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ANALOGUES OF GLP-1

Background of the Invention

The present invention is directed to peptide analogues of glucagon-like peptide-1, the pharmaceutically-acceptable salts thereof, to methods of using such analogues to treat mammals and to pharmaceutical compositions useful therefor comprising said analogues.

Glucagon-like peptide-1 (7-36) amide (GLP-1) is synthesized in the intestinal L-cells by tissue-specific post-translational processing of the glucagon precursor preproglucagon (Varndell, J.M., et al., J. Histochem Cytochem, 1985:33:1080-6) and is released into the circulation in response to a meal. The plasma concentration of GLP-1 rises from a fasting level of approximately 15 pmol/L to a peak postprandial level of 40 pmol/L. It has been demonstrated that, for a given rise in plasma glucose concentration, the increase in plasma insulin is approximately threefold greater when glucose is administered orally compared with intravenously (Kreymann, B., et al., Lancet 1987:2, 1300-4). This alimentary enhancement of insulin release, known as the incretin effect, is primarily humoral and GLP-1 is now thought to be the most potent physiological incretin in humans. In addition to the insulinotropic effect, GLP-1 suppresses glucagon secretion, delays gastric emptying (Wettergren A., et al., Dig Dis Sci 1993:38:665-73) and may enhance peripheral glucose disposal (D'Alessio, D.A. et al., J. Clin Invest 1994:93:2293-6).

In 1994, the therapeutic potential of GLP-1 was suggested following the observation that a single subcutaneous (s/c) dose of GLP-1 could completely normalize postprandial glucose levels in patients with non-insulin-dependent diabetes mellitus (NIDDM) (Gutniak, M.K., et al., Diabetes Care 1994:17:1039-44). This effect was thought to be mediated both by increased insulin release and by a reduction in glucagon secretion. Furthermore, an intravenous infusion of GLP-1 has been shown to delay postprandial gastric emptying in patients with NIDDM (Williams, B., et al., J. Clin Endo Metab 1996:81:327-32). Unlike sulphonylureas, the insulinotropic action of GLP-1 is dependent on plasma glucose concentration (Holz, G.G. 4th, et al., Nature 1993:361:362-5). Thus, the loss of GLP-1-mediated insulin release at low plasma glucose concentration protects against severe

hypoglycemia. This combination of actions gives GLP-1 unique potential therapeutic advantages over other agents currently used to treat NIDDM.

Numerous studies have shown that when given to healthy subjects, GLP-1 potently influences glycemic levels as well as insulin and glucagon concentrations (Orskov, C, Diabetologia 35:701-711, 1992; Holst, J.J., et al., Potential of GLP-1 in diabetes management in Glucagon III, Handbook of Experimental Pharmacology, Lefevbre PJ, Ed. Berlin, Springer Verlag, 1996, p. 311-326), effects which are glucose dependent (Kreymann, B., et al., Lancet ii: 1300-1304, 1987; Weir, G.C., et al., Diabetes 38:338-342, 1989). Moreover, it is also effective in patients with diabetes (Gutniak, M., N. Engl J Med 226:1316-1322, 1992; Nathan, D.M., et al., Diabetes Care 15:270-276, 1992), normalizing blood glucose levels in type 2 diabetic subjects (Nauck, M.A., et al., Diagbetologia 36:741-744, 1993), and improving glycemic control in type 1 patients (Creutzfeldt, W.O., et al., Diabetes Care 19:580-586, 1996), raising the possibility of its use as a therapeutic agent.

GLP-1 is, however, metabolically unstable, having a plasma half-life ($t_{1/2}$) of only 1-2 min *in vivo*. Exogenously administered GLP-1 is also rapidly degraded (Deacon, C.F., et al., Diabetes 44:1126-1131, 1995). This metabolic instability limits the therapeutic potential of native GLP-1. Hence, there is a need for GLP-1 analogues that are more active or are more metabolically stable than native GLP-1.

Summary of the Invention

In one aspect, the present invention is directed to a compound of formula (I),

(R^2R^3)-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-A^{39}-R^1 ,

(I)

wherein

A^7 is L-His, Ura, Paa, Pta, Amp, Tma-His, des-amino-His, or deleted;

A^8 is Ala, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;

A^9 is Glu, N-Me-Glu, N-Me-Asp or Asp;

A^{10} is Gly, Acc, ß-Ala or Aib;

A^{11} is Thr or Ser;

A^{12} is Phe, Acc, Aic, Aib, 3-Pal, 4-Pal, ß-Nal, Cha, Trp or X^1-Phe;

A^{13} is Thr or Ser;

A^{14} is Ser or Aib;

A^{15} is Asp or Glu;

A^{16} is Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala or Cha;

A^{17} is Ser or Thr;

A^{18} is Ser or Thr;

A^{19} is Tyr, Cha, Phe, 3-Pal, 4-Pal, Acc, ß-Nal or X^1-Phe;

A^{20} is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe or X^1-Phe;

A^{21} is Glu or Asp;

A^{22} is Gly, Acc, ß-Ala, Glu or Aib;

A^{23} is Gln, Asp, Asn or Glu;

A^{24} is Ala, Aib, Val, Abu, Tle or Acc;

A^{25} is Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{26} is Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{27} is Glu Asp, Leu, Aib or Lys;

A^{28} is Phe, Pal, ß-Nal, X^1-Phe, Aic, Acc, Aib, Cha or Trp;

A^{29} is Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala or Phe;

A^{30} is Ala, Aib or Acc;

A^{31} is Trp, ß-Nal, 3-Pal, 4-Pal, Phe, Acc, Aib or Cha;

A^{32} is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe, X^1-Phe or Ala;

A^{33} is Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys or X^1-Phe;

A^{34} is Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{35} is Gly, ß-Ala, D-Ala, Gaba, Ava, HN-$(CH_2)_m$-C(O), Aib, Acc or a D-amino acid;

A^{36} is L- or D-Arg, D- or L-Lys, D- or L-hArg, D- or L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) or deleted;

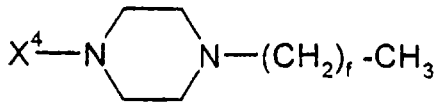
A^{37} is Gly, ß-Ala, Gaba, Ava, Aib, Acc, Ado, Arg, Asp, Aun, Aec, HN-$(CH_2)_m$-C(O), HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), a D-amino acid, or deleted;

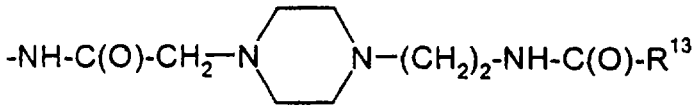
A^{38} is D- or L-Lys, D- or L-Arg, D- or L-hArg, D- or L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) Ava, Ado, Aec or deleted;

A^{39} is D- or L-Lys, D- or L-Arg, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), Ava, Ado, or Aec;

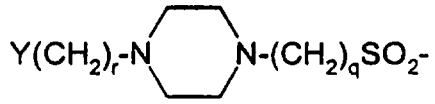
X^1 for each occurrence is independently selected from the group consisting of (C_1-C_6)alkyl, OH and halo;

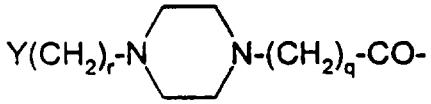
R^1 is OH, NH_2, (C_1-C_{30})alkoxy, or NH-X^2-CH_2-Z^0, wherein X^2 is a (C_1-C_{12})hydrocarbon moiety, and Z^0 is H, OH, CO_2H or $CONH_2$;

X^3 is 



or –C(O)-NHR^{12}, wherein X^4 is, independently for each occurrence, -C(O)-, -NH-C(O)- or -CH_2-, and wherein f is, independently for each occurrence, an integer from 1 to 29 inclusive;

each of R^2 and R^3 is independently selected from the group consisting of H, (C_1-C_{30})alkyl, (C_2-C_{30})alkenyl, phenyl(C_1-C_{30})alkyl, naphthyl(C_1-C_{30})alkyl, hydroxy(C_1-C_{30})alkyl, hydroxy(C_2-C_{30})alkenyl, hydroxyphenyl(C_1-C_{30})alkyl, and hydroxynaphthyl(C_1-C_{30})alkyl; or one of R^2 and R^3 is , (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl, C(O)X^5, , or



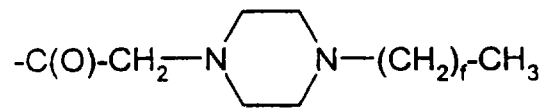
; wherein Y is H, OH or NH_2; r is 0 to 4; q is 0 to 4; and X^5 is (C_1-C_{30})alkyl, (C_2-C_{30})alkenyl, phenyl(C_1-C_{30})alkyl, naphthyl(C_1-C_{30})alkyl, hydroxy(C_1-C_{30})alkyl, hydroxy(C_2-C_{30})alkenyl, hydroxyphenyl(C_1-C_{30})alkyl or hydroxynaphthyl(C_1-C_{30})alkyl;

e is, independently for each occurrence, an integer from 1 to 4 inclusive;

m is, independently for each occurrence, an integer from 5 to 24 inclusive;

n is, independently for each occurrence, an integer from 1 to 5, inclusive;

each of R^{10} and R^{11} is, independently for each occurrence, H, (C_1-C_{30})alkyl, (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl, –C((NH)(NH_2)) or



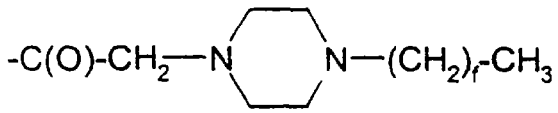
; and

R^{12} and R^{13} each is, independently for each occurrence, (C_1-C_{30})alkyl;

provided that:

when A^7 is Ura, Paa or Pta, then R^2 and R^3 are deleted;

when R^{10} is $(C_1\text{-}C_{30})$acyl, $(C_1\text{-}C_{30})$alkylsulfonyl, $-C((NH)(NH_2))$ or



, then R^{11} is H or $(C_1\text{-}C_{30})$alkyl;

(i) at least one amino acid of a compound of formula (I) is not the same as the native sequence of hGLP-1(7-36, -37 or -38)NH_2 or hGLP-1(7-36, -37 or -38)OH;

(ii) a compound of formula (I) is not an analogue of hGLP-1(7-36, -37 or -38)NH_2 or hGLP-1(7-36, -37 or -38)OH wherein a single position has been substituted by Ala;

(iii) a compound of formula (I) is not ($Arg^{26,34}$, Lys^{38})hGLP-1(7-38)-E, (Lys^{26}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, (Lys^{34}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, ($Lys^{26,34}$-bis(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, (Arg^{26}, Lys^{34}(N_ε-alkanoyl))hGLP-1(8-36, -37 or -38)-E, ($Arg^{26,34}$, Lys^{36}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E or ($Arg^{26,34}$, Lys^{38}(N_ε-alkanoyl))hGLP-1(7-38)-E, wherein E is -OH or -NH_2;

(iv) a compound of formula (I) is not Z^1-hGLP-1(7-36, -37 or -38)-OH, Z^1-hGLP-1(7-36, -37 or -38)-NH_2, wherein Z^1 is selected from the group consisting of:

(a) (Arg^{26}), (Arg^{34}), ($Arg^{26,34}$), (Lys^{36}), (Arg^{26}, Lys^{36}), (Arg^{34}, Lys^{36}), (D-Lys^{36}), (Arg^{36}), (D-Arg^{36}), ($Arg^{26,34}$, Lys^{36}) or ($Arg^{26,36}$, Lys^{34});

(b) (Asp^{21});

(c) at least one of (Aib^8), (D-Ala^8) and (Asp^9); and

(d) (Tyr^7), (N-acyl-His^7), (N-alkyl-His^7), (N-acyl-D-His^7) or (N-alkyl-D-His^7);

(v) a compound of formula (I) is not a combination of any two of the substitutions listed in groups (a) to (d); and

(vi) a compound of formula (I) is not (N-Me-Ala^8)hGLP-1(8-36 or -37), (Glu^{15})hGLP-1(7-36 or -37), (Asp^{21})hGLP-1(7-36 or -37) or (Phe^{31})hGLP-1(7-36 or -37)

or a pharmaceutically acceptable salt thereof.

A preferred group of compounds of the immediately foregoing compound is where A^{11} is Thr; A^{13} is Thr; A^{15} is Asp; A^{17} is Ser; A^{18} is Ser or Lys; A^{21} is Glu; A^{23} is Gln or Glu; A^{27} is Glu, Leu, Aib or Lys; and A^{31} is Trp, Phe or ß-Nal; or a pharmaceutically acceptable salt thereof.

