SUMMARY ~~OF THE INVENTION~~

In a first aspect, the ~~invention~~ present disclosure provides a compound having the formula:

R^1-P^1-P^2-R^2

wherein

R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl or trifluoroacetyl;

R^2 is OH or NH_2;

P^1 is a peptide having the sequence:

H-X2-X3-GTFTSDYSKYLDSΨAAHDFVEWLLSA

wherein:

X2 is selected from Aib, Ala, D-Ala, Ser, N-Me-Ser, Ac3c, Ac4c and Ac5c;

X3 is selected from Gln and His;

P^2 is absent or is a sequence of 1-20 amino acid units independently selected from the group consisting of Ala, Leu, Ser, Thr, Tyr, Cys, Glu, Lys, Arg, Dbu, Dpr and Orn;

or a pharmaceutically acceptable salt or solvate thereof;

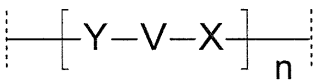
Ψ is a residue of Lys, Arg, Orn or Cys in which the side chain is conjugated to a substituent having the formula $–Z^2$-Z^1;

$–Z^1$ is a fatty chain having a polar group at one end of the chain and a connection to Z^2, –X– at the end of the chain distal from the polar group,

wherein the polar group comprises a carboxylic acid or a carboxylic acid bioisostere, a phosphonic acid, or a sulfonic acid group;

and –X– is a bond, –CO–, –SO–, or $–SO_2–$;

$–Z^2–$ is a spacer of formula:



wherein:

each Y is independently –NH, –NR, –S or –O, where R is alkyl, a protecting group or forms a linkage to another part of the spacer Z^2;

each X is independently a bond, CO–, SO–, or $SO_2–$;

with the proviso that when Y is –S, X is a bond;

each V is independently a bivalent organic moiety linking Y and X;

and n is 1-10;

or a pharmaceutically acceptable salt or solvate thereof.

P^1 may have the sequence:
H-Aib-QGTFTSDYSKYLDSΨAAHDFVEWLLSA

e.g.

H-Aib-QGTFTSDYSKYLDS-K([15-carboxy-pentadecanoyl]-isoGlu)-AAHDFVEWLLSA.

The compound as disclosed herein ~~of the invention~~ may be:
H-H-Aib-QGTFTSDYSKYLDSΨAAHDFVEWLLSA-NH_2

e.g.

H-H-Aib-QGTFTSDYSKYLDS-K([15-carboxy-pentadecanoyl]-isoGlu)-AAHDFVEWLLSA-NH_2.

In a second aspect, the ~~invention~~ present disclosure provides a compound having the formula:
R^1-P^1-P^2-R^2
wherein
R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl or trifluoroacetyl;
R^2 is OH or NH_2;
P^1 is a peptide having the sequence:

His-X2-X3-GTFTSDYSKYL-X15-X16-X17-X18-A-X20-DFI-X24-WLE-X28-A

wherein:
X2 is selected from Aib, Ac3c, Ac4c and Ac5c;
X3 is selected from Gln and His;
X15 is selected from Asp and Glu;
X16 is selected from Glu and Ψ;
X17 is selected from Arg and Ψ;
X18 is selected from Ala and Arg;
X20 is selected from Lys and His;
X24 is selected from Glu and Ψ;
X28 is selected from Ser and Ψ;

and P^2 is absent or is a sequence of 1-20 amino acid units independently selected from the group consisting of Ala, Leu, Ser, Thr, Tyr, Cys, Glu, Lys, Arg, Dbu, Dpr and Orn;

Useful combinations of residues include the following:
X2 is Ac4c and X20 is Lys;
X2 is Aib and X20 is His.

Additionally or alternatively, it may be desirable that X2 is Aib if X15 is E or that X15 is D if X2 is Ac4c.

Particularly interesting substituents Z^2Z^1 include [17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3 and [17-carboxy-heptadecanoyl]-isoGlu-GSGSGG.

