

Claims

1. A glucose-dependent insulinotropic peptide (GIP) analogue consisting of a GIP(3-30) amino acid sequence selected from:

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EGTFISEYSIAibMEKIKQQDFVEWLLAQK – Z (SEQ ID NO:72)
GIP(3-30)[D9E;A13Aib;D15E;H18K;N24E];

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GTFISDYSIAibMDKIKQQDFVEWLLAQK – Z (SEQ ID NO:73)
GIP(3-30)[A13Aib;H18K;N24E];

EGTFISDYSIAibLDKIKQQDFVEWLLAQK – Z (SEQ ID NO:74)
GIP(3-30)[A13Aib;M14L;H18K;N24E];

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EGTFISDYSIAibNleDKIKQQDFVEWLLAQK – Z (SEQ ID NO:75)
GIP(3-30)[A13Aib;M14Nle;H18K;N24E];

EGTFISEYSIAibLEKIKQQEFVEWLLAQK – Z (SEQ ID NO:79)
GIP(3-30)[D9E;A13Aib;M14L;D15E;H18K;D21E;N24E];

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EGTFISEYSIAibNleEKIKQQEFVEWLLAQK – Z (SEQ ID NO:80)
GIP(3-30)[D9E;A13Aib;M14Nle;D15E;H18K;D21E;N24E];

EGTFISEYSIAibLEKIKQQDFVEWLLAQK – Z (SEQ ID NO:84)
GIP(3-30)[D9E; A13Aib; M14L;D15E;H18K;N24E];

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XGTFISEYSIAibLEKIKQQEFVEWLLAQK – Z (SEQ ID NO:85)
GIP(3-30) [E3Glutaric acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E], wherein X is
Glutaric acid;

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XGTFISEYSIAibNleEKIKQQEFVEWLLAQK – Z (SEQ ID NO:86)
GIP(3-30) [E3Glutaric acid;D9E;A13Aib; M14Nle;D15E;H18K;D21E;N24E], wherein X
is Glutaric acid;

XGTFISEYSIAibMEKIKQQEFVEWLLAQK – Z (SEQ ID NO:88)

GIP(3-30) [E3Glutaric acid;D9E;A13Aib;D15E;H18K;D21E;N24E], wherein X is Glutaric acid;

5 EGTFISEYSIAibMEKIKQQEFVEWLLAQK – Z (SEQ ID NO:89)

GIP(3-30)[D9E;A13Aib;D15E;H18K;D21E;N24E];

EGTFISEYSIAibLDKIKQQDFVEWLLAQK – Z (SEQ ID NO:91)

GIP(3-30) [D9E;A13Aib; M14L;H18K;N24E];

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XGTFISDYSIAibMDKIKQQDFVEWLLAQK – Z (SEQ ID NO:92)

wherein X is Glutaric acid, GIP(3-30)[E3Glutaric acid;A13Aib;H18K;N24E];

XGTFISEYSIAibLEKIKQQEFVEWLLAQK – Z (SEQ ID NO:98)

15 GIP(3-30) [E3Succinic acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E], wherein X is Succinic acid, and

XGTFISEYSIAibLEKIKQQEFVEWLLAQK – Z (SEQ ID NO:99)

GIP(3-30) [E3Adipic acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E], wherein X is

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Adipic acid,

wherein Z is a peptide consisting of one or more consecutive amino acid residues of Exendin-4(30-39) (GPSSGAPPPS; SEQ ID NO:61; CE30-39), or is omitted,

wherein a fatty acid molecule is attached, directly or via a linker, to an amino acid residue at any position of said GIP analogue,

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optionally wherein said GIP analogue is C-terminally amidated or has a free C-terminal carboxylic acid,

and wherein said GIP peptide analogue is an antagonist of a glucose-dependent insulinotropic peptide receptor (GIPR).

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2. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule is attached, directly or via a linker, to an amino acid residue at any one of positions 3 to 29 of said GIP(3-30) amino acid sequence.

3. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule is attached, directly or via a linker, to the side chain of a lysine (K) amino acid residue at any one of positions 3 to 29 of said GIP(3-30) amino acid sequence.

