating diabetes mellitus including insulin and a GLP-1/glucagon dual agonist.

[11A] In one aspect, the present invention provides a pharmaceutical composition for treating diabetes mellitus comprising insulin and a GLP-1/glucagon dual agonist.

[12] Another objective of the present disclosure is to provide a method for preventing or treating diabetes, including administering the composition to a subject at high risk of or having diabetes mellitus.

[12A] In another aspect, the present invention provides the use of the composition as disclosed herein, in the manufacture of a medicament for preventing or treating diabetes, wherein the composition disclosed herein is to be administered to a subject, exclusive of humans, at high risk of or having the diabetes mellitus.

[13]

Advantageous Effects of Invention

[14] The long-acting insulin or its analog conjugate and a long-acting GLP-1/glucagon

【Table 4】

SEQ ID NO.	Amino acid sequence	Note
SEQ ID NO. 39	HSQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRNNIA	
SEQ ID NO. 40	HAibQGTFTSDYSKYLD**E**KRA**K**EFVQWLMNTC	Ring formation
SEQ ID NO. 41	CA-SQGTFTSDYSKYLDEEAVRLFIEWLMNTKRNRNNIA	
SEQ ID NO. 42	CA-SQGTFTSDYSKYLDERRAQDFVAWLKNTGPSSGAPPPS	
SEQ ID NO. 43	CA-GQGTFTSDYSRYLEEEAVRLFIEWLKNGGPSSGAPPPS	
SEQ ID NO. 44	CA-GQGTFTSDYSRQMEEEAVRLFIEWLKNGGPSSGAPPPS	
SEQ ID NO. 45	CA-GEGTFTSDLSRQMEEEAVRLFIEWAAHSQGTFTSDYSKYLD	
SEQ ID NO. 46	CA-SQGTFTSDYSRYLDEEAVRLFIEWLMNTK	
SEQ ID NO. 47	CA-SQGTFTSDLSRQLEEEAVRLFIEWLMNK	
SEQ ID NO. 48	CA-GQGTFTSDYSRYLDEEAVXLFIEWLMNTKRNRNNIA	
SEQ ID NO. 49	CA-SQGTFTSDYSRQMEEEAVRLFIEWLMNGGPSSGAPPPSK	
SEQ ID NO. 50	CA-GEGTFTSDLSRQMEEEAVRLFIEWAAHSQGTFTSDYSRYLDK	
SEQ ID NO. 51	CA-SQGTFTSDYSRYLDGGGHGEGTFTSDLSKQMEEEAVK	
SEQ ID NO. 52	CA-SQGTFTSDYSRYLDXEAVXLFIEWLMNTK	
SEQ ID NO. 53	CA-GQGTFTSDYSRYLDEEAVXLFIXWLMNTKRNRNNIA	
SEQ ID NO. 54	CA-GQGTFTSDYSRYLDEEAVRLFIXWLMNTKRNRNNIA	
SEQ ID NO. 55	CA-SQGTFTSDLSRQLEGGGHSQGTFTSDLSRQLEK	
SEQ ID NO. 56	CA-SQGTFTSDYSRYLDEEAVRLFIEWIRNTKRNRNNIA	
SEQ ID NO. 57	CA-SQGTFTSDYSRYLDEEAVRLFIEWIRNGGPSSGAPPPSK	
SEQ ID NO. 58	CA-SQGTFTSDYSRYLD**E**EAV**K**LFIEWIRNTKRNRNNIA	Ring Formation
SEQ ID NO. 59	CA-SQGTFTSDYSRYLD**E**EAV**K**LFIEWIRNGGPSSGAPPPSK	Ring Formation
SEQ ID NO. 60	CA-SQGTFTSDYSRQLEEEAVRLFIEWVRNTKRNRNNIA	

SEQ ID NO. 61	DA-SQGTFTSDYSKYLD**E**KRA**K**EFVQWLMNTK	Ring Formation
SEQ ID NO. 62	HAibQGTFTSDYSKYLDEKRAKEFVCWLMNT	
SEQ ID NO. 63	HAibQGTFTSDYSKYLDEKRAKEFVQWLMNTC	
SEQ ID NO. 64	HAibQGTFTSDYS**K**YLD**E**KRAKEFVQWLMNTC	Ring Formation
SEQ ID NO. 65	HAibQGTFTSDYSKYLD**E**QAA**K**EFICWLMNT	Ring Formation
SEQ ID NO. 66	HAibQGTFTSDYSKYLDEKRAKEFVQWLMNT	
SEQ ID NO. 67	H(d)SQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRNNIA	
SEQ ID NO. 68	CA-SQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRNNIA	
SEQ ID NO. 69	CA-(d)SQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRNNIA	
SEQ ID NO. 70	CA-AibQGTFTSDYSKYLD**E**KRA**K**EFVQWLMNTC	Ring Formation
SEQ ID NO. 71	HAibQGTFTSDYAKYLD**E**KRA**K**EFVQWLMNTC	Ring Formation
SEQ ID NO. 72	YAibQGTFTSDYSKYLD**E**KRA**K**EFVQWLMNTC	Ring Formation

[158] In Table 4, the amino acids of each of SEQ ID NOs.: 40, 58, 59, 61, 64, 65, 70, 71 and 72 form a ring at the amino acids in bold and underlined in each of SEQ ID NOs.: 40, 58, 59, 61, 64, 65, 70, 71 and 72, and the amino acids represented by X mean a non-native amino acid, alpha-methyl-glutamic acid. In addition, CA represents 4-imidazoacetyl, and DA represents desamino-histidyl.

polymer linker is PEG.

