CLAIMS

1. A combination of compounds for use in a method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, wherein said method comprises administering to a mammalian subject a combination of compounds comprising:

(a) a compound having the formula:

R^1-Z-R^2

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

R^2 is OH or NH_2;

and Z is a peptide having the formula I:

His-X2-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-X27-X28-Ala-X30; (I)

wherein

X2 is selected from Aib and Ser;

X12 is selected from Lys, Arg, or Leu;

X16 is selected from Arg and X;

X17 is selected from Arg and X;

X20 is selected from Arg, His, and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and X;

X27 is selected from Leu and X;

X28 is selected from Arg and X;

X30 is X or is absent;

wherein at least one of X16, X17, X20, X24, X27, X28, and X30 is X;

and wherein each residue X is independently selected from the group consisting of Glu, Lys, Ser, Cys, Dbu, Dpr, and Orn;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2;

and

(b) an insulin analogue.

2. Use of (a) a compound having the formula:

R^1-Z-R^2

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula I:
His-X2-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-X27-X28-Ala-X30; (I)
wherein
X2 is selected from Aib and Ser;
X12 is selected from Lys, Arg, or Leu;
X16 is selected from Arg and X;
X17 is selected from Arg and X;
X20 is selected from Arg, His, and X;
X21 is selected from Asp and Glu;
X24 is selected from Ala and X;
X27 is selected from Leu and X;
X28 is selected from Arg and X;
X30 is X or is absent;
wherein at least one of X16, X17, X20, X24, X27, X28, and X30 is X;
and wherein each residue X is independently selected from the group consisting of Glu, Lys, Ser, Cys, Dbu, Dpr, and Orn;
wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2;
and
(b) an insulin analogue;
in the manufacture of a medicament for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight.

3. The use of claim 2, wherein the compound (a) and insulin analogue (b) are formulated for simultaneous or sequential administration.

4. The use of claim 2 or claim 3, wherein the the compound (a) and insulin analogue (b) are formulated as separate medicaments.

5. A method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, said method comprising administering to a mammalian subject a combination of compounds comprising:

(a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

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

R^2 is OH or NH_2;

and Z is a peptide having the formula I:

His-X2-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-X27-X28-Ala-X30; (I)

wherein

X2 is selected from Aib and Ser;

X12 is selected from Lys, Arg, or Leu;

X16 is selected from Arg and X;

X17 is selected from Arg and X;

X20 is selected from Arg, His, and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and X;

X27 is selected from Leu and X;

X28 is selected from Arg and X;

X30 is X or is absent;

wherein at least one of X16, X17, X20, X24, X27, X28, and X30 is X;

and wherein each residue X is independently selected from the group consisting of Glu, Lys, Ser, Cys, Dbu, Dpr, and Orn;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2;

and

(b) an insulin analogue.

6. The combination of compounds for use in a method of treatment, the use, or the method of claims 1-5, wherein said insulin analogue is selected from the group consisting of insulin glulisine, insulin lispro, Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin Lispro, insulin glargine , insulin detemir, insulin isophane, insulin aspart, insulin buccal, hyaluronidase insulin, and insulin protamine.

7. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-6, wherein (a) and (b) are administered in amounts that together are effective.

8. The combination of compounds for use in a method of treatment, the use, or the method of any one of claim 1-7, wherein (a) and (b) are administered within one month of each other.

9. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-8, wherein said condition caused or characterized by excess body weight is selected from the group consisting of obesity, morbid obesity, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea, metabolic syndrome, pre-diabetes, insulin resistance, glucose intolerance, type 2 diabetes, type I diabetes, hypertension, atherogenic dyslipidaemia, atherosclerosis, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke, and microvascular disease.

10. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-9, wherein said method prevents or reduces weight gain or promotes weight loss.

11. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-9, wherein said method improves circulating glucose levels.

12. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-11, wherein said subject has type 1 or type 2 diabetes.

13. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-12, wherein one or more of said residues X is independently selected from Lys, Glu and Cys.

14. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-13, wherein:
X16 is selected from Glu, Lys, and Ser;
X17 is selected from Lys and Cys;
X20 is selected from His, Lys, Arg, and Cys;
X24 is selected from Lys, Glu, and Ala;
X27 is selected from Leu and Lys; and/or
X28 is selected from Ser, Arg, and Lys.

15. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-14, wherein the peptide of formula I includes one or more of the following combinations of residues:

X2 is Aib and X17 is Lys;
X2 is Aib and X17 is Cys;
X2 is Aib and X20 is Cys;
X2 is Aib and X28 is Lys;
X12 is Arg and X17 is Lys;
X12 is Leu and X17 is Lys;
X12 is Lys and X20 is Lys;
X12 is Lys and X17 is Lys;
X16 is Lys and X17 is Lys;
X16 is Ser and X17 is Lys;
X17 is Lys and X20 is Lys;
X17 is Lys and X21 is Asp;
X17 is Lys and X24 is Glu;
X17 is Lys and X27 is Leu;
X17 is Lys and X27 is Lys;
X17 is Lys and X28 is Ser;
X17 is Lys and X28 is Arg;
X20 is Lys and X27 is Leu;
X21 is Asp and X27 is Leu;
X2 is Aib, X12 is Lys, and X16 is Ser;
X12 is Lys, X17 is Lys, and X16 is Ser;
X12 is Arg, X17 is Lys, and X16 is Glu;
X16 is Glu, X17 is Lys, and X20 is Lys;
X16 is Ser, X21 is Asp, and X24 is Glu;
X17 is Lys, X24 is Glu, and X28 is Arg;
X17 is Lys, X24 is Glu, and X28 is Lys;
X17 is Lys, X27 is Leu, and X28 is Ser;
X17 is Lys, X27 is Leu, and X28 is Arg;
X20 is Lys, X24 is Glu, and X27 is Leu;
X20 is Lys, X27 is Leu, and X28 is Ser;
X20 is Lys, X27 is Leu, and X28 is Arg;
X16 is Ser, X20 is His, X24 is Glu, and X27 is Leu;
X17 is Lys, X20 is His, X24 is Glu, and X28 is Ser;
X17 is Lys, X20 is Lys, X24 is Glu, and X27 is Leu; or

X17 is Cys, X20 is Lys, X24 is Glu, and X27 is Leu.

16. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-15, wherein the peptide of formula I contains only one amino acid of the type conjugated to the lipophilic substituent.

17. The combination of compounds for use in a method of treatment, the use, or the method of claim 16, wherein the peptide of formula I contains only one Lys residue, only one Cys residue, or only one Glu residue, andwherein the lipophilic substituent is conjugated to that residue.

18. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-17, wherein the peptide sequence of formula I comprises one or more intramolecular bridges.

19. The combination of compounds for use in a method of treatment, the use, or the method of claim 18, wherein the intramolecular bridge is formed between the side chains of two amino acid residues which are separated by three amino acids in the linear amino acid sequence of formula I.

20. The combination of compounds for use in a method of treatment, the use, or the method of claim 19, wherein the intramolecular bridge is formed between the side chains of residue pairs 16 and 20, 17 and 21, 20 and 24, or 24 and 28.

21. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 18-20, wherein the intramolecular bridge is a salt bridge or a lactam ring.

22. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 18-21, wherein the intramolecular bridge involves a pair of residues selected from the group consisting of:
X16 is Glu and X20 is Lys;
X16 is Glu and X20 is Arg;
X16 is Lys and X20 is Glu;
X16 is Arg and X20 is Glu;
X17 is Arg and X21 is Glu;
X17 is Lys and X21 is Glu;
X17 is Arg and X21 is Asp;
X17 is Lys and X21 is Asp;
X20 is Glu and X24 is Lys;
X20 is Glu and X24 is Arg;

X20 is Lys and X24 is Glu;
X20 is Arg and X24 is Glu;
X24 is Glu and X28 is Lys;
X24 is Glu and X28 is Arg;
X24 is Lys and X28 is Glu; and
X24 is Arg and X28 is Glu.

23. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-22, wherein at least one of X16, X17, X20, and X28 is conjugated to a lipophilic substituent.

24. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-23, wherein X30 is absent.

25. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-23, wherein X30 is present and is conjugated to a lipophilic substituent.

26. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-25, wherein the compound has just one lipophilic substituent, at position 16, 17, 20, 24, 27, 28 or 30, preferably at position 16, 17 or 20, particularly at position 17.

27. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-25, wherein the compound has precisely two lipophilic substituents, each at one of positions 16, 17, 20, 24, 27, 28, and 30.

28. The combination of compounds for use in a method of treatment, the use, or the method of claim 27, wherein the compound has lipophilic substituents at positions 16 and 17, 16 and 20, 16 and 24, 16 and 27, 16 and 28, 16 and 30, 17 and 20, 17 and 24, 17 and 27, 17 and 28, 17 and 30, 20 and 24, 20 and 27, 20 and 28, 20 and 30, 24 and 27, 24 and 28, 24 and 30, 27 and 28, 27 and 30, or 28 and 30.

29. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-12, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IIa:

His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIa)

wherein:

X12 is selected from Lys, Arg, and Leu;

X16 is selected from Ser and X;

X17 is X;

X20 is selected from His and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

and wherein each residue X is independently selected from the group consisting of Glu, Lys, and Cys;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

30. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-12, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

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

R^2 is OH or NH_2;

and Z is a peptide having the formula IIb:

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIb)

wherein:

X12 is selected from Lys, Arg, and Leu;

X16 is selected from Ser and X;

X17 is X;

X20 is selected from His and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

and wherein each residue X is independently selected from the group consisting of Glu, Lys, and Cys;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

31. The combination of compounds for use in a method of treatment, the use, or the method of claim 29, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IIIa:
His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIIa)
wherein:
X12 is selected from Lys And Arg;
X17 is X;
X20 is selected from His and X;
X21 is selected from Asp and Glu;
X24 is selected from Ala and Glu;
X28 is selected from Ser, Lys, and Arg;
and wherein each residue X is independently selected from Glu, Lys, and Cys;
wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

32. The combination of compounds for use in a method of treatment, the use, or the method of claim 30, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IIIb:
His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIIb)
wherein:
X12 is selected from Lys and Arg;
X17 is X;
X20 is selected from His and X;

X21 is selected from Asp and Glu;
X24 is selected from Ala and Glu;
X28 is selected from Ser, Lys, and Arg;
and wherein each residue X is independently selected from Glu, Lys, and Cys;
wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

33. The combination of compounds for use in a method of treatment, the use, or the method of claim 31, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IVa:
His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IVa):
wherein
X12 is selected from Lys and Arg;
X17 is X;
X21 is selected from Asp and Glu;
X24 is selected from Ala and Glu;
X28 is selected from Ser, Lys, and Arg;
wherein X is selected from the group consisting of Glu, Lys, and Cys;
and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

34. The combination of compounds for use in a method of treatment, the use, or the method of claim 32, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IVb:

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IVb)

wherein:

X12 is selected from Lys and Arg;

X17 is X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

wherein X is selected from the group consisting of Glu, Lys, and Cys;

and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

35. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-34, wherein said peptide Z has the sequence:

HSQGTFTSDYSKYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDKKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAKDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLKRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLLKA;

HSQGTFTSDYSRYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSLYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLLRAK;

HSQGTFTSDYSKYLDSKAAHDFVEWLLSAK;

HSQGTFTSDYSKYLDSKAAHDFVEWLKSA;

HSQGTFTSDYSKYLDSKAAHDFVKWLLRA;

HSQGTFTSDYSKYLDSCAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSCAAHDFVEWLLSA;

HSQGTFTSDYSKYLDSKAACDFVEWLLRA;

HSQGTFTSDYSKYLDKSAAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSAK;

H-Aib-QGTFTSDYSKYLDSKAARDFVAWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAKDFVAWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLKA;

H-Aib-QGTFTSDYSKYLDSKAAKDFVAWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVAWLLKA;
H-Aib-QGTFTSDYSKYLDKKAAHDFVAWLLRA;
H-Aib-QGTFTSDYSRYLDSKAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVKWLLSA;
H-Aib-QGTFTSDYSLYLDSKAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSCAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAACDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDK()KAAE()DFVEWLLRA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVE()WLLK()A;
H-Aib-QGTFTSDYSKYLDSKAAK()DFVE()WLLRA;
H-Aib-QGTFTSDYSKYLDSK()AAHE()FVEWLLKA; or
H-Aib-QGTFTSDYSKYLDSK()AAKE()FVEWLLRA.

36. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-35, wherein said peptide Z has the sequence:
HSQGTFTSDYSKYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLD-K*-KAAHDFVEWLLRA;
HSQGTFTSDYSKYLDSKAA-K*-DFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWL-K*-RA;
HSQGTFTSDYSKYLDSKAAHDFVEWLL-K*-A;
HSQGTFTSDYSRYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSLYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWLLRA-K*;
HSQGTFTSDYSKYLDSKAAHDFVEWLLSA-K*;
HSQGTFTSDYSKYLDSKAAHDFVEWL-K*-SA;
HSQGTFTSDYSKYLDSKAAHDFV-K*-WLLRA;
HSQGTFTSDYSKYLDS-C*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLDS-C*-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDSKAA-C*-DFVEWLLRA;
HSQGTFTSDYSKYLD-K*-SAAHDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSA-K*;
H-Aib-QGTFTSDYSKYLDS-K*-AARDFVAWLLRA;
H-Aib-QGTFTSDYSKYLDSKAA-K*-DFVAWLLRA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLL-K*-A;
H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLKA;
H-Aib-QGTFTSDYSKYLDSKAA-K*-DFVAWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVAWLL-K*-A;
H-Aib-QGTFTSDYSKYLD-K*-KAAHDFVAWLLRA;
H-Aib-QGTFTSDYSRYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFV-K*-WLLSA;
H-Aib-QGTFTSDYSLYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-C*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAA-C*-DFVEWLLRA;
H-Aib-QGTFTSDYSKYLD-S*-KAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDK()K*AAE()DFVEWLLRA;
H-Aib-QGTFTSDYSKYLDSK*AAHDFVE()WLLK()A
H-Aib-QGTFTSDYSKYLDSK*AAK()DFVE()WLLRA;
H-Aib-QGTFTSDYSKYLDSK()AAHE()FVEWLLK*A; or
H-Aib-QGTFTSDYSKYLDSK()AAK*E()FVEWLLRA,
wherein "*" indicates the position of a lipophilic substituent.

37. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-36, wherein Z^1 comprises a hydrocarbon chain having 10 to 24 C atoms, 10 to 22 C atoms, or 10 to 20 C atoms.

38. The combination of compounds for use in a method of treatment, the use, or the method of claim 37, wherein Z^1 is a dodecanoyl, 2-butyloctanoyl, tetradecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, or eicosanoyl moiety.

39 The combination of compounds for use in a method of treatment, the use, or the method of any one claims 1-38, wherein Z^2 is or comprises one or more amino acid residues.

40. The combination of compounds for use in a method of treatment, the use, or the method of claim 39, wherein Z^2 is a γ-Glu, Glu, β-Ala or ε-Lys residue, or a 3-aminopropanoyl, 4-aminobutanoyl, 8-aminooctanoyl, or 8-amino-3,6-dioxaoctanoyl moiety.

41. The combination of compounds for use in a method of treatment, the use, or the method of claim 40, wherein the lipophilic substituent is selected from the group consisting of dodecanoyl-γ-Glu, hexadecanoly- γ-Glu, hexadecanoyl-Glu, hexadecanoyl-[3-aminopropanoyl], hexadecanoyl-[8-aminooctanoyl], hexadecanoyl-ε-Lys, 2-butyloctanoyl- γ-Glu, octadecanoyl-γ-Glu, and hexadecanoyl-[4-aminobutanoyl].

42. The combination of compounds for use in a method of treatment, the use, or the method of claim 41, wherein Z has the formula:

HSQGTFTSDYSKYLD-K(Hexadecanoyl-γ-Glu)-KAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWL-K(Hexadecanoyl-γ-Glu)-RA;

HSQGTFTSDYSKYLDSKAA-K(Hexadecanoyl-γ-Glu)-DFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLL-K(Hexadecanoyl-γ-Glu)-A;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AARDFVAWLLRA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLL-K(Hexadecanoyl-γ-Glu)-A;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLKA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVE()WLLK()A;

HSQGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDSKAA-K(Hexadecanoyl-γ-Glu)-DFVAWLLRA;

H-Aib-QGTFTSDYSKYLDS-K(Dodecanoyl-γ-Glu)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[3-aminopropanoyl])-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[8-aminooctanoyl])-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-ε-Lys)-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Hexadecanoyl)-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K([2-Butyloctanoyl]-γ-Glu)-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Hexadecanoyl-[4-Aminobutanoyl])-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Hexadecanoyl-E)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K([2-Butyloctanoyl]-γ-Glu)-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[4-Aminobutanoyl])-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA; or

H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-E)-AAHDFVEWLLSA;

wherein residues marked "()" participate in an intramolecular bond.

43. The combination of compounds for use in a method of treatment, the use, or the method of claim 41, wherein Z has the formula:

H-Aib-QGTFTSDYS-K(Hexadecanoyl-isoGlu)-YLDSKAAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLD-K(Hexadecanoyl-isoGlu)-KAAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDSKAA-K(Hexadecanoyl-isoGlu)-DFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFV-K(Hexadecanoyl-isoGlu)-WLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoLys)-AARDFVAWLLRA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAKDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDE-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHEFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAEDFVEWLLSA; or
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLEA.