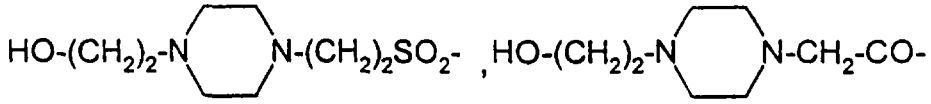
A preferred group of compounds of the immediately foregoing group of compounds is where A^9 is Glu, N-Me-Glu or N-Me-Asp; A^{12} is Phe, Acc, ß-Nal or Aic; A^{16} is Val, Acc or Aib; A^{19} is Tyr or ß-Nal; A^{20} is Leu, Acc or Cha; A^{24} is Ala, Aib

or Acc; A^{25} is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O); A^{28} is Phe or ß-Nal; A^{29} is Ile or Acc; A^{30} is Ala or Aib; A^{32} is Leu, Acc or Cha; and A^{33} is Val, Lys or Acc; or a pharmaceutically acceptable salt thereof.

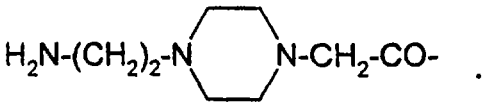
A preferred group of compounds of the immediately foregoing group of compounds is where A^8 is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A^{10} is Gly; A^{12} is Phe, ß-Nal, A6c or A5c; A^{16} is Val, A6c or A5c; A^{20} is Leu, A6c, A5c or Cha; A^{22} is Gly, ß-Ala, Glu or Aib; A^{24} is Ala or Aib; A^{29} is Ile, A6c or A5c; A^{32} is Leu, A6c, A5c or Cha; A^{33} is Val, Lys, A6c or A5c; A^{35} is Aib, ß-Ala, Ado, A6c, A5c, D-Arg or Gly; and A^{37} is Gly, Aib, ß-Ala, Ado, D-Ala Ava, Asp, Aun, D-Asp, D-Arg, Aec, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or deleted; or a pharmaceutically acceptable salt thereof.

A preferred group of compounds of the immediately foregoing group of compounds is where X^4 for each occurrence is -C(O)-; and R^1 is OH or NH_2; or a pharmaceutically acceptable salt thereof.

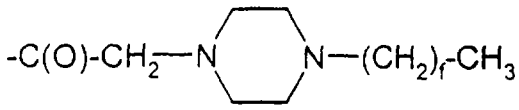
A preferred group of compounds of the immediately foregoing group of compounds or a pharmaceutically acceptable salt thereof is where R^2 is H and R^3 is (C_1-C_{30})alkyl, (C_2-C_{30})alkenyl, (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl,



or

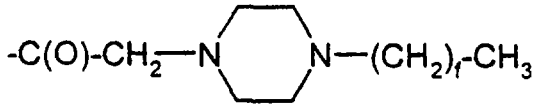


A preferred compound of the formula (I) is where A^8 is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A^{10} is Gly; A^{12} is Phe, ß-Nal A6c or A5c; A^{16} is Val, A6c or A5c; A^{20} is Leu, A6c, A5c or Cha; A^{22} is Gly, ß-Ala, Glu or Aib; A^{24} is Ala or Aib; A^{29} is Ile, A6c or A5c; A^{32} is Leu, A6c, A5c or Cha; A^{33} is Val, Lys, A6c or A5c; A^{35} is Aib, ß-Ala, Ado, A6c, A5c D-Arg or Gly; and A^{37} is Gly, Aib, ß-Ala, Ado, D-Ala, Ava, Asp, Aun, D-Asp, D-Arg, Aec, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or deleted; X^4 for each occurrence is -C(O)-; e for each occurrence is independently 1 or 2; R^1 is OH or NH_2; R^{10} is (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl or



, and R^{11} is H; or a pharmaceutically acceptable salt thereof.

More preferred of the immediately foregoing compounds is where R^{10} is (C_4-C_{20})acyl, (C_4-C_{20})alkylsulfonyl or



, or a pharmaceutically acceptable salt thereof.

A more preferred compound of formula (I) is where said compound is of the formula:

(Aib^{8,35})hGLP-1(7-36)NH_2,

((N$_\alpha$-HEPES-His)^7, Aib^{8,35})hGLP-1(7-36)NH_2,

((N$_\alpha$-HEPA-His)^7, Aib^{8,35})hGLP-1(7-36)NH_2,

(Aib^8, ß-Ala^{35})hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-36)NH_2,

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-38)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-decanoyl))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-dodecanesulfonyl))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-tetradecyl-piperazine)))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-tetradecylamino))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-tetradecanoyl),ß-Ala^{37})hGLP-1(7-37)-OH or

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-36)-OH,

or a pharmaceutically acceptable salt thereof .

More preferred of the immediately foregoing group of compounds is a compound of the formula:

(Aib^{8,35})hGLP-1(7-36)NH_2,

(Aib^8, ß-Ala^{35})hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-36)NH_2,

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$_\epsilon$-tetradecanoyl))hGLP-1(7-38)NH_2,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\epsilon$-decanoyl))hGLP-1(7-36)NH_2, or

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_\varepsilon$-tetradecanoyl),ß-Ala^{37})hGLP-1(7-37) -OH, or a pharmaceutically acceptable salt thereof.

Another more preferred compound of formula (I) is where said compound is of the formula:

(Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH$_2$;

(Aib^{8,24,35})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-Aec-decanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35},Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH$_2$;

(Aib^{8,35},Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH$_2$;

(Aib^{8,35},Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH$_2$;

(Aib^{8,17,35},)hGLP-1(7-36)NH$_2$;

(Aib^{8} ,Arg^{26,34}, ß-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH$_2$;

(Gly^{8}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Ser^{8}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Glu^{22,23}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Lys^{18}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Lys^{33}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Lys^{18}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH$_2$;

(Aib^{8}, ß-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH$_2$;

(Aib^{8,27}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH$_2$;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH$_2$;

(Aib^{8}, Lys^{18,27}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, Lys^{27}, ß-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8}, ß-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35},)hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N^{ε}-decanoyl))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-dodecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8},B-Ala^{35}, Ser^{37}(O-decanoyl))hGLP1(7-37)-NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38}, Lys^{39}(N^{ε}-octanoyl))hGLP-1(7-39)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-octanoyl))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-decanoyl))hGLP-1(7-37)NH_2; or

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-tetradecanoyl))hGLP-1(7-37)NH_2;

or a pharmaceutically acceptable salt thereof.

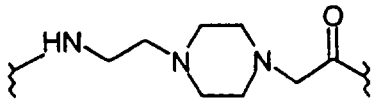
Another more preferred compound of formula (I) is each of the compounds that are specifically enumerated hereinbelow in the Examples section of the present disclosure, or a pharmaceutically acceptable salt thereof.

In another aspect, the present invention provides a pharmaceutical composition comprising an effective amount of a compound of formula (I) as defined hereinabove or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

In yet another aspect, the present invention provides a method of eliciting an agonist effect from a GLP-1 receptor in a subject in need thereof which comprises administering to said subject an effective amount of a compound of formula (I) as defined hereinabove or a pharmaceutically acceptable salt thereof

In a further aspect, the present invention provides a method of treating a disease selected from the group consisting of Type I diabetes, Type II diabetes,

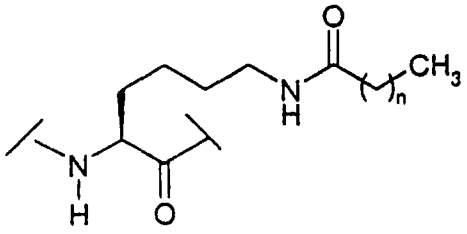
obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis, neurodegenerative disease, renal failure, congestive heart failure, nephrotic syndrome, cirrhosis, pulmonary edema, hypertension, and disorders wherein the reduction of food intake is desired, in a subject in need thereof which comprises administering to said subject an effective amount of a compound of formula (I) as defined hereinabove or a pharmaceutically acceptable salt thereof. A preferred method of the immediately foregoing method is where the disease being treated is Type I diabetes or Type II diabetes.

With the exception of the N-terminal amino acid, all abbreviations (e.g. Ala) of amino acids in this disclosure stand for the structure of -NH-CH(R)-CO-, wherein R is the side chain of an amino acid (e.g., CH_3 for Ala). For the N-terminal amino acid, the abbreviation stands for the structure of (R^2R^3)-N-CH(R)-CO-, wherein R is a side chain of an amino acid and R^2 and R^3 are as defined above, except when A^7 is Ura, Paa or Pta, in which case R^2 and R^3 are not present since Ura, Paa and Pta are considered here as des-amino amino acids. Amp, ß-Nal, Nle, Cha, 3-Pal, 4-Pal and Aib are the abbreviations of the following α-amino acids: 4-amino-phenylalanine, ß-(2-naphthyl)alanine, norleucine, cyclohexylalanine, ß-(3-pyridinyl)alanine, ß-(4-pyridinyl)alanine and α-aminoisobutyric acid, respectively. Other amino acid definitions are: Ura is urocanic acid; Pta is (4-pyridylthio) acetic acid; Paa is *trans*-3-(3-pyridyl) acrylic acid; Tma-His is N,N-tetramethylamidino-histidine; N-Me-Ala is N-methyl-alanine; N-Me-Gly is N-methyl-glycine; N-Me-Glu is N-methyl-glutamic acid; Tle is *tert*-butylglycine; Abu is α-aminobutyric acid; Tba is *tert*-butylalanine; Orn is ornithine; Aib is α-aminoisobutyric acid; ß-Ala is ß-alanine; Gaba is γ-aminobutyric acid; Ava is 5-aminovaleric acid; Ado is 12-aminododecanoic acid, Aic is 2-aminoindane-2-carboxylic acid; Aun is 11-aminoundecanoic acid; and Aec is 4-(2-aminoethyl)-1-carboxymethyl-piperazine, represented by the structure: 

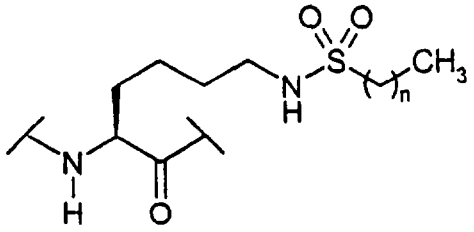
What is meant by Acc is an amino acid selected from the group of 1-amino-1-cyclopropanecarboxylic acid (A3c); 1-amino-1-cyclobutanecarboxylic acid (A4c), 1-amino-1-cyclopentanecarboxylic acid (A5c); 1-amino-1-cyclohexanecarboxylic acid (A6c); 1-amino-1-cycloheptanecarboxylic acid (A7c); 1-amino-1-

cyclooctanecarboxylic acid (A8c); and 1-amino-1-cyclononanecarboxylic acid (A9c). In the above formula, hydroxyalkyl, hydroxyphenylalkyl, and hydroxynaphthylalkyl may contain 1-4 hydroxy substituents. COX^5 stands for $-C=O\cdot X^5$. Examples of $-C=O\cdot X^5$ include, but are not limited to, acetyl and phenylpropionyl.

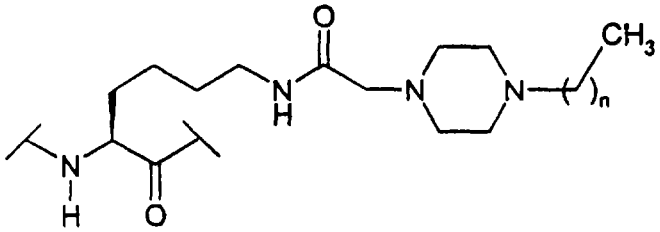
What is meant by Lys(N_ϵ-alkanoyl) is represented by the following structure:



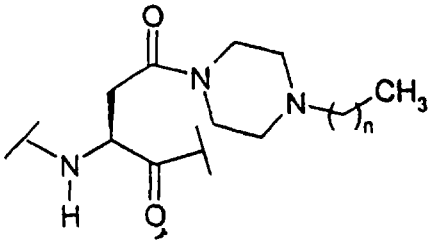
. What is meant by Lys(N_ϵ-alkylsulfonyl) is represented by the following structure:



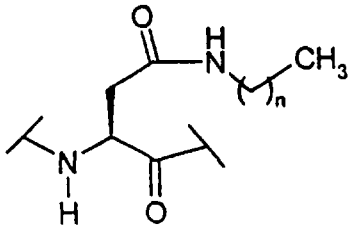
. What is meant by Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) is represented by the following structure:



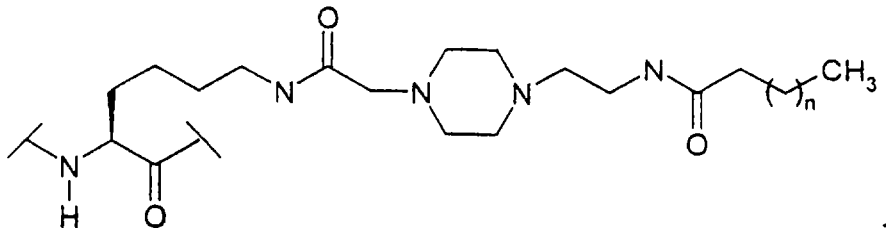
. What is meant by Asp(1-(4-alkyl-piperazine)) is represented by the following structure:



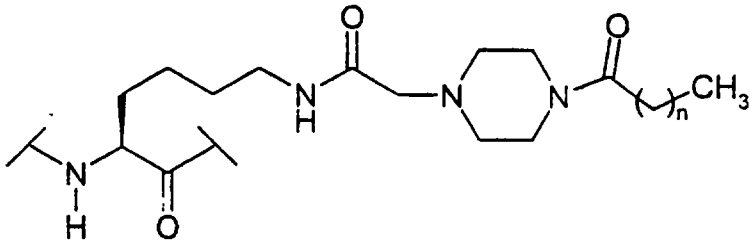
. What is meant by Asp(1-alkylamino) is represented by the following structure:



. What is meant by Lys(N_ϵ-Aec-alkanoyl) is represented by the structure.