P^1 may have a sequence selected from:
H-Aib-QGTFTSDYSKYLDΨRAAKDFIEWLESA
H-Aib-QGTFTSDYSKYLDΨRAAKDFIEWLESA
H-Aib-QGTFTSDYSKYLEΨRAAKDFIEWLESA
H-Ac4c-QGTFTSDYSKYLDΨRAAKDFIEWLESA and
H-Aib-QGTFTSDYSKYLEΨRAAHDFIEWLESA

e.g. from

H-Aib-QGTFTSDYSKYLD-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAAKDFIEWLESA
H-Aib-QGTFTSDYSKYLD-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-RAAKDFIEWLESA
H-Aib-QGTFTSDYSKYLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-RAAKDFIEWLESA
H-Ac4c-QGTFTSDYSKYLD-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-RAAKDFIEWLESA and
H-Aib-QGTFTSDYSKYLE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAAHDFIEWLESA

The compound as disclosed herein ~~of the invention~~ may be selected from:
H-H-Aib-QGTFTSDYSKYLDΨRAAKDFIEWLESA-NH_2
H-H-Aib-QGTFTSDYSKYLDΨRAAKDFIEWLESA-NH_2
H-H-Aib-QGTFTSDYSKYLEΨRAAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDΨRAAKDFIEWLESA-NH_2 and
H-H-Aib-QGTFTSDYSKYLEΨRAAHDFIEWLESA-NH_2

e.g. from

H-Aib-QGTFTSDYSKYLDERAAKDFIΨWLESA
H-Ac4c-QGTFTSDYSKYLDERAAKDFIΨWLESA
H-Ac4c-QGTFTSDYSKYLDERRAKDFIΨWLESA
H-Ac4c-QGTFTSDYSKYLDERAAKDFIEWLEΨA and
H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLEΨA

e.g. from

H-Aib-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA
H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA
H-Ac4c-HGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA
H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA
H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-RAKDFIEWLESA
H-Aib-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA
H-Ac4c-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA
H-Ac4c-QGTFTSDYSKYLDERRAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA
H-Ac4c-QGTFTSDYSKYLDERAAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A and
H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2

The compound as disclosed herein ~~of the invention~~ may be selected from:
H-H-Aib-QGTFTSDYSKYLDEΨAAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDEΨRAKDFIEWLESA-NH_2
H-H-Ac4c-HGTFTSDYSKYLDEΨRAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDEΨAAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDEΨRAKDFIEWLESA-NH_2
H-H-Aib-QGTFTSDYSKYLDERAAKDFIΨWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERAAKDFIΨWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIΨWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERAAKDFIEWLEΨA-NH_2 and
H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLEΨA-NH_2

e.g. from

H-H-Aib-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA-NH_2

H-H-Ac4c-HGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-RAKDFIEWLESA-NH_2

H-H-Aib-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDERRAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2

H-H-Ac4c-QGTFTSDYSKYLDERAAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2 and

H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2

For the avoidance of doubt, in all aspects of the ~~invention~~present disclosure, those positions which are not expressly stated to permit variability are fixed and thus may only include the stated residue.

In all aspects, the compound as disclosed herein ~~of the invention~~ comprises a residue Ψ, i.e. a residue selected from Lys, Arg, Orn and Cys in which the side chain is conjugated to a substituent $-Z^2-Z^1-$ as decribed in more detail below.

The substituent is conjugated to the functional group at the distal end of the side chain from the alpha-carbon. The normal ability of the Lys, Arg, Orn or Cys side chain to participate in interactions mediated by that functional group (e.g. intra- and inter-molecular interactions) may therefore be reduced or completely eliminated by the presence of the substituent. Thus, the overall properties of the compound may be relatively insensitive to changes in the actual amino acid present as residue Ψ. Consequently, it is believed that any of the residues Lys, Arg, Orn and Cys may be present at any position where Ψ is permitted. However, in certain embodiments, it may be advantageous that the amino acid component of Ψ is Lys.