44. A combination of compounds for use in a method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, said method comprising administering to a mammalian subject a combination of compounds comprising:

(a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, $C_{1\text{-}4}$ alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula V:
His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-X28; (V)
wherein:
X17 is X;
X28 is Ser or absent;
wherein X is selected from the group consisting of Glu, Lys, and Cys;
and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and
(b) an insulin analogue.

45. Use of (a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, $C_{1\text{-}4}$ alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula V:

His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-X28; (V)

wherein:

X17 is X;

X28 is Ser or absent;

wherein X is selected from the group consisting of Glu, Lys, and Cys;

and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and

(b) an insulin analogue;

in the manufacture of a medicament for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight.

46. The use of claim 45, wherein the compound (a) and insulin analogue (b) are formulated for simultaneous or sequential administration.

47. The use of claim 45 or claim 46, wherein the the compound (a) and insulin analogue (b) are formulated as separate medicaments.

48. A method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, said method comprising administering to a mammalian subject a combination of compounds comprising:

(a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

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

R^2 is OH or NH_2;

and Z is a peptide having the formula V:

His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-X28; (V)

wherein:

X17 is X;

X28 is Ser or absent;

wherein X is selected from the group consisting of Glu, Lys, and Cys;

and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and
(b) an insulin analogue.

49. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 44-48, wherein said insulin analogue is selected from the group consisting of insulin glulisine (Apidra), insulin lispro (Humalog), Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin Lispro, insulin glargine (Lantus), insulin detemir (Levemir), insulin isophane, insulin aspart, insulin buccal, hyalurinidase, and insulin protamine

50. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-49, wherein (a) and (b) are administered in amounts that together are effective.

51. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-50, wherein (a) and (b) are administered within one month of each other.

52. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-51, wherein said condition caused or characterized by excess body weight is selected from the group consisting of obesity, morbid obesity, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea, metabolic syndrome, pre-diabetes, insulin resistance, glucose intolerance, type 2 diabetes, type 1 diabetes, hypertension, atherogenic dyslipidaemia, atherosclerosis, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke, and microvascular disease.

53. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-52, wherein said method prevents or reduces weight gain or promotes weight loss.

54. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-52, wherein said method improves circulating glucose levels.

55. The combination of compounds in a method of treatment, the use, or the method of any one claims 44-54, wherein said subject has type 1 or type 2 diabetes.

56. The combination of compounds for use in a method of treatment, the use, or the method of claim 55, wherein said subject has type 2 diabetes.

57. The combination of compounds for use in a method of treatment, the use, or the method of any one claims 44-56, wherein Z has the formula:
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLS; or
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLL.

58. A combination of compounds for use in a method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, said method comprising administering to a mammalian subject a combination of compounds comprising:
(a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula VI:
His-Aib-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-Ser-Ala; (VI)
wherein:
X17 is X;
wherein X is selected from the group consisting of Glu, Lys, and Cys;
and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and
(b) an insulin analogue.

59. Use of (a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula VI:
His-Aib-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-Ser-Ala; (VI)
wherein:
X17 is X;
wherein X is selected from the group consisting of Glu, Lys, and Cys;
and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and
(b) an insulin analogue;
in the manufacture of a medicament for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight.

60. The use of claim 59, wherein the compound (a) and insulin analogue (b) are formulated for simultaneous or sequential administration.

61. The use of claim 59 or claim 60, wherein the the compound (a) and insulin analogue (b) are formulated as separate medicaments.

62. A method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight, said method comprising administering to a mammalian subject a combination of compounds comprising:
(a) a compound having the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula VI:
His-Aib-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-Asp-Phe-Val-Glu-Trp-Leu-Leu-Ser-Ala; (VI)
wherein:
X17 is X;
wherein X is selected from the group consisting of Glu, Lys, and Cys;
and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2; and
(b) an insulin analogue.

63. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-62, wherein said insulin analogue is selected from the group consisting of insulin glulisine ,

insulin lispro, Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin lispro, insulin glargine, insulin detemir, NN-1953, IN-105, BIOD-620 and Analog-PH20.

64. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-63, wherein (a) and (b) are administered in amounts that together are effective.

65. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-64, wherein (a) and (b) are administered within one month of each other.

66. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-65, wherein said condition caused or characterized by excess body weight is selected from the group consisting of obesity, morbid obesity, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea, metabolic syndrome, pre-diabetes, insulin resistance, glucose intolerance, type 2 diabetes, type 1 diabetes, hypertension, atherogenic dyslipidaemia, atherosclerosis, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke, and microvascular disease.

67. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-66, wherein said method prevents or reduces weight gain or promotes weight loss.

68. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-66, wherein said method improves circulating glucose levels.

69. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-68, wherein said subject has type 1 or type 2 diabetes.

70. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 58-69, wherein Z has the formula: H-Aib-EGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA.

71. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and insulin glargine.

72. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and insulin detemir.

73. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and glulisine.

74. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and insulin lispro.

75. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and degludec.

76. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and Actraphane.

77. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and LY2963016.

78. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and LY2605541.

79. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and pegylated insulin Lispro.

80. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-5, wherein said combination of compounds includes H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and NN-1953, IN-105, BIOD-620 and Analog-PH20.

81. The combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-80, wherein (a) and (b) are administered within one week, three days, or two days of each other.

82. The combination of compounds for use in a method of treatment, the use, or the method of claim 81, wherein (a) and (b) are administered within one day, 12 hours, or six hours of each other.

83. A compound for use in a method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight in a mammalian subject that is receiving an insulin analogue, said method comprising administering to said subject the compound recited in any one of claims 1-80 in an effective amount.

84. Use of the compound recited in any one of claims 1-80, in the manufacture of a medicament for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treating a condition caused or characterized by excess body weight in a mammalian subject that is receiving an insulin analogue.