The variable n in the foregoing structures is 1-30. What is meant by Lys (Nε-ace-alkanoyl) is represented by the structure:



The full names for other abbreviations used herein are as follows: Boc for t-butyloxycarbonyl, HF for hydrogen fluoride, Fm for formyl, Xan for xanthyl, Bzl for benzyl, Tos for tosyl, DNP for 2,4-dinitrophenyl, DMF for dimethylformamide, DCM for dichloromethane, HBTU for 2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluorophosphate, DIEA for diisopropylethylamine, HOAc for acetic acid, TFA for trifluoroacetic acid, 2ClZ for 2-chlorobenzyloxycarbonyl, 2BrZ for 2-bromobenzyloxycarbonyl, OcHex for O-cyclohexyl, Fmoc for 9-fluorenylmethoxycarbonyl, HOBt for N-hydroxybenzotriazole and PAM resin for 4-hydroxymethylphenylacetamidomethyl resin.

The term "halo" encompasses fluoro, chloro, bromo and iodo.

The term "(C_1-C_{30})hydrocarbon moiety" encompasses alkyl, alkenyl and alkynyl, and in the case of alkenyl and alkynyl there are C_2-C_{30}.

A peptide of this invention is also denoted herein by another format, e.g., (A5c^8)hGLP-1(7-36)NH_2, with the substituted amino acids from the natural sequence placed between the first set of parentheses (e.g., A5c^8 for Ala^8 in hGLP-1). The abbreviation GLP-1 means glucagon-like peptide-1; hGLP-1 means human glucagon-like peptide-1. The numbers between the parentheses refer to the number of amino acids present in the peptide (e.g., hGLP-1(7-36) is amino acids 7 through 36 of the peptide sequence for human GLP-1). The sequence for hGLP-

1(7-37) is listed in Mojsov, S., Int. J. Peptide Protein Res,. 40, 1992, pp. 333-342. The designation "NH_2" in hGLP-1(7-36)NH_2 indicates that the C-terminus of the peptide is amidated. hGLP-1(7-36) means that the C-terminus is the free acid. In hGLP-1(7-38), residues in positions 37 and 38 are Gly and Arg, respectively.

Detailed Description

The peptides of this invention can be prepared by standard solid phase peptide synthesis. See, e.g., Stewart, J.M., et al., Solid Phase Synthesis (Pierce Chemical Co., 2d ed. 1984). The substituents R^2 and R^3 of the above generic formula may be attached to the free amine of the N-terminal amino acid by standard methods known in the art. For example, alkyl groups, e.g., (C_1-C_{30})alkyl, may be attached using reductive alkylation. Hydroxyalkyl groups, e.g., (C_1-C_{30})hydroxyalkyl, may also be attached using reductive alkylation wherein the free hydroxy group is protected with a t-butyl ester. Acyl groups, e.g., COE^1, may be attached by coupling the free acid, e.g., E^1COOH, to the free amine of the N-terminal amino acid by mixing the completed resin with 3 molar equivalents of both the free acid and diisopropylcarbodiimide in methylene chloride for one hour. If the free acid contains a free hydroxy group, e.g., p-hydroxyphenylpropionic acid, then the coupling should be performed with an additional 3 molar equivalents of HOBT.

When R^1 is NH-X^2-CH_2-$CONH_2$, (i.e., Z^0=$CONH_2$), the synthesis of the peptide starts with BocHN-X^2-CH_2-COOH which is coupled to the MBHA resin. If R^1 is NH-X^2-CH_2-COOH, (i.e., Z^0=COOH) the synthesis of the peptide starts with Boc-HN-X^2-CH_2-COOH which is coupled to PAM resin. For this particular step, 4 molar equivalents of Boc-HN-X^2-COOH, HBTU and HOBt and 10 molar equivalents of DIEA are used. The coupling time is about 8 hours.

The protected amino acid 1-(N-tert-butoxycarbonyl-amino)-1-cyclohexane-carboxylic acid (Boc-A6c-OH) was synthesized as follows. 19.1 g (0.133 mol) of 1-amino-1-cyclohexanecarboxylic acid (Acros Organics, Fisher Scientific, Pittsburgh, PA) was dissolved in 200 ml of dioxane and 100 ml of water. To it was added 67 ml of 2N NaOH. The solution was cooled in an ice-water bath. 32.0 g (0.147 mol) of di-tert-butyl-dicarbonate was added to this solution. The reaction mixture was stirred overnight at room temperature. Dioxane was then removed under reduced pressure. 200 ml of ethyl acetate was added to the remaining aqueous solution The mixture was cooled in an ice-water bath. The pH of the aqueous layer was adjusted to about 3 by adding 4N HCl. The organic layer was separated. The

aqueous layer was extracted with ethyl acetate (1 x 100 ml). The two organic layers were combined and washed with water (2 x 150 ml), dried over anhydrous $MgSO_4$, filtered, and concentrated to dryness under reduced pressure. The residue was recrystallized in ethyl acetate/hexanes. 9.2 g of the pure product was obtained. 29% yield.

Boc-A5c-OH was synthesized in an analogous manner to that of Boc-A6c-OH. Other protected Acc amino acids can be prepared in an analogous manner by a person of ordinary skill in the art as enabled by the teachings herein.

In the synthesis of a GLP-1 analogue of this invention containing A5c, A6c and/or Aib, the coupling time is 2 hrs. for these residues and the residue immediately following them. For the synthesis of (Tma-His^7)hGLP-1(7-36)NH_2, HBTU (2 mmol) and DIEA (1.0 ml) in 4 ml DMF are used to react with the N-terminal free amine of the peptide-resin in the last coupling reaction; the coupling time is about 2 hours.

The substituents R^2 and R^3 of the above generic formula can be attached to the free amine of the N-terminal amino acid by standard methods known in the art. For example, alkyl groups, e.g., (C_1-C_{30})alkyl, can be attached using reductive alkylation. Hydroxyalkyl groups, e.g., (C_1-C_{30})hydroxyalkyl, can also be attached using reductive alkylation wherein the free hydroxy group is protected with a t-butyl ester. Acyl groups, e.g., COX^1, can be attached by coupling the free acid, e.g., X^1COOH, to the free amine of the N-terminal amino acid by mixing the completed resin with 3 molar equivalents of both the free acid and diisopropylcarbodiimide in methylene chloride for about one hour. If the free acid contains a free hydroxy group, e.g., p-hydroxyphenylpropionic acid, then the coupling should be performed with an additional 3 molar equivalents of HOBT.

A compound of the present invention can be tested for activity as a GLP-1 binding compound according to the following procedure.

Cell Culture:

RIN 5F rat insulinoma cells (ATCC-# CRL-2058, American Type Culture Collection, Manassas, VA), expressing the GLP-1 receptor, were cultured in Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum, and maintained at about 37 °C in a humidifed atmosphere of 5% CO_2/95% air.

Radioligand Binding:

Membranes were prepared for radioligand binding studies by

homogenization of the RIN cells in 20 ml of ice-cold 50 mM Tris-HCl with a Brinkman Polytron (Westbury, NY) (setting 6, 15 sec). The homogenates were washed twice by centrifugation (39,000 g / 10 min), and the final pellets were resuspended in 50 mM Tris-HCl, containing 2.5 mM $MgCl_2$, 0.1 mg/ml bacitracin (Sigma Chemical, St. Louis, MO), and 0.1% BSA. For assay, aliquots (0.4 ml) were incubated with 0.05 nM (^{125}I)GLP-1(7-36) (~2200 Ci/mmol, New England Nuclear, Boston, MA), with and without 0.05 ml of unlabeled competing test peptides. After a 100 min incubation (25 °C), the bound (^{125}I)GLP-1(7-36) was separated from the free by rapid filtration through GF/C filters (Brandel, Gaithersburg, MD), which had been previously soaked in 0.5% polyethyleneimine. The filters were then washed three times with 5 ml aliquots of ice-cold 50 mM Tris-HCl, and the bound radioactivity trapped on the filters was counted by gamma spectrometry (Wallac LKB, Gaithersburg, MD). Specific binding was defined as the total (^{125}I)GLP-1(7-36) bound minus that bound in the presence of 1000 nM GLP1(7-36) (Bachem, Torrence, CA).

The peptides of this invention can be provided in the form of pharmaceutically acceptable salts. Examples of such salts include, but are not limited to, those formed with organic acids (e.g., acetic, lactic, maleic, citric, malic, ascorbic, succinic, benzoic, methanesulfonic, toluenesulfonic, or pamoic acid), inorganic acids (e.g., hydrochloric acid, sulfuric acid, or phosphoric acid), and polymeric acids (e.g., tannic acid, carboxymethyl cellulose, polylactic, polyglycolic, or copolymers of polylactic-glycolic acids). A typical method of making a salt of a peptide of the present invention is well known in the art and can be accomplished by standard methods of salt exchange. Accordingly, the TFA salt of a peptide of the present invention (the TFA salt results from the purification of the peptide by using preparative HPLC, eluting with TFA containing buffer solutions) can be converted into another salt, such as an acetate salt by dissolving the peptide in a small amount of 0.25 N acetic acid aqueous solution. The resulting solution is applied to a semi-prep HPLC column (Zorbax, 300 SB, C-8). The column is eluted with (1) 0.1N ammonium acetate aqueous solution for 0.5 hrs., (2) 0.25N acetic acid aqueous solution for 0.5 hrs. and (3) a linear gradient (20% to 100% of solution B over 30 min.) at a flow rate of 4 ml/min (solution A is 0.25N acetic acid aqueous solution; solution B is 0.25N acetic acid in acetonitrile/water, 80:20). The fractions containing the peptide are collected and lyophilized to dryness.

As is well known to those skilled in the art, the known and potential uses of GLP-1 is varied and multitudinous (See, Todd, J.F., et al., Clinical Science, 1998, 95, pp. 325-329; and Todd, J.F. et al., European Journal of Clinical Investigation, 1997, 27, pp.533-536). Thus, the administration of the compounds of this invention for purposes of eliciting an agonist effect can have the same effects and uses as GLP-1 itself. These varied uses of GLP-1 may be summarized as follows, treatment of: Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system diseases, restenosis, neurodegenerative diseases, renal failure, congestive heart failure, nephrotic syndrome, cirrhosis, pulmonary edema, hypertension, and disorders wherein the reduction of food intake is desired. GLP-1 analogues of the present invention that elicit an antagonist effect from a subject can be used for treating the following: hypoglycemia and malabsorption syndrome associated with gastroectomy or small bowel resection.

Accordingly, the present invention includes within its scope pharmaceutical compositions comprising, as an active ingredient, at least one of the compounds of formula (I) in association with a pharmaceutically acceptable carrier.

The dosage of active ingredient in the compositions of this invention may be varied; however, it is necessary that the amount of the active ingredient be such that a suitable dosage form is obtained. The selected dosage depends upon the desired therapeutic effect, on the route of administration, and on the duration of the treatment. In general, an effective dosage for the activities of this invention is in the range of $1x10^{-7}$ to 200 mg/kg/day, preferably $1x10^{-4}$ to 100 mg/kg/day, which can be administered as a single dose or divided into multiple doses.

The compounds of this invention can be administered by oral, parenteral (e.g., intramuscular, intraperitoneal, intravenous or subcutaneous injection, or implant), nasal, vaginal, rectal, sublingual or topical routes of administration and can be formulated with pharmaceutically acceptable carriers to provide dosage forms appropriate for each route of administration.