In some embodiments, $-Z^1$ is an acyl group of formula:

A–B–Alk–(CO)–

or a sulfonyl group of formula:

$$A–B–Alk–(SO_2)–;$$

A is –COOH or a carboxylic acid bioisostere;

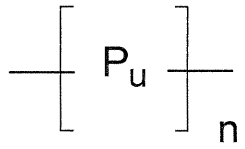
B is a bond, C_6arylene, or C_6arylene–O–;

Alk is a saturated or unsaturated fatty chain of 6 to 18 carbon atoms in length, optionally substituted with one or more substituents selected from fluoro, C_{1-4}alkyl, trifluoromethyl, hydroxymethyl, amino, hydroxyl, C_{1-4}alkoxy, oxo, and carboxyl;

$–Z^2–$ is $–S_A–$, $–S_A–S_B–$, or $–S_B–S_A–$;

$–S_A–$ is a single amino acid residue selected from γ-Glu, α-Glu, α-Asp, β-Asp, Ala, β-Ala (3-aminopropanoic acid), and Gaba (4-aminobutanoic acid);

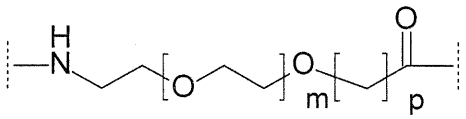
$–S_B–$ is a linker of general formula:



wherein n is 1–10 and each P_U is independently selected from P_U^{i} and P_U^{iii};

each P_U^{i} is independently a natural or unnatural amino acid residue; and

each P_U^{iii} is independently a residue of general formula:



wherein m is 0–5 and p is 1, 3, 4, or 5.

In any aspect of the ~~invention~~present disclosure, R^1 may be selected from H and C_{1-4} alkyl (e.g. methyl).

The compounds of the invention as disclosed herein are glucagon analogue peptides. References herein to a glucagon analogue peptide should be construed as references to a compound of the invention or to a peptide P^1 or P^1-P^2 as the context requires. Reference to a compound of the invention should be taken to include any pharmaceutically acceptable salt (e.g. an acetate or chloride salt) or solvate thereof, unless otherwise stated or excluded by context.

In an aspect, t~~T~~he ~~invention~~ present disclosure provides a composition comprising a compound ~~of the invention~~ as defined herein (including pharmaceutically acceptable salts or solvates thereof, as already described) in admixture with a carrier. In preferred embodiments, the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier. The glucagon analogue peptide may be in the form of a pharmaceutically acceptable salt of the glucagon analogue.

The compounds described herein find use, *inter alia*, in preventing weight gain or promoting weight loss. By "preventing" is meant inhibiting or reducing when compared to the absence of treatment, and is not necessarily meant to imply complete cessation of weight gain. The peptides may cause a decrease in food intake and/or increased energy expenditure, resulting in the observed effect on body weight. Independently of their effect on body weight, the compounds of the invention may have a beneficial effect on glucose control and/or on circulating cholesterol levels, being capable of lowering circulating LDL levels and increasing HDL/LDL ratio. Thus the compounds of the invention can be used for direct or indirect therapy of any condition caused or characterised by excess body weight, such as the treatment and/or prevention of obesity, morbid obesity, obesity linked inflammation, obesity linked gallbladder disease, obesity induced sleep apnea. They may also be used for the prevention of conditions caused or characterised by inadequate glucose control or dyslipidaemia (e.g. elevated LDL levels or reduced HDL/LDL ratio), diabetes (especially Type 2 diabetes), metabolic syndrome, hypertension, atherogenic dyslipidemia, atherosclerosis, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke or microvascular disease. Their effects in these conditions may be as a result of or associated with their effect on body weight, or may be independent thereof.

In an aspect, t~~T~~he ~~invention~~ present disclosure also provides a compound as disclosed herein ~~of the invention~~ for use in a method of medical treatment, particularly for use in a method of treatment of a condition as described above.