85. A method for preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; lowering circulating triacylglycerol levels, lowering circulating free fatty acids or treating a condition caused or characterized by excess body weight in a mammalian subject that is receiving an insulin analogue, said method comprising administering to said subject the compound recited in any one of claims 1-80 in an effective amount.

86. The compound for use in a method of treatment, the use, or the method of any one of claims 1-85, wherein said insulin analogue is selected from the group consisting of insulin glulisine (Apidra), insulin lispro (Humalog), Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin Lispro, insulin glargine (Lantus), insulin detemir (Levemir), NN-1953, IN-105, BIOD-620 and Analog-PH20.

87. The compound for use in a method of treatment, the use, or the method of any one of claims 83-86, wherein said condition caused or characterized by excess body weight is selected from the group consisting of obesity, morbid obesity, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea, metabolic syndrome, pre-diabetes, insulin resistance, glucose intolerance, type 2 diabetes, type I diabetes, hypertension, atherogenic dyslipidaemia, hypertriglyceridemia, hypercholesterolemia, atherosclerosis, arteriosclerosis, coronary heart disease, peripheral artery disease, stroke, and microvascular disease.

88. The compound for use in a method of treatment, the use, or the method of any one of claims 83-87, wherein said method prevents or reduces weight gain or promotes weight loss.

89. The compound for use in a method of treatment, the use, or the method of any one of claims 83-87, wherein said method improves circulating glucose levels.

90. The compound for use in a method of treatment, the use, or the method of any one of claims 83-89, wherein said subject has type 1 or type 2 diabetes.

91. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-91, wherein said compound is part of a composition comprising said compound, or a salt or derivative thereof, in admixture with a carrier.

92. The compound or combination of compounds for use in a method of treatment, the use, or the method of claim 91, wherein said composition is a pharmaceutically acceptable composition, and the carrier is a pharmaceutically acceptable carrier.

93. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-93, wherein said compound is administered in a dosage of 0.1 nmol/kg to 1 µmol/kg.

94. The compound or combination of compounds for use in a method of treatment, the use, or the method of claim 93, wherein said compound is administered in a dosage of 3 nmol/kg to 30 nmol/kg.

95. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-94, wherein said insulin analogue is administered in a dosage of 0.02 U/kg to 20 U/kg.

96. The compound or combination of compounds for use in a method of treatment, the use, or the method of claim 95, wherein said insulin analogue is administered in a dosage of 0.1 U/kg to 0.3 U/kg or in a dosage of about 0.2 U/kg.

97. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-96, wherein said compound is administered every other week, weekly, every other day, daily, twice daily, or three times daily.

98. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-97, wherein said insulin analogue is administered every other week, weekly, every other day, daily, twice daily, or three times daily.

99. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein said compound or combination of compounds is administered in an amount sufficient to reduce food intake in said subject by at least 5%, 10%, 15%, 20%, 25%, 30%, or 50%.

100. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein said combination of compounds is administered in an amount sufficient to reduce the subject's fasting blood glucose level by at least 1, 2, 3, 4, 5, 6, 8, 10, 11, 12, 15, or 20 mM.

101. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein said compound or combination of compounds is administered in an amount sufficient to reduce the subject's HbA1c level by at least 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.8%, 1.0%, 1.5%, or 2.0%.

102. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein administration of said compound or combination of compounds results in a body weight reduction of at least 3%, 5%, 8%, 10%, 12%, 15% or 20% within 1 year of starting administration.

103. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein administration of said compound or combination of compounds results in a body weight reduction of at least 1%, 2%, 3%, 4%, 5%, 6%, 8%, or 10%, 15% within six months of starting administration.

104. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-98, wherein administration of said compound or combination of compounds results in a body weight reduction of at least 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 8%, 10% or 15% within three months of starting administration.

105. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-104, wherein said compound is administered subcutaneously, intravenously, intramuscularly, by inhalation, rectally, buccally, intraperitoneally, intraarticularly, or orally.

107. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-105, where said insulin analogue is administered subcutaneously, intravenously, intramuscularly, by inhalation, rectally, buccally, intraperitoneally, intraarticularly, or orally.

108. The compound or combination of compounds for use in a method of treatment, the use, or the method of any one of claims 1-107, wherein said subject is a human.

109. A kit comprising:
(a) a compound as recited in any of claims 1-80; and
(b) an insulin analogue.

110. The kit of claim 109 further comprising:
(c) instructions for administering (a) and (b) to a mammalian subject in need of preventing or reducing weight gain; promoting weight loss; improving circulating glucose levels, glucose tolerance or circulating cholesterol levels; lowering circulating LDL levels; increasing HDL/LDL ratio; or treatment for a condition caused or characterized by excess body weight.

111. The kit of claim 109 or 110, wherein said insulin analogue is selected from the group consisting of insulin glulisine, insulin lispro, Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin Lispro, insulin glargine (Lantus) insulin detemir (Levemir), NN-1953, IN-105, BIOD-620 and Analog-PH20.

CLAIMS

1. Use of a compound having the formula:

R^1-Z-R^2

wherein R^1 is H, C_{1-4} alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula I:
His-X2-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-X27-X28-Ala-X30; (I)
wherein
X2 is selected from Aib and Ser;
X12 is selected from Lys, Arg, or Leu;
X16 is selected from Arg and X;
X17 is selected from Arg and X;
X20 is selected from Arg, His, and X;
X21 is selected from Asp and Glu;
X24 is selected from Ala and X;
X27 is selected from Leu and X;
X28 is selected from Arg and X;
X30 is X or is absent;
wherein at least one of X16, X17, X20, X24, X27, X28, and X30 is X;
and wherein each residue X is independently selected from the group consisting of Glu, Lys, Ser, Cys, Dbu, Dpr, and Orn;
wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2;
in the manufacture of a medicament for preventing or reducing weight gain or promoting weight loss in a mammalian subject having type 2 diabetes that is receiving an insulin analogue.