Solid dosage forms for oral administration include capsules, tablets, pills, powders and granules. In such solid dosage forms, the active compound is admixed with at least one inert pharmaceutically acceptable carrier such as sucrose, lactose, or starch. Such dosage forms can also comprise, as is normal practice, additional substances other than such inert diluents, e.g., lubricating

agents such as magnesium stearate. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, the elixirs containing inert diluents commonly used in the art, such as water. Besides such inert diluents, compositions can also include adjuvants, such as wetting agents, emulsifying and suspending agents, and sweetening, flavoring and perfuming agents.

Preparations according to this invention for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, or emulsions. Examples of non-aqueous solvents or vehicles are propylene glycol, polyethylene glycol, vegetable oils, such as olive oil and corn oil, gelatin, and injectable organic esters such as ethyl oleate. Such dosage forms may also contain adjuvants such as preserving, wetting, emulsifying, and dispersing agents. They may be sterilized by, for example, filtration through a bacteria-retaining filter, by incorporating sterilizing agents into the compositions, by irradiating the compositions, or by heating the compositions. They can also be manufactured in the form of sterile solid compositions which can be dissolved in sterile water, or some other sterile injectable medium immediately before use.

Compositions for rectal or vaginal administration are preferably suppositories which may contain, in addition to the active substance, excipients such as coca butter or a suppository wax.

Compositions for nasal or sublingual administration are also prepared with standard excipients well known in the art.

Further, a compound of this invention can be administered in a sustained release composition such as those described in the following patents and patent applications. U.S. Patent No. 5,672,659 teaches sustained release compositions comprising a bioactive agent and a polyester. U.S. Patent No. 5,595,760 teaches sustained release compositions comprising a bioactive agent in a gelable form. U.S. Application No. 08/929,363 filed September 9, 1997, teaches polymeric sustained release compositions comprising a bioactive agent and chitosan. U.S Application No. 08/740,778 filed November 1, 1996, teaches sustained release compositions comprising a bioactive agent and cyclodextrin. U.S. Application No 09/015,394 filed January 29, 1998, teaches absorbable sustained release

compositions of a bioactive agent. U.S. Application No. 09/121,653 filed July 23, 1998, teaches a process for making microparticles comprising a therapeutic agent such as a peptide in an oil-in-water process. U.S. Application No. 09/131,472 filed August 10, 1998, teaches complexes comprising a therapeutic agent such as a peptide and a phosphorylated polymer. U.S. Application No. 09/184,413 filed November 2, 1998, teaches complexes comprising a therapeutic agent such as a peptide and a polymer bearing a non-polymerizable lactone. The teachings of the foregoing patents and applications are incorporated herein by reference.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Also, all publications, patent applications, patents and other references mentioned herein are incorporated by reference.

The following examples describe synthetic methods for making a peptide of this invention, which methods are well-known to those skilled in the art. Other methods are also known to those skilled in the art. The examples are provided for the purpose of illustration and is not meant to limit the scope of the present invention in any manner.

Boc-ßAla-OH, Boc-D-Arg(Tos)-OH and Boc-D-Asp(OcHex) were purchased from Nova Biochem, San Diego, California. Boc-Aun-OH was purchased from Bachem, King of Prussia, PA. Boc-Ava-OH and Boc-Ado-OH were purchased from Chem-Impex International, Wood Dale, IL. Boc-Nal-OH was purchased from Synthetech, Inc. Albany, OR.

Example 1

$(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$

The title peptide was synthesized on an Applied Biosystems (Foster City, CA) model 430A peptide synthesizer which was modified to do accelerated Boc-chemistry solid phase peptide synthesis. See Schnolzer, et al., Int. J. Peptide Protein Res., 90:180 (1992). 4-methylbenzhydrylamine (MBHA) resin (Peninsula, Belmont, CA) with the substitution of 0.91 mmol/g was used. The Boc amino acids (Bachem, CA, Torrance, CA; Nova Biochem., LaJolla, CA) were used with the following side chain protection: Boc-Ala-OH, Boc-Arg(Tos)-OH, Boc-Asp(OcHex)-OH, Boc-Tyr(2BrZ)-OH, Boc-His(DNP)-OH, Boc-Val-OH, Boc-Leu-OH, Boc-Gly-OH, Boc-Gln-OH, Boc-Ile-OH, Boc-Lys(2ClZ)-OH, Boc-Thr(Bzl)-OH, Boc-Ser(Bzl)-OH, Boc-Phe-OH, Boc-Aib-OH, Boc-Glu(OcHex)-OH and Boc-Trp(Fm)-OH The

synthesis was carried out on a 0.20 mmol scale. The Boc groups were removed by treatment with 100% TFA for 2 x 1 min. Boc amino acids (2.5 mmol) were pre-activated with HBTU (2.0 mmol) and DIEA (1.0 mL) in 4 mL of DMF and were coupled without prior neutralization of the peptide-resin TFA salt. Coupling times were 5 min. except for the Boc-Aib-OH residues and the following residues, Boc-Lys(2ClZ)-OH and Boc-His(DNP)-OH wherein the coupling times were 2 hours.

At the end of the assembly of the peptide chain, the resin was treated with a solution of 20% mercaptoethanol/10% DIEA in DMF for 2 x 30 min. to remove the DNP group on the His side chain. The N-terminal Boc group was then removed by treatment with 100% TFA for 2 x 2 min. After neutralization of the peptide-resin with 10% DIEA in DMF (1 x 1 min), the formyl group on the side chain of Trp was removed by treatment with a solution of 15% ethanolamine/ 15% water/ 70% DMF for 2 x 30 min. The peptide-resin was washed with DMF and DCM and dried under reduced pressure. The final cleavage was done by stirring the peptide-resin in 10 mL of HF containing 1 mL of anisole and dithiothreitol (24 mg) at 0°C for 75 min. HF was removed by a flow of nitrogen. The residue was washed with ether (6 x 10 mL) and extracted with 4N HOAc (6 x 10 mL).

The peptide mixture in the aqueous extract was purified on reverse-phase preparative high pressure liquid chromatography (HPLC) using a reverse phase VYDAC® C_{18} column (Nest Group, Southborough, MA). The column was eluted with a linear gradient (20% to 50% of solution B over 105 min.) at a flow rate of 10 mL/min (Solution A = water containing 0.1% TFA; Solution B = acetonitrile containing 0.1% of TFA). Fractions were collected and checked on analytical HPLC. Those containing pure product were combined and lyophilized to dryness. 135 mg of a white solid was obtained. Purity was 98.6% based on analytical HPLC analysis. Electro-spray mass spectrometer (MS(ES))S analysis gave the molecular weight at 3339.7 (in agreement with the calculated molecular weight of 3339.7).

Example 2

(N_α-HEPES-His)^7, Aib^{8,35})hGLP-1(7-36)NH_2

The title compound (HEPES is (4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid)) can be synthesized as follows: after assembly of the peptide (Aib^{8,35})hGLP-1(7-36)NH_2 on MBHA resin (0.20 mmol) according to the procedure of Example 1, the peptide-resin is treated with 100% TFA (2 x 2 min.) and washed with DMF and DCM. The resin is then neutralized with 10% DIEA in DMF for 2 min

After washing with DMF and DCM, the resin is treated with 0.23 mmol of 2-chloro-1-ethanesulfonyl chloride and 0.7 mmol of DIEA in DMF for about 1 hour. The resin is washed with DMF and DCM and treated with 1.2 mmol of 2-hydroxyethylpiperazine for about 2 hours. The resin is washed with DMF and DCM and treated with different reagents ((1) 20% mercaptoethanol / 10% DIEA in DMF and (2) 15% ethanolamine / 15% water / 70% DMF) to remove the DNP group on the His side chain and formyl group on the Trp side chain as described above before the final HF cleavage of the peptide from the resin.

Example 3

$((N_{\alpha}\text{-HEPA-His})^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$

The title compound (HEPA is (4-(2-hydroxyethyl)-1-piperazineacetyl)) can be made substantially according to the procedure described in Example 2 for making $((N_{\alpha}\text{-HEPES-His})^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ except that 2-bromoacetic anhydride is used in place of 2-chloro-1-ethanesulfonyl chloride.

Example 4

$(Aib^{8}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$

The title compound was synthesized substantially according to the procedure described for Example 1 using the appropriate protected amino acids. MS (ES) gave the molecular weight at 3325.7, calculated MW = 3325.8, purity = 99%, yield = 85 mg.

The synthesis of other compounds of the present invention can be accomplished in substantially the same manner as the procedure described for the synthesis of $(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ in Example 1 above, but using the appropriate protected amino acids depending on the desired peptide.

Example 5

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{\epsilon}\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$

The Boc amino acids used were the same as those in the synthesis of $(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ described in Example 1 except that Fmoc-Lys(Boc)-OH was used in this example. The first amino acid residue was coupled to the resin manually on a shaker. 2.5 mmol of Fmoc-Lys(Boc)-OH was dissolved in 4 mL of 0.5N HBTU in DMF. To the solution was added 1 mL of DIEA. The mixture was shaken for about 2 min. To the solution was then added 0.2 mmol of MBHA resin (substitution = 0.91 mmol/g). The mixture was shaken for about 1 hr. The resin was washed with DMF and treated with 100% TFA for 2x2 min to remove the Boc

protecting group. The resin was washed with DMF. Myristic acid (2.5 mmol) was pre-activated with HBTU (2.0 mmol) and DIEA (1.0 mL) in 4 mL of DMF for 2 min and was coupled to the Fmoc-Lys-resin. The coupling time was about 1 hr. The resin was washed with DMF and treated with 25% piperidine in DMF for 2x20 min to remove the Fmoc protecting group. The resin was washed with DMF and transferred to the reaction vessel of the peptide synthesizer. The following steps synthesis and purification procedures for the peptide were the same as those in the synthesis of (Aib^{8,35})hGLP-1(7-36)NH_2 in Example 1. 43.1 mg of the title compound were obtained as a white solid. Purity was 98% based on analytical HPLC analysis. Electro-spray mass spectrometer analysis gave the molecular weight at 3577.7 in agreement with the calculated molecular weight 3578.7.

Examples 6-8

Examples 6-8 were synthesized substantially according to the procedure described for Example 5 using the appropriate protected amino acid and the appropriate acid in place of the Myristic acid used in Example 5.

Example 6: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_ϵ-tetradecanoyl))hGLP-1(7-36)NH_2; Yield = 89.6 mg; MS(ES) = 3577.2, Calculated MW = 3578.7; Purity 96%.

Example 7: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ϵ-tetradecanoyl))hGLP-1(7-38)NH_2; Yield = 63.3 mg; MS(ES) = 3818.7; Calculated MW = 3819.5; Purity 96%.

Example 8: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ϵ-decanoyl))hGLP-1(7-36)NH_2; Yield = 57.4 mg; MS(ES) = 3521.5; Calculated MW = 3522.7; Purity 98%; Acid = decanoic acid.

The syntheses of other compounds of the present invention containing Lys(N_ϵ-alkanoyl) residue can be carried out in an analogous manner to the procedure described for Example 5, (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ϵ-tetradecanoyl))hGLP-1(7-36)NH_2. Fmoc-Lys(Boc)-OH amino acid is used for the residue of Lys(N_ϵ-alkanoyl) in the peptide, while Boc-Lys(2ClZ)-OH amino acid is used for the residue of Lys. If the Lys(N_ϵ-alkanoyl) residue is not at the C-terminus, the peptide fragment immediately prior to the Lys(N_ϵ-alkanoyl) residue is assembled on the resin on the peptide synthesizer first. The appropriate acid corresponding to the desired alkanoyl can be purchased from Aldrich Chemical Co., Inc. Milwaukee, WI, USA, e.g., octanoic acid, decanoic acid, lauric acid and palmitic acid.

Example 9

($Aib^{8,35}$, $Arg^{26,34}$, $Lys^{36}(N_\epsilon$-dodecanesulfonyl))hGLP-1(7-36)NH_2

The Boc amino acids to be used in this synthesis are the same as those used in the synthesis of Example 5. The first amino acid residue is coupled to the resin manually on a shaker. 2.5 mmol of Fmoc-Lys(Boc)-OH is dissolved in 4 mL of 0.5N HBTU in DMF. To the solution is added 1 mL of DIEA. The mixture is shaken for about 2 min. To the solution is then added 0.2 mmol of MBHA resin(substitution = 0.91 mmol/g). The mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 100% TFA for 2x2 min to remove the Boc protecting group. The resin is washed with DMF and to it is added 0.25 mmol of 1-dodecanesulfonyl chloride in 4 mL of DMF and 1 mL of DIEA. The mixture is shaken for about 2 hrs. The resin is washed with DMF and treated with 25% piperidine in DMF for 2 x 20 min to remove the Fmoc protecting group. The resin is washed with DMF and transferred to the reaction vessel of the peptide synthesizer. The synthesis of the rest of the peptide and purification procedures are the same as those described in Example 1.