The ~~invention~~ present disclosure also provides the use of a compound as disclosed herein ~~of the invention~~ in the preparation of a medicament for the treatment of a condition as described above. In an aspect, the present disclosure provides the use of a compound as disclosed herein in the manufacture of a medicament for preventing weight gain or promoting weight loss in an individual in need thereof. In another aspect, the present disclosure provides the use of a compound as disclosed herein in the manufacture of a medicament for lowering circulating LDL levels, and/or increasing HDL/LDL ratio in an individual in need thereof. In yet another aspect, the present disclosure provides the use of a compound as disclosed herein in the manufacture of a medicament for treatment of a condition caused or characterised by excess body weight. In a further aspect, the present disclosure provides the use of a compound as disclosed herein in the manufacture of a medicament for prevention or

treatment of obesity, morbid obesity, morbid obesity prior to surgery, obesity linked inflammation, obesity linked gallbladder disease, obesity induced sleep apnea, diabetes, metabolic syndrome, hypertension, atherogenic dyslipidimia, atherosclerois, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke or microvascular disease.

The compound as disclosed herein ~~of the invention~~ may be administered as part of a combination therapy with an agent for treatment of diabetes, obesity, dyslipidaemia or hypertension.

In such cases, the two active agents may be given together or separately, and as part of the same pharmaceutical formulation or as separate formulations.

Thus the compound as disclosed herein ~~of the invention~~ can be used in combination with an anti-diabetic agent including but not limited to a biguanide (e.g. metformin), a sulfonylurea, a meglitinide or glinide (e.g. nateglinide), a DPP-IV inhibitor, an SGLT2 inhibitor, a glitazone, an insulin, or an

insulin analogue. Examples of insulin analogues include but are not limited to Lantus™, Novorapid™, Humalog™, Novomix™, Actraphane HM™, Levemir™ and Apidra™.

The compound can further be used in combination with an anti-obesity agent including but not limited to a glucagon-like peptide receptor 1 agonist, peptide YY or analogue thereof, cannabinoid receptor 1 antagonist, lipase inhibitor, melanocortin receptor 4 agonist, melanin concentrating hormone receptor 1 antagonist, phentermine (alone or in combination with topiramate), a combination of norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (e.g. a combination of bupropion and naltrexone), or a serotonergic agent (e.g. lorcaserin).

The compound can further be used in combination with an anti-hypertension agent including but not limited to an angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, diuretic, beta-blocker, or calcium channel blocker.

The compound can be used in combination with an anti-dyslipidaemia agent including but not limited to a statin, a fibrate, a niacin or a cholesterol absorbtion inhibitor.

In an aspect, the present disclosure provides a therapeutic kit comprising a compound as disclosed herein or a composition comprising the compound in admixture with a carrier as disclosed herein. Thus the ~~invention~~ present disclosure further provides a composition or therapeutic kit comprising a compound as disclosed herein ~~of the invention~~ and for example an anti-diabetic agent, anti-obesity agent, anti-hypertension agent or anti-dyslipidaemia agent as described above. Also provided is such a composition or therapeutic kit for use in a method of medical treatment, especially for treament of a condition as described above.

The compound as disclosed herein ~~of the invention~~ may be made by synthetic chemistry. Accordingly in an aspect, the ~~invention~~ present disclosure provides a method of synthesis of a compound as disclosed herein~~of the invention~~.

The ~~invention~~ present disclosure may also be made by a combination of recombinant and synthetic methods. The method may comprise expressing a precursor peptide sequence, optionally purifying the compund thus produced, and adding or modifying one or more amino acids to produce a compound as disclosed herein ~~of the invention~~ or a compound comprising the amino acid sequence P^1 or P^1-P^2. The step of modification may comprise introduction of an Orn residue (e.g. by modiication of a precursor residue) and/or introduction of a substituent Z2Z1 at the site of a residue Ψ. Accordingly in an aspect, the present disclosure provides a method of producing a compound as dislosed herein, the method comprising expressing a precursor peptide sequence from a nucleic acid construct that encodes the precursor peptide,

recovering the expression product, and modifying the precursor peptide to yield a compound as disclosed herein.

The precursor peptide may be expressed from a nucleic acid encoding the precursor peptide in a cell or a cell-free expression system comprising such a nucleic acid.