2. The use of claim 1, wherein

said compound having formula R1-Z-R2 is administered in a dosage of 3 nmol/kg to 30 nmol/kg; and/or

said insulin analogue is administered in a dosage of 0.02 U/kg to 0.3 U/kg or in a dosage of about 0.2 U/kg.

3. The use of claim 1, wherein the compound having formula R^1-Z-R^2 and the insulin analogue are formulated for simultaneous or sequential administration and/or wherein the compound having formula R^1-Z-R^2 and the insulin analogue are formulated as separate medicaments.

4. The use of any preceding claim,

wherein one or more of said residues X is independently selected from Lys, Glu and Cys; and/or wherein

X16 is selected from Glu, Lys, and Ser;

X17 is selected from Lys and Cys;

X20 is selected from His, Lys, Arg, and Cys;

X24 is selected from Lys, Glu, and Ala;

X27 is selected from Leu and Lys; and/or

X28 is selected from Ser, Arg, and Lys; and/or

wherein the peptide of formula I includes one or more of the following combinations of residues:

X2 is Aib and X17 is Lys;

X2 is Aib and X17 is Cys;

X2 is Aib and X20 is Cys;

X2 is Aib and X28 is Lys;

X12 is Arg and X17 is Lys;

X12 is Leu and X17 is Lys;

X12 is Lys and X20 is Lys;

X12 is Lys and X17 is Lys;

X16 is Lys and X17 is Lys;

X16 is Ser and X17 is Lys;

X17 is Lys and X20 is Lys;

X17 is Lys and X21 is Asp;

X17 is Lys and X24 is Glu;

X17 is Lys and X27 is Leu;

X17 is Lys and X27 is Lys;

X17 is Lys and X28 is Ser;

X17 is Lys and X28 is Arg;

X20 is Lys and X27 is Leu;

X21 is Asp and X27 is Leu;

X2 is Aib, X12 is Lys, and X16 is Ser;

X12 is Lys, X17 is Lys, and X16 is Ser;

X12 is Arg, X17 is Lys, and X16 is Glu;

X16 is Glu, X17 is Lys, and X20 is Lys;

X16 is Ser, X21 is Asp, and X24 is Glu;

X17 is Lys, X24 is Glu, and X28 is Arg;

X17 is Lys, X24 is Glu, and X28 is Lys;

X17 is Lys, X27 is Leu, and X28 is Ser;

X17 is Lys, X27 is Leu, and X28 is Arg;

X20 is Lys, X24 is Glu, and X27 is Leu;

X20 is Lys, X27 is Leu, and X28 is Ser;

X20 is Lys, X27 is Leu, and X28 is Arg;
X16 is Ser, X20 is His, X24 is Glu, and X27 is Leu;
X17 is Lys, X20 is His, X24 is Glu, and X28 is Ser;
X17 is Lys, X20 is Lys, X24 is Glu, and X27 is Leu; or
X17 is Cys, X20 is Lys, X24 is Glu, and X27 is Leu.

5. The use of any preceding claim, wherein the peptide of formula I contains only one amino acid of the type conjugated to the lipophilic substituent, optionally wherein the peptide of formula I contains only one Lys residue, only one Cys residue, or only one Glu residue, and wherein the lipophilic substituent is conjugated to that residue.

6. The use of any preceding claim, wherein the peptide sequence of formula I comprises one or more intramolecular bridges, optionally wherein the intramolecular bridge is formed between the side chains of two amino acid residues which are separated by three amino acids in the linear amino acid sequence of formula I, optionally wherein the intramolecular bridge is formed between the side chains of residue pairs 16 and 20, 17 and 21, 20 and 24, or 24 and 28, optionally wherein the intramolecular bridge involves a pair of residues selected from the group consisting of:
X16 is Glu and X20 is Lys;
X16 is Glu and X20 is Arg;
X16 is Lys and X20 is Glu;
X16 is Arg and X20 is Glu;
X17 is Arg and X21 is Glu;
X17 is Lys and X21 is Glu;
X17 is Arg and X21 is Asp;
X17 is Lys and X21 is Asp;
X20 is Glu and X24 is Lys;
X20 is Glu and X24 is Arg;
X20 is Lys and X24 is Glu;
X20 is Arg and X24 is Glu;
X24 is Glu and X28 is Lys;
X24 is Glu and X28 is Arg;
X24 is Lys and X28 is Glu; and
X24 is Arg and X28 is Glu
and/or optionally wherein the intramolecular bridge is a salt bridge or a lactam ring.

7. The use of any preceding claim, wherein:
a) at least one of X16, X17, X20, and X28 is conjugated to a lipophilic substituent; or
b) X30 is absent; or
c) wherein X30 is present and is conjugated to a lipophilic substituent.

8. The use of any preceding claim, wherein

a) the compound has just one lipophilic substituent, at position 16, 17, 20, 24, 27, 28 or 30, preferably at position 16, 17 or 20, particularly at position 17; or

b) the compound has precisely two lipophilic substituents, each at one of positions 16, 17, 20, 24, 27, 28, and 30; or

c) the compound has lipophilic substituents at positions 16 and 17, 16 and 20, 16 and 24, 16 and 27, 16 and 28, 16 and 30, 17 and 20, 17 and 24, 17 and 27, 17 and 28, 17 and 30, 20 and 24, 20 and 27, 20 and 28, 20 and 30, 24 and 27, 24 and 28, 24 and 30, 27 and 28, 27 and 30, or 28 and 30.