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4. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule is attached, directly or via a linker, to an amino acid residue at any one of positions 11, 12, 13, 16, 17, 18, or 20, of said GIP(3-30) amino acid sequence.

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5. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule is attached, directly or via a linker, to an amino acid residue at any one of positions 12, 13, 16, 17, or 18 of said GIP(3-30) amino acid sequence, or said functional variant thereof.

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6. The GIP analogue according to any of the preceding claims, wherein a fatty acid molecule is attached to the side chain amino group of the K amino acid residue at position 18 ('18K') of said GIP(3-30) amino acid sequence.

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7. The GIP analogue according to any of the preceding claims, wherein said fatty acid molecule is a straight-chain fatty acid or a branched fatty acid and/or wherein said fatty acid molecule is a monoacyl fatty acid molecule or a diacyl fatty acid molecule; such as wherein said fatty acid molecule comprises an acyl group of the formula $\text{CH}_3(\text{CH}_2)_n\text{CO}-$, wherein n is an integer of 4 to 24; such as

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wherein said fatty acid molecule comprises one or more acyl groups selected from $\text{CH}_3(\text{CH}_2)_6\text{CO}-$, $\text{CH}_3(\text{CH}_2)_8\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{10}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{12}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{14}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{16}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{18}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{20}\text{CO}-$ and $\text{CH}_3(\text{CH}_2)_{22}\text{CO}-$; such as wherein said fatty acid molecule comprises an acyl group of the formula $\text{COOH}(\text{CH}_2)_n\text{CO}-$ (dicarboxylic acid), wherein n is an integer of 4 to 24;

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wherein said fatty acid molecule comprises two acyl groups individually selected from $\text{HOOC-CH}_3(\text{CH}_2)_{10}\text{CO}-$ (dodecanoyl, C12), $\text{HOOC-CH}_3(\text{CH}_2)_{12}\text{CO}-$ (1-tetradecanoyl, C14), $\text{HOOC-CH}_3(\text{CH}_2)_{14}\text{CO}-$ (hexadecanoyl, C16), $\text{HOOC-CH}_3(\text{CH}_2)_{15}\text{CO}-$ (15-carboxy-pentadecanoyl, C17), $\text{HOOC-CH}_3(\text{CH}_2)_{16}\text{CO}-$ (octadecanoyl, C18), $\text{HOOC-CH}_3(\text{CH}_2)_{17}\text{CO}-$ (17-carboxy-heptadecanoyl, C19), $\text{HOOC-CH}_3(\text{CH}_2)_{18}\text{CO}-$ (eicosanoyl, C20), $\text{HOOC-CH}_3(\text{CH}_2)_{19}\text{CO}-$ (19-carboxy-nonadecanoyl, C21) and

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HOOC-CH₃(CH₂)₂₀CO- (behenyl, C22).

8. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule comprises an acyl group selected from COOH(CH₂)₁₄CO-,
5 COOH(CH₂)₁₆CO-, COOH(CH₂)₁₈CO- and COOH(CH₂)₂₀CO-.

9. The GIP analogue according to any one of the preceding claims, wherein said fatty acid molecule is attached to the epsilon amino group of the side chain of a lysine amino acid residue of said GIP analogue directly.

10. The GIP analogue according to any one of the preceding claims, wherein the fatty acid molecule is attached to an amino acid residue via a linker, such as wherein such as wherein said linker comprises a γ-Glu, one or more 8-amino-3,6-dioxaoctanoic acid (AEEAc), or combinations thereof,
15 such as wherein said linker comprises or consists of γGlu, such as wherein said linker comprises or consists of a [8-amino-3,6-dioxaoctanoic acid]_n (AEEAc)_n, wherein n is an integer of 1 to 50, such as an integer of 1-2, 2-3, 3-4, 4-5, 5-6, 6-7, 7-8, 8-9, 9-10, 10-11, 11-12, 12-13, 13-14, 14-15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-45, 45-50, preferably wherein n is 1, 2 or 3.