The syntheses of other compounds of the present invention containing Lys(N_ϵ-alkylsulfonyl) residue can be carried out in an analogous manner to the procedure described in Example 9. Fmoc-Lys(Boc)-OH amino acid is used for the residue of Lys(N_ϵ-alkylsulfonyl) in the peptide, while Boc-Lys(2ClZ)-OH amino acid is used for the residue of Lys. If the Lys(N_ϵ-alkylsulfonyl) residue is not at the C-terminus, the peptide fragment immediately prior to the Lys(N_ϵ-alkylsulfonyl) residue is assembled on the resin on the peptide synthesizer first. The appropriate akylsulfonyl chloride can be obtained from Lancaster Synthesis Inc., Windham, NH, USA, e.g., 1-octanesulfonyl chloride, 1-decanesulfonyl chloride, 1-dodecanesulfonyl chloride, 1-hexadecanesulfonyl chloride and 1-octadecylsulfonyl chloride.

Example 10

($Aib^{8,35}$, $Arg^{26,34}$, $Lys^{36}(N_\epsilon$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

The Boc amino acids to be used for this example are the same as those used in the synthesis of Example 5. The first amino acid residue is coupled to the resin manually on a shaker. 2.5 mmol of Fmoc-Lys(Boc)-OH is dissolved in 4 mL of 0.5N HBTU in DMF. To the solution is added 1 mL of DIEA. The mixture is shaken for about 2 min. To the solution is then added 0.2 mmol of MBHA (substitution =

0.91 mmol/g) resin. The mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 100% TFA for 2x2 min to remove the Boc protecting group. The resin is washed with DMF. The 2-bromoacetic acid (2.5 mmol) is pre-activated with HBTU (2.0 mmol) and DIEA (1 mL) in 4 mL of DMF for about 2 min and is added to the resin. The mixture is shaken for about 10 min and washed with DMF. The resin is then treated with 1.2 mmol of piperazine in 4 mL of DMF for about 2 hrs. The resin is washed with DMF and treated with 2 mmol of 1-iodotetradecane for about 4 hrs. After washing with DMF, the resin is treated with 3 mmol of acetic anhydride and 1 mL of DIEA in 4 mL of DMF for about 0.5 hr. The resin is washed with DMF and treated with 25% piperidine in DMF for 2x20 min. The resin is washed with DMF and transferred to the reaction vessel of the peptide synthesizer to continue the synthesis. The remaining synthesis and purification procedures for the peptide are the same as the procedures described for Example 1.

The syntheses of other compounds of the present invention containing Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) residue are carried out in an analogous manner as the procedure described for the synthesis of Example 10. Fmoc-Lys(Boc)-OH amino acid is used for the residue of Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) in the peptide, while Boc-Lys(2ClZ)-OH amino acid is used for the residue of Lys. The corresponding iodoalkane is used for the residue of Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) during the alkylation step. If the Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) residue is not at the C-terminus, the peptide fragment immediately prior to the Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) residue is assembled on the resin on the peptide synthesizer first.

Example 11

($Aib^{8,35}$, $Arg^{26,34}$, Asp^{36}(1-(4-tetradecyl-piperazine)))hGLP-1(7-36)NH_2

The Boc amino acids to be used in this example are the same as the amino acids used in synthesis of Example 5 except Fmoc-Asp(O-tBu)-OH is used at position 36. The first amino acid residue is coupled to the resin manually on a shaker. 2.5 mmol of Fmoc-Asp(O-tBu)-OH is dissolved in 4 mL of 0.5N HBTU in DMF. To the solution is added 1 mL of DIEA. The mixture is shaken for about 2 min. To the solution is then added 0.2 mmol of MBHA (substitution = 0.91 mmol/g) resin. The mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 100% TFA for 2x15 min to remove the tBu protecting group. The resin is washed with DMF and is treated with HBTU (0.6 mmol) and DIEA (1mL) in 4 mL

of DMF for about 15 min. 0.6 mmol of piperazine is added to the reaction mixture and the mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 3 mmol of 1-iodotetradecane for about 4 hrs. After washing with DMF, the resin is treated with 3 mmol of acetic anhydride and 1 mL of DIEA in 4 mL of DMF for about 0.5 hr. The resin is washed with DMF and treated with 25% piperidine in DMF for 2x20 min to remove the Fmoc protecting group. The resin is washed with DMF and transferred to the reaction vessel of the peptide synthesizer to continue the synthesis. The remaining synthesis and purification procedures for the peptide are the same as those for the synthesis of Example 1.

The syntheses of other compounds of the present invention comprising Asp(1-(4-alkylpiperazine)) or Glu(1-(4-alkylpiperazine)) residue are carried out in an analogous manner as the procedure described for the synthesis of Example 11. Fmoc-Asp(O-tBu)-OH or Fmoc-Glu(O-tBu)-OH amino acid is used for the residue of Asp(1-(4-alkylpiperazine)) or Glu(1-(4-alkylpiperazine)) in the peptide, while Boc-Asp(OcHex)-OH or Boc-Glu(OcHex)-OH amino acid is used for the residue of Asp or Glu. The corresponding iodoalkane is used for the residue of Lys(N_ϵ-(2-(4-alkyl-1-piperazine)-acetyl)) during the alkylation step. If the Asp(1-(4-alkylpiperazine)) or Glu(1-(4-alkylpiperazine)) residue is not at the C-terminus, the peptide fragment immediately prior to the Asp(1-(4-alkylpiperazine)) or Glu(1-(4-alkylpiperazine)) residue is assembled on the resin on the peptide synthesizer first.

Example 12

($Aib^{8,35}$, $Arg^{26,34}$, Asp^{36}(1-tetradecylamino))hGLP-1(7-36)NH_2

The Boc amino acids to be used for this example are the same as those used in Example 5. The first amino acid residue is coupled to the resin manually on a shaker. 2.5 mmol of Fmoc-Asp(O-tBu)-OH is dissolved in 4 mL of 0.5N HBTU in DMF. To the solution is added 1 mL of DIEA. The mixture is shaken for about 2 min. To the solution is then added 0.2 mmol of MBHA (substitution = 0.91 mmol/g) resin. The mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 100% TFA for 2x15 min to remove the t-Bu protecting group. The resin is washed with DMF and is treated with HBTU (0.6 mmol) and DIEA (1mL) in 4 mL of DMF for about 15 min. 0.6 mmol of 1-tetradecaneamine is added to the reaction mixture and the mixture is shaken for about 1 hr. The resin is washed with DMF and treated with 25% piperidine in DMF for 2x20 min to remove the Fmoc protecting group. The resin is washed with DMF and transferred to the reaction

vessel of the peptide synthesizer to continue the synthesis. The remaining synthesis and purification procedures for the peptide of this example are the same as those described for the synthesis of Example 1.

The syntheses of other compounds of the present invention containing Asp(1-alkylamino) or Glu(1-alkylamino) residue are carried out in an analogous manner as described for the synthesis of Example 12. Fmoc-Asp(O-tBu)-OH or Fmoc-Glu(O-tBu)-OH amino acid is used for the residue of Asp(1-alkylamino) or Glu(1-alkylamino), respectively, in the peptide, while Boc-Asp(OcHex)-OH or Boc-Glu(OcHex)-OH amino acid is used for the residue of Asp or Glu, respectively. If the Asp(1-alkylamino) or Glu(1-alkylamino) residue is not at the C-terminus, the peptide fragment immediately prior to the Asp(1-alkylamino) or Glu(1-alkylamino) residue is assembled on the resin on the peptide synthesizer first.

Example 13

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-tetradecanoyl),ß-Ala^{37})hGLP-1(7-37)-OH

The Boc amino acids used are the same as those in the synthesis of (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-tetradecanoyl))hGLP-1(7-36)NH_2 (Example 5). 270 mg of Boc-ß-Ala-PAM resin (Novabiochem, San Diego, California, substitution=0.74 mmol/g) was used. The Boc protecting group on Boc-ß-Ala-PAM resin was deblocked on a shaker with 100%TFA for 2x2 min first. The remainder of the synthesis and purification procedures were the same as that in Example 5. 83.0 mg of the title peptide was obtained as white solid. Purity was 99% based on analytical HPLC analysis. Electro-spray mass spectrometer analysis gave the molecular weight at 3650.5 in agreement with the calculated weight 3650.8.

Example 14

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-tetradecanoyl))hGLP-1(7-36)-OH

The Boc amino acids to be used are the same as those in the synthesis of (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-tetradecanoyl))hGLP-1(7-36)NH_2 (Example 5). Fmoc-Lys(Boc)-OH (2.5 mmol) is pre-activated with HBTU (2.0 mmol), HOBt (2.0 mmol and DIEA (2.5 ml) in DMF (4 ml) for about 2 min. This amino acid is coupled to 235 mg of PAM resin (Chem-Impex, Wood Dale, IL; substitution = 0.85 mmol/g) manually on a shaker. The coupling time is about 8 hrs. The remainder of the synthesis and purification procedures are the same as those in Example 5 Electro-spray mass spectrometer analysis gave the molecular weight at 3579.15 in agreement with the calculated weight 3579.5.

The syntheses of other analogs of hGLP-1(7-36)-OH, hGLP-1(7-37)-OH and hGLP-1(7-38)-OH of the instant invention which contain Lys(N_ε-alkanoyl) residue can be carried out in an analogous manner according to the procedure described for the synthesis of Example 14. Fmoc-Lys(Boc)-OH amino acid is used for the residue of Lys(N_ε-alkanoyl) in the peptide, while Boc-Lys(2ClZ)-OH amino acid is used for the residue of Lys.

Example 366

(Aib^8, ß-Ala^{35}, Aec^{37})hGLP-1(7-37)NH_2

A mixture of MBHA resin (0.2mmol, substitution=0.91mmol/g), Fmoc-Aec-OH (0.40g, 0.829 mmol), HBTU (1.5 mL @ 0.5M in DMF) and DIEA (0.5mL) in a reaction vessel was shaken on a shaker for 4h at room temperature. The resin was then washed with DMF and treated with 25% piperidine in DMF for 2X20min. The resin was washed with DMF and DCM and transferred to the reaction vessel of the peptide synthesizer to continue the assembly of the rest of the peptide according the procedure described for Example 1. The purification procedure was also the same as the one described in Example 1. Electro-spry mass spectrometer analysis gave the molecular weight at 3494.8 in agreement with the calculated molecular weight 3494.99. Purity 93%; Yield 79.1mg.

Example 367

(Aib^8, ß-Ala^{35}, Aec^{38})hGLP-1(7-38)NH_2

Example 367 was synthesized substantially according to the procedure described for Example 366. MS(ES)=3551.7, calculated MW=3552.04; Purity 97%; Yield 97.4mg.

Example 368:

(Aib^8, ß-Ala^{35}, Aec^{37,38})hGLP-1(7-38)NH_2

A mixture of MBHA resin (0.2mmol, substitution=0.91mmol/g), Fmoc-Aec-OH (0.289g, 0.6 mmol), HBTU (1.12 mL @ 0.5M in DMF) and DIEA (0.4mL) in a reaction vessel was shaken on a shaker for 2h at room temperature. The resin was then washed with DMF and treated with 30% piperidine in DMF for 2X15min. The resin was washed with DMF. To the reaction vessel were added Fmoc-Aec-OH (0.289g, 0.6 mmol), HBTU (1.12 mL @ 0.5M in DMF) and DIEA (0.4mL). The mixture was shaken at room temperature for 2h. The resin was washed with DMF

and treated with 30% piperidine in DMF for 2X15min. The resin was washed with DMF and DCM and transferred to the reaction vessel of the peptide synthesizer to continue the assembly of the rest of the peptide according the procedure described for Example 1. The purification procedure was also the same as the one described in Example 1. Electro-spry mass spectrometer analysis gave the molecular weight at 3663.9 in agreement with the calculated molecular weight 3664.26. Purity 100%; Yield 75.3mg.

Example 369

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-Aec-decanoyl))hGLP-1(7-36)NH$_2$

A mixture of MBHA resin (0.2mmol, substitution=0.91mmol/g), Boc-Lys(Fmoc)-OH (1.17g, 2.5mmol), HBTU (4 mL @ 0.5M in DMF) and DIEA (1mL) in a reaction vessel was shaken on a shaker at room temperature for 10min. The resin was washed with DMF and treated with 25% piperidine in DMF for 2X15min. The resin was washed with DMF. To the reaction vessel were added Fmoc-Aec-OH (0.289g, 0.6 mmol), HBTU (1.12 mL @ 0.5M in DMF) and DIEA (0.4mL). The mixture was shaken at room temperature for 10min. The resin was washed with DMF and treated with 30% piperidine in DMF for 2X15min. The resin was washed with DMF and treated with a mixture of decanoic acid (431mg, 2.5 mmol), HBTU (4 mL @ 0.5M in DMF) and DIEA (1mL) for 10 min. The resin was washed with DMF and treated with 100% TFA for 2X2 min. The resin was washed with DMF and DCM and transferred to the reaction vessel of the peptide synthesizer to continue the assembly of the rest of the peptide according the procedure described for Example 1. The purification procedure was also the same as the one described in Example 1. Electro-spry mass spectrometer analysis gave the molecular weight at 3677.0 in agreement with the calculated molecular weight 3677.25. Purity 97.6%;Yield 44.8mg.