9. The use according to claim 1, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, $C_{1\text{-}4}$ alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IIa:
His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIa)
wherein:
X12 is selected from Lys, Arg, and Leu;
X16 is selected from Ser and X;
X17 is X;
X20 is selected from His and X;
X21 is selected from Asp and Glu;
X24 is selected from Ala and Glu;
X28 is selected from Ser, Lys, and Arg;
and wherein each residue X is independently selected from the group consisting of Glu, Lys, and Cys; wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:
(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or
(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

10. The use of claim 1, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

wherein R^1 is H, $C_{1\text{-}4}$ alkyl, acetyl, formyl, benzoyl, or trifluoroacetyl;
R^2 is OH or NH_2;
and Z is a peptide having the formula IIb:
His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-X16-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIb)

wherein:

X12 is selected from Lys, Arg, and Leu;

X16 is selected from Ser and X;

X17 is X;

X20 is selected from His and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

and wherein each residue X is independently selected from the group consisting of Glu, Lys, and Cys;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

11. The use of claim 9, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

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

R^2 is OH or NH_2;

and Z is a peptide having the formula IIIa:

His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIIa)

wherein:

X12 is selected from Lys And Arg;

X17 is X;

X20 is selected from His and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

and wherein each residue X is independently selected from Glu, Lys, and Cys;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

12. The use of claim 10, wherein said compound has the formula:

$$R^1\text{-}Z\text{-}R^2$$

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

R^2 is OH or NH_2;

and Z is a peptide having the formula IIIb:

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-X20-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IIIb)

wherein:

X12 is selected from Lys and Arg;

X17 is X;

X20 is selected from His and X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

and wherein each residue X is independently selected from Glu, Lys, and Cys;

wherein the side chain of at least one residue X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

13. The use of claim 11, wherein said compound has the formula:

R^1-Z-R^2

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

R^2 is OH or NH_2;

and Z is a peptide having the formula IVa:

His-Aib-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IVa):

wherein

X12 is selected from Lys and Arg;

X17 is X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

wherein X is selected from the group consisting of Glu, Lys, and Cys;

and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

14. The use of claim 12, wherein said compound has the formula:

R^1-Z-R^2

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

R^2 is OH or NH_2;

and Z is a peptide having the formula IVb:

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-X12-Tyr-Leu-Asp-Ser-X17-Ala-Ala-His-X21-Phe-Val-X24-Trp-Leu-Leu-X28-Ala; (IVb)

wherein:

X12 is selected from Lys and Arg;

X17 is X;

X21 is selected from Asp and Glu;

X24 is selected from Ala and Glu;

X28 is selected from Ser, Lys, and Arg;

wherein X is selected from the group consisting of Glu, Lys, and Cys;

and wherein the side chain of X is conjugated to a lipophilic substituent having the formula:

(i) Z^1, wherein Z^1 is a lipophilic moiety conjugated directly to the side chain of X; or

(ii) Z^1Z^2, wherein Z^1 is a lipophilic moiety, Z^2 is a spacer, and Z^1 is conjugated to the side chain of X via Z^2.

15. The use of any preceding claim, wherein said peptide Z has the sequence:

HSQGTFTSDYSKYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDKKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAKDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLKRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLLKA;

HSQGTFTSDYSRYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSLYLDSKAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSKAAHDFVEWLLRAK;

HSQGTFTSDYSKYLDSKAAHDFVEWLLSAK;

HSQGTFTSDYSKYLDSKAAHDFVEWLKSA;

HSQGTFTSDYSKYLDSKAAHDFVKWLLRA;

HSQGTFTSDYSKYLDSCAAHDFVEWLLRA;

HSQGTFTSDYSKYLDSCAAHDFVEWLLSA;

HSQGTFTSDYSKYLDSKAACDFVEWLLRA;

HSQGTFTSDYSKYLDKSAAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSAK;

H-Aib-QGTFTSDYSKYLDSKAARDFVAWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAKDFVAWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLRA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLKA;

H-Aib-QGTFTSDYSKYLDSKAAKDFVAWLLSA;

H-Aib-QGTFTSDYSKYLDSKAAHDFVAWLLKA;

H-Aib-QGTFTSDYSKYLDKKAAHDFVAWLLRA;

H-Aib-QGTFTSDYSRYLDSKAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVKWLLSA;
H-Aib-QGTFTSDYSLYLDSKAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSCAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAACDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDK()KAAE()DFVEWLLRA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVE()WLLK()A;
H-Aib-QGTFTSDYSKYLDSKAAK()DFVE()WLLRA;
H-Aib-QGTFTSDYSKYLDSK()AAHE()FVEWLLKA; or
H-Aib-QGTFTSDYSKYLDSK()AAKE()FVEWLLRA; or
wherein said peptide Z has the sequence:
HSQGTFTSDYSKYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLD-K*-KAAHDFVEWLLRA;
HSQGTFTSDYSKYLDSKAA-K*-DFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWL-K*-RA;
HSQGTFTSDYSKYLDSKAAHDFVEWLL-K*-A;
HSQGTFTSDYSRYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSLYLDS-K*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWLLRA-K*;
HSQGTFTSDYSKYLDSKAAHDFVEWLLSA-K*;
HSQGTFTSDYSKYLDSKAAHDFVEWL-K*-SA;
HSQGTFTSDYSKYLDSKAAHDFV-K*-WLLRA;
HSQGTFTSDYSKYLDS-C*-AAHDFVEWLLRA;
HSQGTFTSDYSKYLDS-C*-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDSKAA-C*-DFVEWLLRA;
HSQGTFTSDYSKYLD-K*-SAAHDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLLSA-K*;
H-Aib-QGTFTSDYSKYLDS-K*-AARDFVAWLLRA;
H-Aib-QGTFTSDYSKYLDSKAA-K*-DFVAWLLRA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLL-K*-A;
H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDS-K*-AAHDFVEWLLKA;
H-Aib-QGTFTSDYSKYLDSKAA-K*-DFVAWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVAWLL-K*-A;
H-Aib-QGTFTSDYSKYLD-K*-KAAHDFVAWLLRA;
H-Aib-QGTFTSDYSRYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFV-K*-WLLSA;
H-Aib-QGTFTSDYSLYLDS-K*-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-C*-AAHDFVEWLLSA;

H-Aib-QGTFTSDYSKYLDSKAA-C*-DFVEWLLRA;
H-Aib-QGTFTSDYSKYLD-S*-KAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDK()K*AAE()DFVEWLLRA;
H-Aib-QGTFTSDYSKYLDSK*AAHDFVE()WLLK()A
H-Aib-QGTFTSDYSKYLDSK*AAK()DFVE()WLLRA;
H-Aib-QGTFTSDYSKYLDSK()AAHE()FVEWLLK*A; or
H-Aib-QGTFTSDYSKYLDSK()AAK*E()FVEWLLRA,
wherein "*" indicates the position of a lipophilic substituent.