11. The GIP analogue according to any one of the preceding claims, wherein the fatty acid molecule is attached to an amino acid residue via a linker, and wherein the combination of linker and fatty acid is selected from

- i. [15-Carboxy pentadecanoyl]-γGlu
- 25 ii. [17-carboxy-heptadecanoyl]-γ-Glu-AEEAc-AEEAc-, and
- iii. [17-carboxy-heptadecanoyl]-γGlu-γGlu

12. The GIP analogue according to any one of the preceding claims, wherein said GIP analogue is

30 EGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS (SEQ ID NO: 18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

wherein a fatty acid molecule is attached to an amino acid residue, directly or via a linker, at any position of SEQ ID NO: 18,

optionally wherein said GIP analogue is C-terminally amidated or has a free C-terminal carboxylic acid.

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13. The GIP analogue according to any one of the preceding claims, wherein said GIP analogue is a pharmaceutically acceptable salt of

EGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS (SEQ ID NO: 18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

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wherein a fatty acid molecule is attached to an amino acid residue, directly or via a linker, at any position of SEQ ID NO: 18,

optionally wherein said GIP analogue is C-terminally amidated or has a free C-terminal carboxylic acid.

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14. The GIP analogue according to any one of the preceding claims, having an amino acid sequence selected from

EGTFISEYSIAibMEKIKQQDFVEWLLAQKPSSGAPPPS (SEQ ID NO:33) GIP(3-30)+Cex(31-39) [D9E;A13Aib;D15E;H18K;N24E],

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EGTFISDYSIAibMDKIKQQDFVEWLLAQKPSSGAPPPS; (SEQ ID NO:12) GIP(3-30)+Cex(31-39) [A13Aib;H18K(C16-diacid);N24E],

EGTFISDYSIAibLDKIKQQDFVEWLLAQKPSSGAPPPS (SEQ ID NO:13) GIP(3-30)+Cex(31-39) [A13Aib;M14L;H18K(C16-diacid);N24E],

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EGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

EGTFISEYSIAibNleEKIKQQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:19) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle; D15E;H18K;D21E;N24E],

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XGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS, wherein X is glutaric acid

(SEQ ID NO:25) GIP(3-30)+Cex(31-39) [E3Glutaric acid;D9E;A13Aib;
M14L;D15E;H18K;D21E;N24E],

5 **XGTFISEYSIAibNleEKIKQQEFVEWLLAQKPSSGAPPPS**, wherein X is glutaric acid
(SEQ ID NO:26) GIP(3-30)-Cex(31-39) [E3Glutaric acid;D9E;
A13Aib;M14Nle;D15E;H18K;D21E;N24E],

10 **XGTFISEYSIAibMEKIKQQEFVEWLLAQKPSSGAPPPS**, wherein X is glutaric acid
(SEQ ID NO:28) GIP(3-30)-Cex(31-39) [E3Glutaric acid;D9E;A13Aib;
D15E;H18K;D21E;N24E],

EGTFISEYSIAibMEKIKQQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:29) GIP(3-30)-
Cex(31-39) [D9E;A13Aib;D15E;H18K; D21E;N24E],

15 **EGTFISEYSIAibLDKIKQQDFVEWLLAQKPSSGAPPPS** (SEQ ID NO:30) GIP(3-
30)Cex(31-39) [D9E;A13Aib;M14L;H18K; N24E],

20 **XGTFISDYSIAibMDKIKQQDFVEWLLAQKPSSGAPPPS**, wherein X is glutaric acid
(SEQ ID NO:32) GIP(3-30)Cex(31-39) [E3Glutaric acid;A13Aib;H18K(C16-
diacid);N24E],

EGTFISEYSIAibLEKIKQQDFVEWLLAQKPSSGAPPPS (SEQ ID NO:50) GIP(3-
30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;N24E],

25 **XGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS**, wherein X is succinic acid
(SEQ ID NO:48) GIP(3-30)Cex(31-39) [E3Succinic acid;D9E;A13Aib;
M14L;D15E;H18K;D21E;N24E], and

30 **XGTFISEYSIAibLEKIKQQEFVEWLLAQKPSSGAPPPS**, wherein X is adipic acid
(SEQ ID NO:49) GIP(3-30)Cex(31-39) [E3Adipic acid;D9E;A13Aib;
M14L;D15E;H18K;D21E;N24E],

wherein a fatty acid molecule is attached, directly or via a linker, to an amino acid residue at any position of said amino acid sequence,

optionally wherein said amino acid sequence is C-terminally amidated or has a free C-terminal carboxylic acid.