The following examples can be made according to the appropriate procedures described hereinabove.

Example 15: (Aib^{35})hGLP-1(7-36)NH$_2$

Example 16: (ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 17 ((N$^{\alpha}$-Me-His)^{7}, Aib^{8,35})hGLP-1(7-36)NH$_2$

Example 18: ((N$^{\alpha}$-Me-His)^{7}, Aib^{8}, ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 19: ((N$^{\alpha}$-Me-His)^{7}, Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH$_2$

Example 20: ((N$^{\alpha}$-Me-His)^{7}, Aib^{8}, Arg^{26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 21 (Aib^{8}, A6c^{35})hGLP-1(7-36)NH_2

Example 22: (Aib^{8}, A5c^{35})hGLP-1(7-36)NH_2

Example 23: (Aib^{8}, D-Ala^{35})hGLP-1(7-36)NH_2

Example 24: (Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH_2

Example 25: (Aib^{8,35}, A5c^{32})hGLP-1(7-36)NH_2

Example 26: (Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH_2

Example 27: (Aib^{8,24,35})hGLP-1(7-36)NH_2

Example 28: (Aib^{8,30,35})hGLP-1(7-36)NH_2

Example 29: (Aib^{8,25,35})hGLP-1(7-36)NH_2

Example 30: (Aib^{8,35}, A6c^{16,20})hGLP-1(7-36)NH_2

Example 31: (Aib^{8,35}, A6c^{16,29,32})hGLP-1(7-36)NH_2

Example 32: (Aib^{8,35}, A6c^{20,32})hGLP-1(7-36)NH_2

Example 33: (Aib^{8,35}, A6c^{20})hGLP-1(7-36)NH_2

Example 34: (Aib^{8,35}, Lys^{25})hGLP-1(7-36)NH_2

Example 35: (Aib^{8,24,35}, A6c^{20})hGLP-1(7-36)NH_2

Example 36: (Aib^{8,35}, A6c^{29,32})hGLP-1(7-36)NH_2

Example 37: (Aib^{8,24,35}, A6c^{29,32})hGLP-1(7-36)NH_2

Example 38: (Aib^{8,35}, A6c^{12})hGLP-1(7-36)NH_2

Example 39: (Aib^{8,35}, Cha^{20})hGLP-1(7-36)NH_2

Example 40: (Aib^{8,35}, A6c^{33})hGLP-1(7-36)NH_2

Example 41 (Aib^{8,35}, A6c^{20,32})hGLP-1(7-36)NH_2

Example 42: (Aib^{8}, A6c^{16,20}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 43: (Aib^{8,35}, ß-Ala^{22})hGLP-1(7-36)NH_2

Example 44: (Aib^{8,22,35})hGLP-1(7-36)NH_2

Example 45: (Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2

Example 46: (Aib^{8,24,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2

Example 47 (Aib^{8,24,25,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2

Example 48 (Aib^{8,24,25,35}, A6c^{16,20,32}, Glu^{23})hGLP-1(7-36)NH_2

Example 49: (Aib^{8}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 50: (Aib^{8}, A5c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 51: (Aib^{8}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 52: (Aib^{8,24}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 53 (Aib^{8,30}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 54 (Aib^{8,25}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 55: (Aib^{8}, A6c^{16,20}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 56: (Aib^{8}, A6c^{16,29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 57: (Aib^{8}, A6c^{20,32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 58: (Aib^{8}, A6c^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 59: (Aib^{8}, Lys^{25}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 60: (Aib^{8,24}, A6c^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 61: (Aib^{8}, A6c^{29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 62: (Aib^{8,24}, A6c^{29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 63: (Aib^{8}, A6c^{12}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 64: (Aib^{8}, Cha^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 65 (Aib^{8} , A6c^{33}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 66: (Aib^{8}, A6c^{20,32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 67: (Aib^{8}, ß-Ala^{22,35})hGLP-1(7-36)NH_2

Example 68: (Aib^{8,22}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 69: (Aib^{8}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 70: (Aib^{8,24}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 71: (Aib^{8,24}, Glu^{23}, A6c^{32}, Lys^{34}(N_ε-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 72: (Aib^{8,24,25}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 73: (Aib^{8,24,25}, A6c^{16,20,32}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 74: (Aib^{8,35}, D-Arg^{36})hGLP-1(7-36)NH_2

Example 75: (Aib^{8,35}, D-Lys^{36})hGLP-1(7-36)NH_2

Example 76: (Aib^{8}, ß-Ala^{35}, D-Arg^{36})hGLP-1(7-36)NH_2

Example 77: (Aib^{8}, ß-Ala^{35}, D-Lys^{36})hGLP-1(7-36)NH_2

Example 78: (Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2

Example 79: (Aib^{8}, Arg^{26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 80: (Aib^{8,35}, Arg^{25,26,34})hGLP-1(7-36)NH_2

Example 81: (Aib^{8}, Arg^{25,26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 82: (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N^{ε}-tetradecanoyl))hGLP-1(7-36)OH

Example 83: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-tetradecanoyl))hGLP-1(7-37)OH

Example 84: (Aib^{8,35,37}, Arg^{26,34}, Lys^{36}(N^{ε}-tetradecanoyl))hGLP-1(7-37)OH

Example 85: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-tetradecanoyl), D-Ala^{37})hGLP-1(7-37)OH

Example 86: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N^{ε}-tetradecanoyl))hGLP-1(7-38)OH

Example 87: (Aib^{8,35}, Arg^{26,34}, ß-Ala^{37}, Lys^{38}(N^{ε}-tetradecanoyl))hGLP-1(7-38)OH

Example 88: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)OH

Example 89 (Aib^{8}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{37})hGLP-1(7-37)OH

Example 90. (Aib^{8,37}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-37)OH

Example 91: (Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)OH

Example 92: (Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)NH$_2$

Example 93 (Aib^{8}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl), D-Ala^{37})hGLP-1(7-37)OH

Example 94: (Aib^{8,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)OH

Example 95: (Aib^{8}, Arg^{26,34}, ß-Ala^{37}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)OH

Example 96: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 97 (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 98: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 99: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 100: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 101: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 102: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 103: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 104: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 105: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-decanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 106: (Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 107: (Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 108: (Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 109: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 110: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 111. (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 112. (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 113: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 114: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 115: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 116: (Aib^{8}, Lys^{26}(N$^{\varepsilon}$-decanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 117: (Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 118: (Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 119: (Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 120: (Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 121 (Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 122: (Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 123: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 124: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 125: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 126: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 127: (Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 128: (Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 129: (Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 130: (Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 131: (Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 132: (Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 133: (Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 134: (Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 135: (Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 136: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 137 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 138: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH$_2$

Example 139 (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH$_2$

Example 140: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH$_2$

Example 141 (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH$_2$

Example 142: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH$_2$

Example 143: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH$_2$

Example 144: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH$_2$

Example 145: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH$_2$

Example 146: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH$_2$

Example 147 (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH$_2$

Example 148: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH$_2$

Example 149: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH$_2$

Example 150 (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH$_2$

Example 151: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH$_2$

Example 152: (Aib$^{8,35\ 37}$, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH_2

Example 153: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 154: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 155: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 156: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 157: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 158: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 159: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2

Example 160: (Aib^{8}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 161: (Aib^{8}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 162: (Aib^{8}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 163: (Aib^{8}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 164: (Aib^{8}, Glu^{23}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 165: (Aib^{8}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 166: (Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 167: (Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 168 (Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 169: (Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-decanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 170: (Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 171: (Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 172. (Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 173: (Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-decanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 174: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 175: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 176: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2

Example 177: (Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 178 (Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 179: (Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 180: (Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 181: (Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 182: (Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 183: (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 184: (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 185 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$- hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 186 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 187: (Aib^{8}, Lys^{25}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 188: (Aib^{8}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH$_2$

Example 189: (Aib^{8}, Lys^{25}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 190: (Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 191: (Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 192: (Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 193: (Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 194: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH$_2$

Example 195: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH$_2$

Example 196: (Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH$_2$

Example 197: (Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 198: (Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 199: (Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 200: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 201: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 202: (Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 203: (Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 204: (Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 205: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 206: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 207: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 208: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 209: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH$_2$

Example 210: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 211: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 212: (Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 213: (Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 214: (Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 215: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 216: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 217: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 218: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 219: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 220: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 221: (Aib^{8,24,35}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 222: (Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 223: (Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 224: (Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 225: (Aib^{8,35}, Glu^{23}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 226: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 227: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 228: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 229: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 230: (Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 231 (Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 232: (Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 233: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 234 (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 235: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 236: (Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 237: (Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 238: (Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$

Example 239: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 240: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 241: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 242: (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 243 (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 244: (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$

Example 245: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$

Example 246: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$

Example 247 ($Aib^{8,35}$, Glu^{23}, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 248: ($Aib^{8,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 249 ($Aib^{8,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 250: ($Aib^{8,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 251: ($Aib^{8,24,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 252 ($Aib^{8,24,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 253: ($Aib^{8,24,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 254: ($Aib^{8,24,30,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2

Example 255 ($Aib^{8,24,30,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2

Example 256: ($Aib^{8,24,30,35}$, Glu^{23}, $Arg^{26,34}$, $A6c^{32}$, $Lys^{36}(N^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2

Example 257: ($(N^{\alpha}$-HEPES-$His)^7$, Aib^{35})hGLP-1(7-36)NH_2

Example 258 ($(N^{\alpha}$-HEPES-$His)^7$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 259 ($(N^{\alpha}$-HEPES-$His)^7$, Aib^8, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 260: ($(N^{\alpha}$-HEPA-$His)^7$, Aib^{35})hGLP-1(7-36)NH_2

Example 261: ($(N^{\alpha}$-HEPA-$His)^7$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 262: ($(N^{\alpha}$-HEPA-$His)^7$, Aib^8, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 263: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, Aib^{35})hGLP-1(7-36)NH_2

Example 264: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 265: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Aib^{8,35}$)hGLP-1(7-36)NH_2

Example 266: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, Aib^8, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 267: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Arg^{26,34}$, Aib^{35})hGLP-1(7-36)NH_2

Example 268 ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Arg^{26,34}$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 269: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Aib^{8,35}$, $Arg^{26,34}$)hGLP-1(7-36)NH_2

Example 270: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, Aib^8, $Arg^{26,34}$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 271: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Arg^{25,26,34}$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 272: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, $Aib^{8,35}$, $Arg^{25,26,34}$)hGLP-1(7-36)NH_2

Example 273: ($(N^{\alpha}$-tetradecanoyl-$His)^7$, Aib^8, $Arg^{25,26,34}$, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 274: ($Aib^{8,35}$, $Lys^{26}(N^{\varepsilon}$-octanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2

Example 275 ($Aib^{8,35}$, $Lys^{26}(N^{\varepsilon}$-dodecanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2

Example 276: (Aib^{8,35}, Lys^{26}(N^{ε}-hexadecanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2

Example 277: (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-octanesulfonyl))hGLP-1(7-36)NH_2

Example 278 (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-dodecanesulfonyl))hGLP-1(7-36)NH_2

Example 279: (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-hexadecanesulfonyl))hGLP-1(7-36)NH_2

Example 280: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-octanesulfonyl))hGLP-1(7-36)NH_2

Example 281: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-hexadecanesulfonyl))hGLP-1(7-36)NH_2

Example 282: (Aib^{8,35}, Asp^{26}(1-(4-decylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2

Example 283 (Aib^{8,35}, Asp^{26}(1-(4-dodecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2

Example 284: (Aib^{8,35}, Asp^{26}(1-(4-tetradecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2

Example 285: (Aib^{8,35}, Asp^{26}(1-(4-hexadecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2

