

Claims

1. A peptidic compound having the formula (I):

5 H₂N-His-X2-X3-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-X14-X15-
Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-X28-Gly-Gly-Pro-
Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-R¹ (I)

10 X2 represents an amino acid residue selected from Ser, D-Ser and Aib,
X3 represents an amino acid residue selected from Gln and His,
X14 represents an amino acid residue with a functionalized -NH₂ side chain group, selected from the group consisting of Lys, Orn, Dab, or Dap, wherein the -NH₂ side chain group is functionalized by -Z-C(O)-
15 R⁵, wherein
Z represents a linker in all stereoisomeric forms and
R⁵ is a moiety comprising up to 50 carbon atoms and heteroatoms selected from N and O,
X15 represents an amino acid residue selected from Glu and Asp,
20 X28 represents an amino acid residue selected from Ala and Lys,
R¹ is NH₂ or OH,
or a salt or solvate thereof.

- 25 2. A compound of claim 1, wherein
 R¹ is NH₂
 or a salt or solvate thereof.
- 30 3. A compound according to any one of claims 1 - 2, wherein the peptidic
 compound has a relative activity of at least 0.1% compared to that of
 natural glucagon at the glucagon receptor.
4. A compound according to any one of claims 1 - 3, wherein the peptidic

compound exhibits a relative activity of at least 0.1% compared to that of GLP-1(7-36)-amide at the GLP-1 receptor.

5. A compound of any one of claims 1 - 4, wherein
5 X14 represents Lys wherein the -NH₂ side chain group is functionalized with a group -Z-C(O)R⁵, wherein Z represents a group selected from γE, γE-γE, AEEAc-AEEAc-γE and AEEAc-AEEAc-AEEAc and R⁵ represents a group selected from pentadecanoyl, heptadecanoyl or
10 16-carboxy-hexadecanoyl.
6. A compound of any one of claims 1 - 5, wherein
X14 represents Lys wherein the -NH₂ side chain group is functionalized with a group -Z-C(O)R⁵, wherein
15 Z represents a group selected from γE, γE-γE, AEEAc-AEEAc-γE and AEEAc-AEEAc-AEEAc and R⁵ represents a group selected from pentadecanoyl or heptadecanoyl.
7. A compound of any one of claims 1 - 6, wherein
20 X2 represents Ser,
X3 represents an amino acid residue selected from Gln and His,
X14 represents Lys wherein the -NH₂ side chain group is functionalized by (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-
25 butyryl-,
X15 represents Glu,
X28 represents Ala,
R¹ represents NH₂,
or a salt or solvate thereof.
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8. A compound of any one of claims 1 - 6, wherein
X2 represents D-Ser,

X3 represents an amino acid residue selected from Gln and His,
X14 represents Lys wherein the -NH₂ side chain group is
functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-
Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-
carboxy-4-hexadecanoylamino-butyrylamino)-butyryl,
X15 represents an amino acid residue selected from Glu and Asp,
X28 represents an amino acid residue selected from Ala and Lys,
R¹ represents NH₂,
or a salt or solvate thereof.

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9. A compound of any one of claims 1 - 6, wherein

X2 represents Aib,
X3 represents an amino acid residue selected from Gln and His,
X14 represents Lys wherein the -NH₂ side chain group is
functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-
Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-
carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-, (2-{2-[2-(2-{2-
[(4S)-4-Carboxy-4-hexadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-
acetylamino]-ethoxy}-ethoxy)-acetyl, (2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-
octadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-
ethoxy}-ethoxy)-acetyl, [2-(2-{2-[2-(2-{2-[2-(2-Octadecanoylamino-
ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetylamino}-ethoxy)-
ethoxy]-acetyl-,
X15 represents an amino acid residue selected from Glu and Asp,
X28 represents an amino acid residue selected from Ala and Lys,
R¹ represents NH₂,
or a salt or solvate thereof.

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10. A compound of any one of claims 1 - 6, wherein

X2 represents an amino acid residue selected from Ser, D-Ser and
Aib,
X3 represents Gln,

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X14 represents Lys wherein the -NH₂ side chain group is functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-,

5 X15 represents an amino acid residue selected from Glu and Asp,
X28 represents an amino acid residue selected from Ala and Lys,
R¹ represents NH₂,
or a salt or solvate thereof.