DETAILED DESCRIPTION OF THE INVENTION

Throughout this specification, the conventional one letter and three letter codes for naturally occurring amino acids are used, as well as generally accepted abbreviations for other amino

H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2

25. A compound according to claim 24 which is selected from:
H-H-Aib-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA-NH_2
H-H-Ac4c-HGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu-Peg3-Peg3)-RAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-AAKDFIEWLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDE-K([17-carboxy-heptadecanoyl]-isoGlu)-RAKDFIEWLESA-NH_2
H-H-Aib-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERAAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERRAKDFI-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-WLESA-NH_2
H-H-Ac4c-QGTFTSDYSKYLDERAAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2 and
H-H-Ac4c-QGTFTSDYSKYLDERRAKDFIEWLE-K([17-carboxy-heptadecanoyl]-isoGlu-GSGSGG)-A-NH_2

26. A composition comprising a compound according to any one of the preceding claims in admixture with a carrier.

27. A composition according to claim 26 wherein the composition is a pharmaceutical composition, and the carrier is a pharmaceutically acceptable carrier.

28. A compound according to any one of claims 1 to 25 for use in a method of medical treatment.

29. Use of a~~A~~ compound according to any one of claims 1 to 25 ~~for use~~ in the manufacture of a medicament for ~~a method of~~ preventing weight gain or promoting weight loss in an individual in need thereof.

30. Use of a~~A~~ compound according to any one of claims 1 to 25 ~~for use~~ in the manufacture of a medicament for ~~a method of~~ lowering circulating LDL levels, and/or increasing HDL/LDL ratio in an individual in need thereof.

31. Use of a~~A~~ compound according to any one of claims 1 to 25 ~~for use~~ in the manufacture of a medicament for ~~a method of~~ treatment of a condition caused or characterised by excess body weight.

32. Use of a~~A~~ compound according to any one of claims 1 to 25 ~~for use~~ in the manufacture of a medicament for ~~a method of~~ prevention or treatment of obesity, morbid obesity, morbid obesity prior to surgery, obesity linked inflammation, obesity linked gallbladder disease, obesity induced sleep apnea, diabetes, metabolic syndrome, hypertension, atherogenic dyslipidimia, atherosclerois, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke or microvascular disease.

33. ~~A compound for~~ The use according to any one of claims 29 to 32 wherein the compound is to be administered as part of a combination therapy together with an agent for treatment of diabetes, obesity, dyslipidemia or hypertension.

34. ~~A compound for~~ The use according to claim 33 wherein the agent for treatment of diabetes is a biguanide (e.g. metformin), a sulfonylurea, a meglitinide or glinide (e.g. nateglinide), a DPP-IV inhibitor, an SGLT2 inhibitor, a glitazone, a different GLP-1 agonist, an insulin or an insulin analogue.

35. ~~A compound for~~ The use according to claim 33, wherein the agent for treatment of obesity is a glucagon-like peptide receptor 1 agonist, peptide YY receptor agonist or analogue thereof, cannabinoid receptor 1 antagonist, lipase inhibitor, melanocortin receptor 4 agonist, melanin concentrating hormone receptor 1 antagonist, phentermine, a combination of norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (e.g. a combination of phentermine and topiramate), a combination of bupropion and naltrexone, or a serotonergic agent.

36. ~~A compound for~~The use according to claim 33 wherein the agent for treatment of hypertension is an angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, diuretic, beta-blocker, or calcium channel blocker.

37. ~~A compound for~~ The use according to claim 33 wherein the agent for treatment of dyslipidaemia is a statin, a fibrate, a niacin and/or a cholesterol absorbtion inhibitor.

38. A therapeutic kit comprising a compound according to any of claims 1 to 25 or a composition according to claim 26 or 27.

39. A method of synthesis of a compound according to any one of claims 1 to 25.

40. A method of producing a compound according to any one of claims 1 to 25, the method comprising expressing a precursor peptide sequence from a nucleic acid construct that encodes the precursor peptide, recovering the expression product, and modifying the precursor peptide to yield a compound according to any one of claims 1 to 25.