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15. The GIP peptide analogue of any one of the preceding claims selected from :

EGTFISEYSIAibMEKIK(C16-diacid)QQDFVEWLLAQKPSSGAPPPS (SEQ ID NO:33) GIP(3-30)+Cex(31-39) [D9E;A13Aib;D15E;H18K;N24E],

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EGTFISEYSIAibLEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;

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H18K;D21E;N24E],

EGTFISEYSIAibNleEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:19) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle;D15E;H18K; D21E;N24E],

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EGTFISEYSIAibNleEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:19) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle; D15E;H18K;D21E;N24E],

XGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS, wherein X is glutaric acid (SEQ ID NO:25) GIP(3-30)+Cex(31-39) [E3Glutaric acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

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XGTFISEYSIAibNleEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:26) GIP(3-30)-Cex(31-39) [E3Glutaric acid;D9E; A13Aib;M14Nle;D15E;H18K;D21E;N24E],

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XGTFISEYSIAibMEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS, wherein X is glutaric acid (SEQ ID NO:28)

GIP(3-30-Cex(31-39) [E3Glutaric acid;D9E;A13Aib; D15E;H18K;D21E;N24E],

EGTFISEYSIAibMEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS
(SEQ ID NO:29) GIP(3-30)-Cex(31-39) [D9E;A13Aib;D15E;H18K; D21E;N24E],

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EGTFISEYSIAibLDKIK(2xAEEAc+yGlu-C18-diacid)QQDFVEWLLAQKPSSGAPPPS
(SEQ ID NO:30) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;H18K; N24E],

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XGTTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS,
wherein X is glutaric acid (SEQ ID NO:25) GIP(3-30)Cex(31-39) [E3Glutaric
acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS
(SEQ ID NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

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XGTTFISEYSIAibLEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS, wherein X is
glutaric acid (SEQ ID NO:25) GIP(3-30)Cex(31-39) [E3Glutaric
acid;D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

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EGTFISEYSIAibLEKIK(SGGGG-C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ
ID NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(ALEA-C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID
NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

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EGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQDFVEWLLAQKPSSGAPPPS
(SEQ ID NO:50) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;N24E],

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XGTTFISEYSIAibNleEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS, wherein X is
glutaric acid;(SEQ ID NO:26) GIP(3-30)Cex(31-39) [E3Glutaric
acid;D9E;A13Aib;M14Nle; D15E;H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(Aib-C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID
NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E; N24E],

EGTFISEYSIAibLEKIK(KAAAEKAAAEKAAAE-C16-diacid
/18K)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18) GIP(3-30)Cex(31-39)
[D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

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XGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS,
wherein X is succinic acid (SEQ ID NO:48) GIP(3-30)Cex(31-39) [E3Succinic
acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

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XGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid
)QQEFVEWLLAQKPSSGAPPPS, wherein X is adipic acid (SEQ ID NO:49) GIP(3-
30)Cex(31-39) [E3Adipic acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

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EGTFISDYSIAibMDKIK(C16-diacid)QQDFVEWLLAQKPSSGAPPPS (SEQ ID
NO:12) GIP(3-30)+Cex(31-39) [A13Aib;H18K(C16-diacid);N24E],

EGTFISDYSIAibLDKIK(C16-diacid)QQDFVEWLLAQKPSSGAPPPS (SEQ ID NO:13)
GIP(3-30)+Cex(31-39) [A13Aib;M14L;H18K(C16-diacid);N24E],

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EGTFISDYSIAibLDKIK(2xAEEAc+yGlu-C18-
diacid)QQDFVEWLLAQKPSSGAPPPS(SEQ ID NO:13) GIP(3-30)+Cex(31-39)
[A13Aib;M14L;H18K(2xAEEAc+yGlu-C18-diacid);N24E],

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XGTFISDYSIAibMDKIK(C16-diacid)QQDFVEWLLAQKPSSGAPPPS, wherein X is
glutaric acid (SEQ ID NO:32) GIP(3-30)Cex(31-39) [E3Glutaric
acid;A13Aib;H18K(C16-diacid);N24E],

optionally wherein said GIP analogue is C-terminally amidated or has a free C-
terminal carboxylic acid.