10 11. A compound of any one of claims 1 - 6, wherein

X2 represents an amino acid residue selected from Ser, D-Ser and Aib,

X3 represents His,

15 X14 represents Lys wherein the -NH₂ side chain group is functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-, (2-{2-[2-(2-{2-
[(4S)-4-Carboxy-4-hexadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, (2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-
20 octadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, [2-(2-{2-[2-(2-{2-[2-(2-Octadecanoylamino-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetyl-,

25 X15 represents an amino acid residue selected from Glu and Asp,
X28 represents an amino acid residue selected from Ala and Lys,
R¹ represents NH₂,
or a salt or solvate thereof.

12. A compound of any one of claims 1 - 6, wherein

30 X2 represents an amino acid residue selected from Ser, D-Ser and Aib,

X3 represents an amino acid residue selected from Gln and His,

X14 represents Lys wherein the -NH₂ side chain group is functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-, (2-{2-[2-(2-{2-
5 [(4S)-4-Carboxy-4-hexadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, (2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-octadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, [2-(2-{2-[2-(2-{2-[2-(2-Octadecanoylamino-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetyl-,
10 ethoxy]-acetyl-,

X15 represents Glu,

X28 represents an amino acid residue selected from Ala and Lys,

R¹ represents NH₂,

or a salt or solvate thereof.

15 13. A compound of any one of claims 1 - 6, wherein

X2 represents an amino acid residue selected from D-Ser and Aib,

X3 represents an amino acid residue selected from Gln and His,

X14 represents Lys wherein the -NH₂ side chain group is

functionalized by (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-,
20 butyryl-,

X15 represents Asp,

X28 represents Ala,

25 R¹ represents NH₂,

or a salt or solvate thereof.

14. A compound of any one of claims 1 - 6, wherein

X2 represents an amino acid residue selected from Ser, D-Ser and Aib,
30 Aib,

X3 represents an amino acid residue selected from Gln and His,

X14 represents Lys wherein the -NH₂ side chain group is

- functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-, (2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-hexadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, (2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-octadecanoylamino-butyrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl, [2-(2-{2-[2-(2-{2-[2-(2-Octadecanoylamino-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetyl-,
- 5
- 10 X15 represents an amino acid residue selected from Glu and Asp,
X28 represents Ala,
R¹ represents NH₂,
or a salt or solvate thereof.
- 15 15. A compound of any one of claims 1 - 6, wherein
X2 represents an amino acid residue selected from D-Ser and Aib,
X3 represents an amino acid residue selected from Gln and His,
X14 represents Lys wherein the -NH₂ side chain group is
functionalized by (S)-4-Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl-,
- 20
- X15 represents Glu,
X28 represents Lys,
R¹ represents NH₂,
- 25 or a salt or solvate thereof.
16. A compound of any one of claims 1 - 6, wherein
X2 represents Aib,
X3 represents His,
- 30 X14 represents Lys wherein the -NH₂ side chain group is
functionalized by (S)-4-Carboxy-4-hexadecanoylamino-butyryl-, (S)-4-

Carboxy-4-octadecanoylamino-butyryl-, (S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylamino)-butyryl,
X15 represents an amino acid residue selected from Glu and Asp,
X28 represents Ala,
5 R¹ represents NH₂,
or a salt or solvate thereof.

10 17. The compound of any one of claims 1 - 16, selected from the
compounds of SEQ ID NO: 6-31, as well as salts and solvates thereof.

18. The compound of any one of claims 1 - 17, selected from the
compounds of SEQ ID NO: 6-29 and 31, as well as salts and solvates
thereof.

15 19. The compound of claim 1, wherein the compound is represented by
SEQ ID NO: 11, or a salt or solvate thereof.

20 20. The compound of claim 1, wherein the compound is represented by
SEQ ID NO: 12, or a salt or solvate thereof.

21. The compound of claim 1, wherein the compound is represented by
SEQ ID NO: 20, or a salt or solvate thereof.

25 22. The compound of any one of claims 1 - 21 for use in medicine,
particularly in human medicine.

30 23. The compound of any one of claims 1 - 21 for use according to claim
22, which is present as an active agent in a pharmaceutical
composition together with at least one pharmaceutically acceptable
carrier.