16. The use of any preceding claim, wherein

Z^1 comprises a hydrocarbon chain having 10 to 24 C atoms, 10 to 22 C atoms, or 10 to 20 C atoms, optionally wherein Z^1 is a dodecanoyl, 2-butyloctanoyl, tetradecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, or eicosanoyl moiety; and/or

wherein Z^2 is or comprises one or more amino acid residues, optionally wherein Z^2 is a γ-Glu, Glu, β-Ala or ε-Lys residue, or a 3-aminopropanoyl, 4-aminobutanoyl, 8-aminooctanoyl, or 8-amino-3,6-dioxaoctanoyl moiety, optionally wherein the lipophilic substituent is selected from the group consisting of dodecanoyl-γ-Glu, hexadecanoly- γ-Glu, hexadecanoyl-Glu, hexadecanoyl-[3-aminopropanoyl], hexadecanoyl-[8-aminooctanoyl], hexadecanoyl-ε-Lys, 2-butyloctanoyl- γ-Glu, octadecanoyl-γ-Glu, and hexadecanoyl-[4-aminobutanoyl]; optionally

wherein Z has the formula:
HSQGTFTSDYSKYLD-K(Hexadecanoyl-γ-Glu)-KAAHDFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWL-K(Hexadecanoyl-γ-Glu)-RA;
HSQGTFTSDYSKYLDSKAA-K(Hexadecanoyl-γ-Glu)-DFVEWLLRA;
HSQGTFTSDYSKYLDSKAAHDFVEWLL-K(Hexadecanoyl-γ-Glu)-A;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AARDFVAWLLRA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFVEWLL-K(Hexadecanoyl-γ-Glu)-A;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLKA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVE()WLLK()A;
HSQGTFTSDYSKYLDS-K(Hexadecanoyl-γ-Glu)-AAHDFVEWLLRA;
H-Aib-QGTFTSDYSKYLDSKAA-K(Hexadecanoyl-γ-Glu)-DFVAWLLRA;
H-Aib-QGTFTSDYSKYLDS-K(Dodecanoyl-γ-Glu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[3-aminopropanoyl])-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[8-aminooctanoyl])-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-ε-Lys)-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDS-K(Hexadecanoyl)-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDS-K([2-Butyloctanoyl]-γ-Glu)-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDS-K(Hexadecanoyl-[4-Aminobutanoyl])-AAHDFVEWLLSA;

HSQGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;
HSQGTFTSDYSKYLDS-K(Hexadecanoyl-E)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K([2-Butyloctanoyl]-γ-Glu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-[4-Aminobutanoyl])-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Octadecanoyl- γ-Glu)-AAHDFVEWLLSA; or
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-E)-AAHDFVEWLLSA;

wherein residues marked "()" participate in an intramolecular bond; or wherein Z has the formula:

H-Aib-QGTFTSDYS-K(Hexadecanoyl-isoGlu)-YLDSKAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLD-K(Hexadecanoyl-isoGlu)-KAAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAA-K(Hexadecanoyl-isoGlu)-DFVEWLLSA;
H-Aib-QGTFTSDYSKYLDSKAAHDFV-K(Hexadecanoyl-isoGlu)-WLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoLys)-AARDFVAWLLRA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAKDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDE-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHEFVEWLLSA;
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAEDFVEWLLSA; or
H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLEA.

17. The use according to claim 16, wherein Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH2.

18. The use of any preceding claim, wherein said insulin analogue is selected from the group consisting of insulin glulisine (Apidra), insulin lispro (Humalog), Degludec, Actraphane HM, LY2963016, LY2605541, pegylated insulin Lispro, insulin glargine (Lantus), insulin detemir (Levemir), insulin isophane, insulin aspart, insulin buccal, hyaluronidase insulin, insulin protamine, NN-1953, IN-105, BIOD-620 and Analog-PH20.

19. The use according to claim 18, wherein

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is insulin glargine; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is insulin detemir; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is glulisine; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is insulin lispro; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is degludec; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is Actraphane ;or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is LY2963016; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is LY2605541; or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is pegylated insulin Lispro or

Z has the formula H-H-Aib-QGTFTSDYSKYLDS-K(Hexadecanoyl-isoGlu)-AAHDFVEWLLSA-NH_2 and said insulin analogue is NN-1953, IN-105, BIOD-620 and Analog-PH20.

20. The use of any preceding claim, wherein

said compound or combination of compounds is administered in an amount sufficient to reduce food intake in said subject by at least 5%, 10%, 15%, 20%, 25%, 30%, or 50%; or

said combination of compounds is administered in an amount sufficient to reduce the subject's fasting blood glucose level by at least 1, 2, 3, 4, 5, 6, 8, 10, 11, 12, 15, or 20 mM; or

said compound or combination of compounds is administered in an amount sufficient to reduce the subject's HbA1c level by at least 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.8%, 1.0%, 1.5%, or 2.0%; or

administration of said compound or combination of compounds results in a body weight reduction of at least 3%, 5%, 8%, 10%, 12%, 15% or 20% within 1 year of starting administration; or

administration of said compound or combination of compounds results in a body weight reduction of at least 1%, 2%, 3%, 4%, 5%, 6%, 8%, or 10%, 15% within six months of starting administration; or

administration of said compound or combination of compounds results in a body weight reduction of at least 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 8%, 10% or 15% within three months of starting administration.

21. The use according to any preceding claim, wherein said subject is a human.