Example 286 (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2

Example 287 (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2

Example 288: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2

Example 289: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2

Example 290. (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2

Example 291 (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2

Example 292: (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2

Example 293 (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2

Example 294. (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2

Example 295: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2

Example 296: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2

Example 297 (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2

Example 298. (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2

Example 299: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2

Example 300: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2

Example 301. (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2

Example 302 (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2

Example 303: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2

Example 304: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2

Example 305 (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2

Example 306 (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2

Example 307: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2

Example 308: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2

Example 309: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2

Example 310 (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2

Example 311: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2

Example 312. (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2

Example 313: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2

Example 314: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2

Example 315: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2

Example 316: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2

Example 317 (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2

Example 318. (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2

Example 319: (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2

Example 320 (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2

Example 321: (Aib^{8,35}, Arg^{26,34}, Glu^{36}(1-dodecylamino))hGLP-1(7-36)NH_2

Example 322: (Aib^{8,35}, Glu^{26}(1-dodecylamino), Arg^{34})hGLP-1(7-36)NH_2

Example 323 (Aib^{8,35}, Arg^{26}, Glu^{34}(1-dodecylamino))hGLP-1(7-36)NH_2

Example 324: (Aib^{8,35,37}, Arg^{26,34}, Glu^{38}(1-dodecylamino))hGLP-1(7-38)NH_2

Example 325 (Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 326: (Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 327: (Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 328: (Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 329. (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 330: (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-(2-(4-dodecyl-1-piperazine)-acetyl))hGLP-1(7-36)NH_2

Example 331: (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 332: (Aib^{8,35}, Arg^{26}, Lys^{34}(N^{ε}-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 333 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 334 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 335: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 336 (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 337 (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 338: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 339: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 340 (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 341 (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 342: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 343: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 344 (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 345 (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 346: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 347: Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 348 (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 349 (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 350: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 351: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 352: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 353 (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 354: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 355: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2

Example 356: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 357 (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 358: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 359: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 360: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 361: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 362: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 363: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2

Example 364: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH

Example 365: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH

Example 370 (Aib^{8,35},Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2

Example 371 (Aib^{8,35},Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2

Example 372 (Aib^{8,35},Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2

Example 373 (Aib^{8,17,35},)hGLP-1(7-36)NH_2

Example 374 (Aib^{8} ,Arg^{26,34}, ß-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2

Example 375 (Gly^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 376 (Ser^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 377 (Aib^{8}, Glu^{22,23}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 378 (Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2

Example 379 (Aib^{8}, Lys^{18}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 380 (Aib^{8}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 381 (Aib^{8}, Lys^{33}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 382 (Aib^{8}, Lys^{18}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 383 (Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2

Example 384 (Aib^{8}, ß-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2

Example 385 (Aib^{8,27}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 386 (Aib^{8,27}, ß-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2

Example 387 (Aib^{8,27}, ß-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2

Example 388 (Aib^{8}, Lys^{18,27}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 389 (Aib^{8}, Lys^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 390 (Aib^{8}, ß-Ala^{35}, Arg^{36})hGLP-1(7-38)NH_2

Example 391 (Aib^{8}, Arg^{26,34}, ß-Ala^{35},)hGLP-1(7-36)NH_2

Example 392 (Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2

Example 393 (Aib^{8}, ß-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2

Example 394 (Aib^{8}, Phe^{31}, ß-Ala^{35})hGLP-1(7-36)NH_2

Example 395 (Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2

Example 396 (Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2

Example 397 (Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2

Example 398 (Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2

Example 399 (Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2

Example 400 (Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2

Example 401 (Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2

Example 402 (Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36) NH_2

Example 403 (Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2

Example 404 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(7-36)NH_2

Example 405 (Aib^{8},B-Ala^{35},Ser^{37}(O-decanoyl))hGLP1(7-37)-NH_2

Example 406 (Aib^{8,27}, ß-Ala^{35,37}, Arg^{38}, Lys^{39}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-39)NH_2

Example 407 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-37)NH_2

Example 408 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-37)NH_2

Example 409 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-37)NH_2

Example 410 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(7-37)NH_2

Example 411 (Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(8-37)NH_2

Physical data for a representative sampling of the compounds exemplified herein are given in Table 1.

Example Number	Mol. Wt. Expected	Mol. Wt. MS(ES)	Purity (HPLC)
24	3351.8	3352.2	88%
26	3340.17	3340.9	99%
27	3353.81	3353.9	99%
29	3353.81	3353.9	99%
45	3352.6	3352.5	97%
51	3326.74	3326.6	99%
78	3395.81	3395.5	96%
136	3494	3494	99%
364	3523.02	3523.6	99%
365	3580.13	3580.3	95%
369	3677.25	3677	97%
370	3692.28	3692.4	98%
371	3807.37	3807.3	98%
372	3579.11	3579.7	97.90%
373	3337.81	3338.5	94%
374	3779.3	3779.5	94%
375	3297.7	3297.5	99%
376	3327.7	3327.4	98%
377	3398.8	3398.7	97.50%
378	3311.6	3311	93%
379	3366.85	3366.5	97%
380	3309.8	3309.4	99%
381	3354.8	3354.5	97.70%
382	3350.9	3350.3	97.20%
383	3311.73	3310.7	92%
384	3481.95	3481.3	94.30%
385	3281.76	3281.6	98%
386	3509.02	3509.1	99.40%
387	3665.2	3665.1	99%
388	3365.91	3365	97%
389	3324.79	3324.2	95%
390	3539	3539.2	93%
391	3381.74	3381.3	97%

392	3410.89	3409.8	99%
393	3481.95	3481.1	90%
394	3286.76	3286.2	99.20%
395	3300.76	3299.4	93%
396	3350.81	3349.4	99%
397	3400.87	3400.1	99%
398	3406.84	3406.4	99%
399	3356.77	3356.6	99%
400	3384.87	3384.43	94%
401	3400.87	3401.3	99%
402	3466.03	3466.9	97.40%
403	3522.05	3522.06	93%
404	3550.11	3550.2	98%
405	3567.09		99%
406	3763.38	3763.2	95%
407	3636.15	3635.8	99%
408	3664.21	3663.3	99%
409	3720.32	3719.5	99%
410	3692.27	3691.7	99%
411	3555.13	3554.4	99%

TABLE 1

CLAIMS

What is claimed is:

1. A compound of formula (I),

(R^2R^3)-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-A^{39}-R^1 ,

(I)

wherein

A^7 is L-His, Ura, Paa, Pta, Amp, Tma-His, des-amino-His, or deleted;

A^8 is Ala, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;

A^9 is Glu, N-Me-Glu, N-Me-Asp or Asp;

A^{10} is Gly, Acc, ß-Ala or Aib;

A^{11} is Thr or Ser;

A^{12} is Phe, Acc, Aic, Aib, 3-Pal, 4-Pal, ß-Nal, Cha, Trp or X^1-Phe;

A^{13} is Thr or Ser;

A^{14} is Ser or Aib;

A^{15} is Asp or Glu;

A^{16} is Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala or Cha;

A^{17} is Ser or Thr;

A^{18} is Ser or Thr;

A^{19} is Tyr, Cha, Phe, 3-Pal, 4-Pal, Acc, ß-Nal or X^1-Phe;

A^{20} is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe or X^1-Phe;

A^{21} is Glu or Asp;

A^{22} is Gly, Acc, ß-Ala, Glu or Aib;

A^{23} is Gln, Asp, Asn or Glu;

A^{24} is Ala, Aib, Val, Abu, Tle or Acc;

A^{25} is Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-$N(R^{10}R^{11})$)-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{26} is Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-$N(R^{10}R^{11})$)-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{27} is Glu Asp, Leu, Aib or Lys;

A^{28} is Phe, Pal, ß-Nal, X^1-Phe, Aic, Acc, Aib, Cha or Trp;

A^{29} is Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala or Phe;

A^{30} is Ala, Aib or Acc;

A^{31} is Trp, ß-Nal, 3-Pal, 4-Pal, Phe, Acc, Aib or Cha;

A^{32} is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe, X^1-Phe or Ala;

A^{33} is Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys or X^1-Phe;

A^{34} is Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O);

A^{35} is Gly, ß-Ala, D-Ala, Gaba, Ava, HN-$(CH_2)_m$-C(O), Aib, Acc or a D-amino acid;

A^{36} is L- or D-Arg, D- or L-Lys, D- or L-hArg, D- or L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) or deleted;

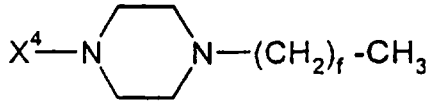
A^{37} is Gly, ß-Ala, Gaba, Ava, Aib, Acc, Ado, Arg, Asp, Aun, Aec, HN-$(CH_2)_m$-C(O), HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), a D-amino acid, or deleted;

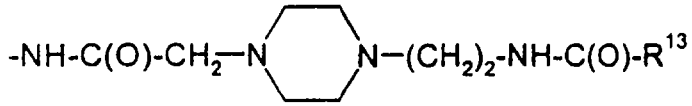
A^{38} is D- or L-Lys, D- or L-Arg, D- or L-hArg, D- or L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) Ava, Ado, Aec or deleted;

A^{39} is D- or L-Lys, D- or L-Arg, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), Ava, Ado, or Aec;

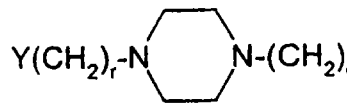
X^1 for each occurrence is independently selected from the group consisting of (C_1-C_6)alkyl, OH and halo;

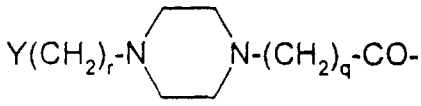
R^1 is OH, NH_2, (C_1-C_{30})alkoxy, or NH-X^2-CH_2-Z^0, wherein X^2 is a (C_1-C_{12})hydrocarbon moiety, and Z^0 is H, OH, CO_2H or $CONH_2$;

X^3 is ,



or –C(O)-NHR[12], wherein X^4 is, independently for each occurrence, -C(O)-, -NH-C(O)- or -CH_2-, and wherein f is, independently for each occurrence, an integer from 1 to 29 inclusive;

each of R^2 and R^3 is independently selected from the group consisting of H, (C_1-C_{30})alkyl, (C_2-C_{30})alkenyl, phenyl(C_1-C_{30})alkyl, naphthyl(C_1-C_{30})alkyl, hydroxy(C_1-C_{30})alkyl, hydroxy(C_2-C_{30})alkenyl, hydroxyphenyl(C_1-C_{30})alkyl, and hydroxynaphthyl(C_1-C_{30})alkyl; or one of R^2 and R^3 is , (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl, C(O)X^5, , or



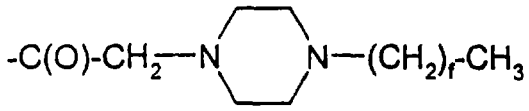
; wherein Y is H, OH or NH_2; r is 0 to 4; q is 0 to 4; and X^5 is $(C_1\text{-}C_{30})$alkyl, $(C_2\text{-}C_{30})$alkenyl, phenyl$(C_1\text{-}C_{30})$alkyl, naphthyl$(C_1\text{-}C_{30})$alkyl, hydroxy$(C_1\text{-}C_{30})$alkyl, hydroxy$(C_2\text{-}C_{30})$alkenyl, hydroxyphenyl$(C_1\text{-}C_{30})$alkyl or hydroxynaphthyl$(C_1\text{-}C_{30})$alkyl;

e is, independently for each occurrence, an integer from 1 to 4 inclusive;

m is, independently for each occurrence, an integer from 5 to 24 inclusive;

n is, independently for each occurrence, an integer from 1 to 5, inclusive;

each of R^{10} and R^{11} is, independently for each occurrence, H, $(C_1\text{-}C_{30})$alkyl, $(C_1\text{-}C_{30})$acyl, $(C_1\text{-}C_{30})$alkylsulfonyl, –C((NH)(NH_2)) or



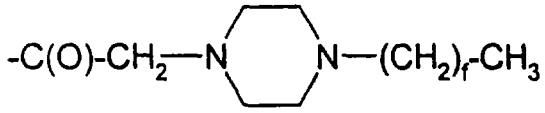
; and

R^{12} and R^{13} each is, independently for each occurrence, $(C_1\text{-}C_{30})$alkyl;

provided that:

when A^7 is Ura, Paa or Pta, then R^2 and R^3 are deleted;

when R^{10} is $(C_1\text{-}C_{30})$acyl, $(C_1\text{-}C_{30})$alkylsulfonyl, –C((NH)(NH_2)) or



, then R^{11} is H or $(C_1\text{-}C_{30})$alkyl;

(i) at least one amino acid of a compound of formula (I) is not the same as the native sequence of hGLP-1(7-36, -37 or -38)NH_2 or hGLP-1(7-36, -37 or -38)OH;

(ii) a compound of formula (I) is not an analogue of hGLP-1(7-36, -37 or -38)NH_2 or hGLP-1(7-36, -37 or -38)OH wherein a single position has been substituted by Ala;

(iii) a compound of formula (I) is not ($Arg^{26,34}$, Lys^{38})hGLP-1(7-38)-E, (Lys^{26}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, (Lys^{34}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, ($Lys^{26,34}$-bis(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E, (Arg^{26}, Lys^{34}(N_ε-alkanoyl))hGLP-1(8-36, -37 or -38)-E, ($Arg^{26,34}$, Lys^{36}(N_ε-alkanoyl))hGLP-1(7-36, -37 or –38)-E or ($Arg^{26,34}$, Lys^{38}(N_ε-alkanoyl))hGLP-1(7-38)-E, wherein E is -OH or -NH_2;

(iv) a compound of formula (I) is not Z^1-hGLP-1(7-36, -37 or -38)-OH, Z^1-hGLP-1(7-36, -37 or -38)-NH_2, wherein Z^1 is selected from the group consisting of:

(e) (Arg^{23}), (Arg^{34}), ($Arg^{26,34}$), (Lys^{36}), (Arg^{26}, Lys^{36}), (Arg^{34}, Lys^{36}), (D-Lys^{36}), (Arg^{35}), (D-Arg^{36}), ($Arg^{26,34}$, Lys^{36}) or ($Arg^{26,36}$, Lys^{34});

(f) (Asp^{21});

(g) at least one of (Aib^{8}), (D-Ala^{8}) and (Asp^{9}); and

(h) (Tyr^{7}), (N-acyl-His^{7}), (N-alkyl-His^{7}), (N-acyl-D-His^{7}) or (N-alkyl-D-His^{7});

(v) a compound of formula (I) is not a combination of any two of the substitutions listed in groups (a) to (d); and

(vi) a compound of formula (I) is not (N-Me-Ala^{8})hGLP-1(8-36 or -37), (Glu^{15})hGLP-1(7-36 or -37), (Asp^{21})hGLP-1(7-36 or -37) or (Phe^{31})hGLP-1(7-36 or -37)

or a pharmaceutically acceptable salt thereof.