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16. The GIP analogue according to any one of the preceding claims, wherein said GIP
analogue is a pharmaceutically acceptable salt of an amino acid sequence selected
from:

EGTFISEYSIAibMEKIK(C16-diacid)QQDFVEWLLAQKPSSGAPPPS (SEQ ID

NO:33) GIP(3-30)+Cex(31-39) [D9E;A13Aib;D15E;H18K;N24E],

EGTFISEYSIAib**LEKIK**(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18)
GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

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EGTFISEYSIAib**LEKIK**(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS
(SEQ ID NO:18) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;
H18K;D21E;N24E],

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EGTFISEYSIAib**NleEKIK**(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID
NO:19) GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle;D15E;H18K; D21E;N24E],

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EGTFISEYSIAib**NleEKIK**(2xAEEAc+yGlu-C18-
diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:19) GIP(3-30)+Cex(31-39)
[D9E;A13Aib;M14Nle; D15E;H18K;D21E;N24E],

XGTFISEYSIAib**LEKIK**(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS,
wherein X is glutaric acid (SEQ ID NO:25) GIP(3-30)+Cex(31-39) [E3Glutaric
acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

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XGTFISEYSIAib**NleEKIK**(2xAEEAc+yGlu-C18-
diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:26) GIP(3-30)-Cex(31-39)
[E3Glutaric acid;D9E; A13Aib;M14Nle;D15E;H18K;D21E;N24E],

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XGTFISEYSIAib**MEKIK**(2xAEEAc+yGlu-C18-
diacid)QQEFVEWLLAQKPSSGAPPPS, wherein X is glutaric acid (SEQ ID NO:28)
GIP(3-30)-Cex(31-39) [E3Glutaric acid;D9E;A13Aib; D15E;H18K;D21E;N24E],

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EGTFISEYSIAib**MEKIK**(2xAEEAc+yGlu-C18-diacid)QQEFVEWLLAQKPSSGAPPPS
(SEQ ID NO:29) GIP(3-30)-Cex(31-39) [D9E;A13Aib;D15E;H18K; D21E;N24E],

EGTFISEYSIAib**LDKIK**(2xAEEAc+yGlu-C18-diacid)QQDFVEWLLAQKPSSGAPPPS
(SEQ ID NO:30) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;H18K; N24E],

XGTFISEYSIAibLEKIK(2xAEAAc+yGlu-C18-diacid)**QQEFVEWLLAQKPSSGAPPPS**,
wherein X is glutaric acid (SEQ ID NO:25) GIP(3-30)Cex(31-39) [E3Glutaric
acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

5 **EGTFISEYSIAibLEKIK**(2xAEAAc+yGlu-C18-diacid)**QQEFVEWLLAQKPSSGAPPPS**
(SEQ ID NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

XGTFISEYSIAibLEKIK(C16-diacid)**QQEFVEWLLAQKPSSGAPPPS**, wherein X is
glutaric acid (SEQ ID NO:25) GIP(3-30)Cex(31-39) [E3Glutaric
10 acid;D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(SGGGG-C16-diacid)**QQEFVEWLLAQKPSSGAPPPS** (SEQ
ID NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

15 **EGTFISEYSIAibLEKIK**(ALEA-C16-diacid)**QQEFVEWLLAQKPSSGAPPPS** (SEQ ID
NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;D21E;N24E],

EGTFISEYSIAibLEKIK(2xAEAAc+yGlu-C18-diacid)**QQDFVEWLLAQKPSSGAPPPS**
(SEQ ID NO:50) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E; H18K;N24E],
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XGTFISEYSIAibNleEKIK(C16-diacid)**QQEFVEWLLAQKPSSGAPPPS**, wherein X is
glutaric acid;(SEQ ID NO:26) GIP(3-30)Cex(31-39) [E3Glutaric
acid;D9E;A13Aib;M14Nle; D15E;H18K;D21E;N24E],

25 **EGTFISEYSIAibLEKIK**(Aib-C16-diacid)**QQEFVEWLLAQKPSSGAPPPS** (SEQ ID
NO:18) GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E; N24E],