[Claim 20] The use of the composition of any one of claims 1 to 19, in the manufacture of a medicament for preventing or treating diabetes, wherein the composition of any one of claims 1 to 19 is to be administered to a subject, exclusive of humans, at high risk of or having the diabetes mellitus.

[Claim 21] The use according to claim 20, wherein the administering step is to be performed by combined administration of the long-acting insulin conjugate and the long-acting GLP-1/glucagon dual agonist conjugate.

[Claim 22] The use according to claim 21, wherein the combined administration is to be performed by simultaneously, sequentially, or reversely administrating the long-acting insulin conjugate and the long-acting GLP-1/glucagon dual agonist conjugate.ucagon dual agonist.

<210> 39
<211> 37
<212> PRT
<213> Homo sapiens

<220>
<223> oxyntomodulin

<400> 39
His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 40
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 40
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

<210> 41
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 41
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala

35

<210> 42
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 42
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Ala Trp Leu Lys Asn Thr Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 43
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 43
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 44
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 44

Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 45
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 45
Xaa Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ala Ala His Ser Gln Gly Thr
20 25 30

Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp
35 40

<210> 46
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 46
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Thr Lys
20 25 30

<210> 47
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)

<223> Xaa = 4-imidazoacetyl.

<400> 47
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Lys
20 25

<210> 48
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (20)
<223> Xaa = alpha-methyl-glutamic acid

<400> 48
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Xaa Leu Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 49
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 49
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser Lys
35 40

<210> 50

<211> 43
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 50
Xaa Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ala Ala His Ser Gln Gly Thr
20 25 30

Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Lys
35 40

<210> 51
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 51
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Gly
1 5 10 15

Gly Gly His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met
20 25 30

Glu Glu Glu Ala Val Lys
35

<210> 52
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (16)
<223> Xaa = alpha-methyl-glutamic acid

<220>
<221> VARIANT
<222> (20)
<223> Xaa = alpha-methyl-glutamic acid

<400> 52
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Xaa
  1   5   10   15

Glu Ala Val Xaa Leu Phe Ile Glu Trp Leu Met Asn Thr Lys
             20   25   30

<210> 53
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (20)
<223> Xaa = alpha-methyl-glutamic acid

<220>
<221> VARIANT
<222> (24)
<223> Xaa = alpha-methyl-glutamic acid

<400> 53
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
  1   5   10   15

Glu Ala Val Xaa Leu Phe Ile Xaa Trp Leu Met Asn Thr Lys Arg Asn
             20   25   30

Arg Asn Asn Ile Ala
         35

<210> 54
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT

<222> (24)
<223> Xaa = alpha-methyl-glutamic acid

<400> 54
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Xaa Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 55
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 55
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu Glu Gly
1 5 10 15

Gly Gly His Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu
20 25 30

Glu Lys

<210> 56
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 56
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ile Arg Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 57
<211> 40
<212> PRT

<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 57
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ile Arg Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser Lys
35 40

<210> 58
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 58
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Lys Leu Phe Ile Glu Trp Ile Arg Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 59
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 59
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Lys Leu Phe Ile Glu Trp Ile Arg Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser Lys
35 40

<210> 60
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<400> 60
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Val Arg Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 61
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = desamino-histidyl.

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 61
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Lys
20 25 30

<210> 62
<211> 29
<212> PRT

<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<400> 62
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Cys Trp Leu Met Asn Thr
20 25

<210> 63
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<400> 63
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

<210> 64
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (12), (16)
<223> amino acids at position 12 and position 16 form a ring

<400> 64
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

<210> 65
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative'

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 65
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Cys Trp Leu Met Asn Thr
20 25

<210> 66
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<400> 66
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr
20 25

<210> 67
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = d-serine.

<400> 67
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn

```
            20                  25                  30

Arg Asn Asn Ile Ala
        35


<210>    68
<211>    37
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    oxyntomodulin derivative

<220>
<221>    VARIANT
<222>    (1)
<223>    Xaa = 4-imidazoacetyl


<400>    68
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
  1               5                  10                  15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
            20                  25                  30

Arg Asn Asn Ile Ala
        35


<210>    69
<211>    37
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    oxyntomodulin derivative

<220>
<221>    VARIANT
<222>    (1)
<223>    Xaa = 4-imidazoacetyl


<220>
<221>    VARIANT
<222>    (2)
<223>    Xaa = d-serine.


<400>    69
Xaa Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
  1               5                  10                  15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
            20                  25                  30

Arg Asn Asn Ile Ala
        35


<210>    70
<211>    30
<212>    PRT
<213>    Artificial Sequence

<220>
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<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (1)
<223> Xaa = 4-imidazoacetyl.

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 70
Xaa Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

<210> 71
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)
<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 71
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ala Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

<210> 72
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> oxyntomodulin derivative

<220>
<221> VARIANT
<222> (2)

<223> Xaa = aminoisobutyric acid

<220>
<221> VARIANT
<222> (16), (20)
<223> amino acids at position 16 and position 20 form a ring

<400> 72

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Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
  1               5                  10                  15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
            20                  25                  30
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