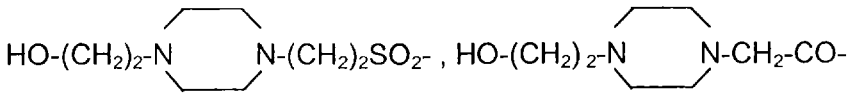
2. A compound according to claim 1, wherein A^{11} is Thr; A^{13} is Thr; A^{15} is Asp; A^{17} is Ser; A^{18} is Ser; A^{21} is Glu; A^{23} is Gln or Glu; A^{27} is Glu; and A^{31} is Trp; or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 2, wherein A^{9} is Glu, N-Me-Glu or N-Me-Asp; A^{12} is Phe, Acc or Aic; A^{16} is Val, Acc or Aib; A^{19} is Tyr; A^{20} is Leu, Acc or Cha; A^{24} is Ala, Aib or Acc; A^{25} is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) or HN-CH($(CH_2)_e$-X^3)-C(O); A^{26} is Phe; A^{29} is Ile or Acc; A^{30} is Ala or Aib; A^{32} is Leu, Acc or Cha; and A^{33} is Val or Acc; or a pharmaceutically acceptable salt thereof.

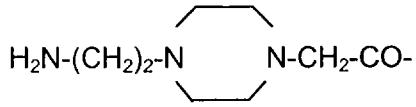
4. A compound according to claim 3, wherein A^{8} is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A^{10} is Gly; A^{12} is Phe, A6c or A5c; A^{16} is Val, A6c or A5c; A^{20} is Leu, A6c, A5c or Cha; A^{22} is Gly, ß-Ala or Aib; A^{24} is Ala or Aib; A^{29} is Ile, A6c or A5c; A^{32} is Leu, A6c, A5c or Cha; A^{33} is Val, A6c or A5c; A^{35} is Aib, ß-Ala, Ado, A6c, A5c or Gly; and A^{37} is Gly, Aib, ß-Ala, Ado, D-Ala or deleted; or a pharmaceutically acceptable salt thereof.

5. A compound according to claim 4 or a pharmaceutically acceptable salt thereof, wherein X^4 for each occurrence is -C(O)-; e for each occurrence is independently 1 or 2; and R^1 is OH or NH_2.

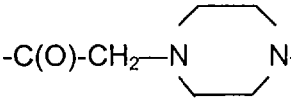
6. A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein R^2 is H and R^3 is (C_1-C_{30})alkyl, (C_2-C_{30})alkenyl, (C_1-C_{30})acyl, (C_1-C_{30})alkylsulfonyl,



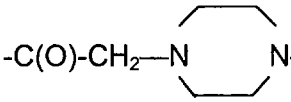
or



7. A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein R^{10} is $(C_1\text{-}C_{30})$acyl, $(C_1\text{-}C_{30})$alkylsulfonyl or



8. A compound according to claim 7 or a pharmaceutically acceptable salt thereof, wherein R^{10} is $(C_4\text{-}C_{20})$acyl, $(C_4\text{-}C_{20})$alkylsulfonyl or



9. A compound according to claim 1 wherein said compound is
$(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$,
$((N_\alpha\text{-HEPES-His})^7, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$,
$((N_\alpha\text{-HEPA-His})^7, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^8, ß\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26}, Lys^{34}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}38)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-decanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-dodecanesulfonyl}))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-(2-(4-tetradecyl-1-piperazine)-acetyl})))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1\text{-}(4\text{-tetradecyl-piperazine})))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1\text{-tetradecylamino}))hGLP\text{-}1(7\text{-}36)NH_2$,
$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-tetradecanoyl}),ß\text{-}Ala^{37})hGLP\text{-}1(7\text{-}37)\text{-}OH$ or
$(Aib^{8,35}, Arg^{26\,34}, Lys^{36}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}36)\text{-}OH$, or a pharmaceutically acceptable salt thereof.

10. A compound according to claim 9 wherein said compound is

$(Aib^{8}, ß\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$,

$(Aib^{8,35}, Arg^{26}, Lys^{34}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$,

$(Aiba^{8,35,37}, Arg^{26,34}, Lys^{38}(N_\varepsilon\text{-tetradecanoyl}))hGLP\text{-}1(7\text{-}38)NH_2$,

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-decanoyl}))hGLP\text{-}1(7\text{-}36)NH_2$, or

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_\varepsilon\text{-tetradecanoyl}),ß\text{-}Ala^{37})hGLP\text{-}1(7\text{-}37)\text{-}OH$, or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

12. Use of an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof in the preparation of a medicament to elicit an agonist effect from a GLP-1 receptor in a subject in need thereof.

13. Use of an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof in the preparation of a medicament to treat a disease selected from the group consisting of Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis and neurodegenerative disease, in a subject in need thereof.

14. Use according to claim 13 wherein said disease is Type I diabetes or Type II diabetes.

15. A compound according to claim 1 wherein said compound is

$(Aib^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(ß\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N^{\alpha}\text{-Me-His})^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N^{\alpha}\text{-Me-His})^{7}, Aib^{8}, ß\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N^{\alpha}\text{-Me-His})^{7}, Aib^{8,35}, Arg^{26,34})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N^{\alpha}\text{-Me-His})^{7}, Aib^{8}, Arg^{26,34}, ß\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, A6c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, A5c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, D\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A5c^{32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, Glu^{23})hGLP\text{-}1(7\text{-}36)NH_2$;

(Aib^{8,24,35})hGLP-1(7-36)NH_2;

(Aib$^{8\ 30,35}$)hGLP-1(7-36)NH_2;

(Aib$^{8,25\ 35}$)hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{16,20})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{16,29,32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{20,32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{20})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, A6c^{20})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{29,32})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, A6c^{29,32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{12})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Cha^{20})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{33})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{20,32})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{16,20}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, ß-Ala^{22})hGLP-1(7-36)NH_2;

(Aib^{8,22,35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,24,25,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,24,25,35}, A6c^{16,20,32}, Glu^{23})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A5c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,30}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,25}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{16,20}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{16,29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{20,32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, A6c^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, A6c^{29,32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{12}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Cha^{20}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8} , A6c^{33}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{20,32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{22,35})hGLP-1(7-36)NH_2;

(Aib^{8,22}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, Glu^{23}, A6c^{32}, Lys^{34}(N_ϵ-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24,25}, Glu^{23}, A6c^{32}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24,25}, A6c^{16,20,32}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8,35}, D-Lys^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, D-Lys^{36})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-36)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-37)OH;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl), D-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-38)OH;

(Aib^{8,35}, Arg^{26,34}, ß-Ala^{37},Lys^{38}(N^ϵ-tetradecanoyl))hGLP-1(7-38)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-38)OH;

(Aib^{8}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl), ß-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,37}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl))hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, Lys^{36}(N^ϵ-tetradecanoyl), D-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)OH;

(Aib^{8}, Arg^{26,34}, ß-Ala^{37}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)OH;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-decanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N$^{\varepsilon}$-decanoyl), Arg^{34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg$^{25\,26,34}$, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg$^{25\,26,34}$, Lys^{38}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg$^{25\,26\,34}$, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg$^{25\,26\,34}$, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib$^{8\ 35}$, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-decanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-decanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$- hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl), ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg$^{25,26\ 34}$, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{34}(N$_{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-octanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-tetradecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanoyl), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH$_2$;

(Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib$^{8,24,30\ 35}$, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N$^{\varepsilon}$-hexadecanoyl))hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPES-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPES-His)^{7}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPES-His)^{7}, Aib^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPA-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPA-His)^{7}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-HEPA-His)^{7}, Aib^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8,35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Arg^{26,34}, Aib^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Arg^{26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8}, Arg^{26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Arg^{25,26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8,35}, Arg^{25,26,34})hGLP-1(7-36)NH_2;

((N$^{\alpha}$-tetradecanoyl-His)^{7}, Aib^{8}, Arg^{25,26,34}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-octanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-dodecanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N$^{\varepsilon}$-hexadecanesulfonyl), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-octanesulfonyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-dodecanesulfonyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-hexadecanesulfonyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanesulfonyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-hexadecanesulfonyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Asp^{26}(1-(4-decylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Asp^{26}(1-(4-dodecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Asp^{26}(1-(4-tetradecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Asp^{26}(1-(4-hexadecylpiperazine)), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-decylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-dodecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-tetradecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-hexadecylpiperazine)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-decylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-dodecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-tetradecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-hexadecylpiperazine)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Glu^{36}(1-dodecylamino))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{26}(1-dodecylamino), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Glu^{34}(1-dodecylamino))hGLP-1(7-36)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Glu^{38}(1-dodecylamino))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

Aib^{8,35}, Arg^{25,34}, Lys^{26}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-decyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-dodecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-tetradecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N$^{\varepsilon}$-(2-(4-hexadecyl-1-piperazine)-acetyl)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8,35},Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

(Aib^{8,35},Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

(Aib^{8,35},Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

(Aib^{8,17,35},)hGLP-1(7-36)NH_2;

(Aib^{8} ,Arg^{26,34}, ß-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2;

(Gly^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Ser^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{22,23}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{33}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8,27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg$^{38\ 39}$)hGLP-1(7-39)NH_2;

(Aib^{8}, Lys^{18,27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35},)hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8},B-Ala^{35},Ser^{37}(O-decanoyl))hGLP1(7-37)-NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38}, Lys^{39}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-39)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-tetradecanoyl))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(7-37)NH_2; or

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N$^{\varepsilon}$-dodecanoyl))hGLP-1(8-37)NH_2;

or a pharmaceutically acceptable salt thereof.

16. A compound according to claim 15 wherein said compound is

(Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH_2;

(Aib^{8,24,35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg$^{26\ 34}$)hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-octanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N$^{\varepsilon}$-decanoyl))hGLP-1(7-36)OH;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{36}(N$^{\varepsilon}$-Aec-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35},Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

(Aib^{8,35},Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

(Aib^{8,35},Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

(Aib^{8,17,35},)hGLP-1(7-36)NH_2;

(Aib^{8} ,Arg^{26,34}, ß-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2;

(Gly^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Ser^{8}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{22,23}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{33}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, Leu^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8,27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2;

(Aib^{8}, Lys^{18,27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{27}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35},)hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, ß-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, ß-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N^{ε}-decanoyl))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N^{ε}-decanoyl))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N^{ε}-dodecanoyl))hGLP-1(7-36)NH_2;

(Aib^{8},B-Ala^{35}, Ser^{37}(O-decanoyl))hGLP1(7-37)-NH_2;

(Aib^{8,27}, ß-Ala^{35,37}, Arg^{38}, Lys^{39}(N^{ε}-octanoyl))hGLP-1(7-39)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-octanoyl))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-decanoyl))hGLP-1(7-37)NH_2; or

(Aib^{8}, Arg^{26,34}, ß-Ala^{35}, Lys^{37}(N^{ε}-tetradecanoyl))hGLP-1(7-37)NH_2;

or a pharmaceutically acceptable salt thereof.

17. Use of a compound as claimed in any of claims 1 to 10, or 15 or 16, in the preparation of a medicament for the treatment of disease.

18. Use as claimed in claim 17, in which the disease is selected from the group consisting of Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis and neurodegenerative disease.