EGTFISEYSIAibLEKIK(KAAAEKAAAEKAAAE-C16-diacid
/18K)**QQEFVEWLLAQKPSSGAPPPS** (SEQ ID NO:18) GIP(3-30)Cex(31-39)
30 [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],

XGTFISEYSIAibLEKIK(2xAEAAc+yGlu-C18-diacid)**QQEFVEWLLAQKPSSGAPPPS**,
wherein X is succinic acid (SEQ ID NO:48) GIP(3-30)Cex(31-39) [E3Succinic
acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

XGTFISEYSIAibLEKIK(2xAEEAc+yGlu-C18-diacid
)**QQEFVEWLLAQKPSSGAPPPS**, wherein X is adipic acid (SEQ ID NO:49) GIP(3-
30)Cex(31-39) [E3Adipic acid;D9E;A13Aib; M14L;D15E;H18K;D21E;N24E],

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EGTFISDYSIAibMDKIK(C16-diacid)**QQDFVEWLLAQKPSSGAPPPS** (SEQ ID
NO:12) GIP(3-30)+Cex(31-39) [A13Aib;H18K(C16-diacid);N24E],

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EGTFISDYSIAibLDKIK(C16-diacid)**QQDFVEWLLAQKPSSGAPPPS** (SEQ ID NO:13)
GIP(3-30)+Cex(31-39) [A13Aib;M14L;H18K(C16-diacid);N24E],

EGTFISDYSIAibLDKIK(2xAEEAc+yGlu-C18-
diacid)**QQDFVEWLLAQKPSSGAPPPS**(SEQ ID NO:13) GIP(3-30)+Cex(31-39)
[A13Aib;M14L;H18K(2xAEEAc+yGlu-C18-diacid);N24E],

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XGTFISDYSIAibMDKIK(C16-diacid)**QQDFVEWLLAQKPSSGAPPPS**, wherein X is
glutaric acid (SEQ ID NO:32) GIP(3-30)Cex(31-39) [E3Glutaric
acid;A13Aib;H18K(C16-diacid);N24E],

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optionally wherein said GIP analogue is C-terminally amidated or has a free C-
terminal carboxylic acid.

17. The GIP analogue of any one of the preceding claims, wherein said GIP analogue is
EGTFISEYSIAib**LEKIK**(C16-diacid)**QQEFVEWLLAQKPSSGAPPPS** (SEQ ID NO:18)
GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],
optionally wherein said GIP analogue is C-terminally amidated or has a free C-
terminal carboxylic acid.

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18. The GIP analogue according to any one of the preceding claims, wherein said GIP analogue is

EGTFISEYSIAibLEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18)
GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E], wherein said GIP
analogue has a free C-terminal carboxylic acid.

19. The GIP analogue according to any one of the preceding claims, wherein said GIP analogue is a pharmaceutically acceptable salt of

EGTFISEYSIAibLEKIK(C16-diacid)QQEFVEWLLAQKPSSGAPPPS (SEQ ID NO:18)
GIP(3-30)Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E], wherein said GIP
analogue has a free C-terminal carboxylic acid.

20. The GIP analogue according to any of the preceding claims, wherein the GIP analogue has a free N-terminus and/or wherein said GIP analogue is C-terminally amidated or has a free C-terminal carboxylic acid.

21. The GIP peptide analogue according to any one of the preceding claims, which is a pharmaceutically acceptable salt of said GIP analogue.

22. The GIP peptide analogue according to any one of the preceding claims, wherein said pharmaceutically acceptable salt of said GIP analogue is selected from Na, Cl, acetate and trifluoroacetate (TFA).

23. Use of the GIP analogue according to any of the preceding claims for the manufacture of a medicament for the treatment of a condition selected from metabolic syndrome, obesity, pre-diabetes, type I diabetes, type 2 diabetes, insulin resistance, elevated fasting glucose, hyperglycemia, elevated fasting serum triglyceride levels, low levels of very low-density lipoprotein (VLDL), low high-density lipoprotein (HDL) levels, dyslipidemia, increased/decreased low-density lipoprotein (LDL), high cholesterol levels, abnormal deposition of lipids, a cardiovascular disease, elevated blood pressure and atherosclerosis.