24. The compound of any one of claims 1 - 21 for use according to claim

22 or 23, together with at least one additional therapeutically active agent, wherein the additional therapeutically active agent is selected from the series of Insulin and Insulin derivatives, GLP-1, GLP-1 analogues and GLP-1 receptor agonists, polymer bound GLP-1 and GLP-1 analogues, dual GLP1/glucagon agonists, dual GLP1/GIP agonists, PYY3-36 or analogues thereof, pancreatic polypeptide or analogues thereof, Glucagon receptor agonists, GIP receptor agonists or antagonists, ghrelin antagonists or inverse agonists, Xenin and analogues thereof, DDP4 inhibitors, SGLT2 inhibitors, dual SGLT2 / SGLT1 inhibitors, Biguanides, Thiazolidinediones, dual PPAR agonists, Sulfonylureas, Meglitinides, alpha-glucosidase inhibitors, Amylin and Amylin analogues, GPR119 agonists, GPR40 agonists, GPR120 agonists, GPR142 agonists, systemic or low-absorbable TGR5 agonists, Cycloset, inhibitors of 11-beta-HSD, activators of glucokinase, inhibitors of DGAT, inhibitors of protein tyrosinephosphatase 1, inhibitors of glucose-6-phosphatase, inhibitors of fructose-1,6-bisphosphatase, inhibitors of glycogen phosphorylase, inhibitors of phosphoenol pyruvate carboxykinase, inhibitors of glycogen synthase kinase, inhibitors of pyruvate dehydrogenase kinase, alpha2-antagonists, CCR-2 antagonists, modulators of glucose transporter-4, Somatostatin receptor 3 agonists, HMG-CoA-reductase inhibitors, fibrates, nicotinic acid and the derivatives thereof, nicotinic acid receptor 1 agonists, PPAR-alpha, gamma or alpha/gamma agonists or modulators, PPAR-delta agonists, ACAT inhibitors, cholesterol absorption inhibitors, bile acid-binding substances, IBAT inhibitors, MTP inhibitors, modulators of PCSK9, LDL receptor up-regulators by liver selective thyroid hormone receptor β agonists, HDL-raising compounds, lipid metabolism modulators, PLA2 inhibitors, ApoA-I enhancers, thyroid hormone receptor agonists, cholesterol synthesis inhibitors, omega-3 fatty acids and derivatives thereof, active substances for the treatment of obesity, such as Sibutramine, Tesofensine, Orlistat, CB-1receptor antagonists, MCH-1 antagonists,

- MC4 receptor agonists and partial agonists, NPY5 or NPY2 antagonists, NPY4 agonists, beta-3-agonists, leptin or leptin mimetics, agonists of the 5HT2c receptor, or the combinations of bupropione/naltrexone (CONTRAVE), bupropione/zonisamide (EMPATIC), bupropione/phentermine or pramlintide/metreleptin, QNEXA (Phentermine+ topiramate), lipase inhibitors, angiogenesis inhibitors, H3 antagonists, AgRP inhibitors, triple monoamine uptake inhibitors (norepinephrine and acetylcholine), MetAP2 inhibitors, nasal formulation of the calcium channel blocker diltiazem, antisense against production of fibroblast growth factor receptor 4, prohibitin targeting peptide-1, drugs for influencing high blood pressure, chronic heart failure or atherosclerosis, such as angiotensin II receptor antagonists, ACE inhibitors, ECE inhibitors, diuretics, beta-blockers, calcium antagonists, centrally acting hypertensives, antagonists of the alpha-2-adrenergic receptor, inhibitors of neutral endopeptidase, thrombocyte aggregation inhibitors.
25. The compound of any one of claims 1 - 21 for use in the treatment of glucose intolerance, insulin resistance, pre-diabetes, increased fasting glucose (hyperglycemia), type 2 diabetes, hypertension, dyslipidemia, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke or any combination of these individual disease components.
26. The compound of any one of claims 1 - 21 which is suitable for use in control of appetite, feeding and calory intake, increase of energy expenditure, prevention of weight gain, promotion of weight loss, reduction of excess body weight, or which is for use in the treatment of obesity, including morbid obesity.
27. The compound of any one of claims 1 - 21 for use in the treatment or prevention of hyperglycemia, type 2 diabetes, obesity.
28. The compound of any one of claims 1 - 21 for use in the simultaneous

treatment of diabetes and obesity.

29. A pharmaceutical composition comprising at least one compound
according to any one of claims 1 – 21 or a physiologically acceptable
5 salt or a solvate of any of them.