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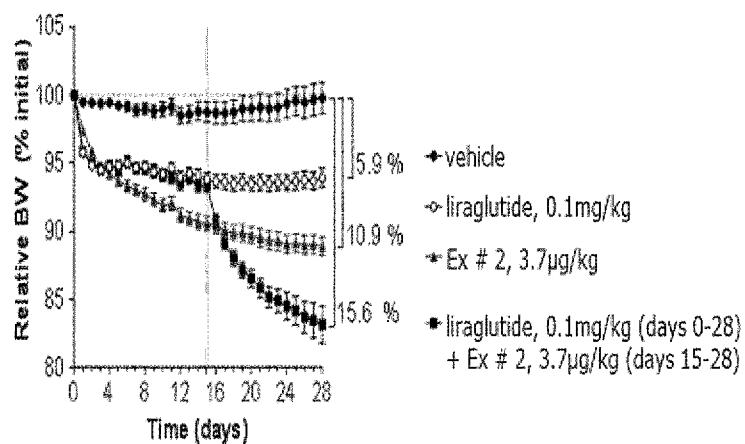
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(54) Title: NOVEL AMYLIN AND CALCITONIN RECEPTOR AGONIST

**Fig. 1**

(57) **Abstract:** The present invention relates to peptides comprising an amino acid sequence SEQ ID NO: 1 (EASELSTAALGRL-SAELH ELATLPRTEGPESP), analogues and derivatives thereof and pharmaceutical compositions comprising such peptides and derivatives. This invention further regards the use of these peptides according to SEQ ID NO : 1, analogues and derivatives thereof as medicaments.

NOVEL AMYLIN AND CALCITONIN RECEPTOR AGONIST**TECHNICAL FIELD**

The present invention relates to peptides comprising an amino acid sequence SEQ ID NO: 1 (EASELSTAALGRLSAELHELATLPRTEGPESP).

5 BACKGROUND

It has been known for a long time that when traditional insulin is used to treat diabetes, it is associated with an increase in body weight. Insulin has to be injected subcutaneously up to several times per day. *Thus, an antidiabetic therapeutic approach should not only lower fasting and postprandial blood glucose levels but optimally also induce weight loss.* Type 2 diabetes is generally treated in the early phases with diet and exercise. As the condition progresses, various oral anti-diabetic agents are added. Novel hormone-based therapies for type 2 diabetes are now emerging resembling an endogenous mode of action, such as glucagon like peptide (GLP)-1 and amylin analogues. These agents do not only improve glucose homeostasis but also very promisingly exert beneficial effects on body weight. In obese individuals, fasting amylin concentrations are elevated in conjunction with hyperinsulinemia and in patients with type 2 diabetes, amylin, like insulin, is relatively deficient depending on the severity of β -cell secretory failure. Amylin receptor agonists are useful in reducing food intake and treating obesity. Human amylin is a 37 amino acid long polypeptide which has physico-chemical properties that make its use as a drug troublesome. In particular, it has a tendency for fibrillogenesis, i.e. the formation of fibrils, *in vitro* and/or *ex vivo* and becomes ineffective due to precipitation. Pramlintide is a drug product marketed by Amylin Pharmaceuticals as Symlin® and a human amylin analogue and receptor agonist used in the treatment of diabetes as an add-on to insulin. Pramlintide is chemically unstable at neutral pH and it is therefore provided in an acidic solution.

The calcitonin receptor is found in many tissues throughout the body and it is believed to be involved in regulation of bone metabolism. Salmon calcitonin is currently sold under the tradename Miacalcic®. The product is used against hypercalcaemia, osteoporosis (including post-menopausal osteoporosis and glucocorticoid-related osteoporosis), osteitis deformans (Pagets disease) and is administered once daily either by injection or nasally. The calcitonin is bound to specific receptors in the membrane of the skeleton, the kidneys and in the central nervous system (CNS). Calcitonin is chemically unstable at neutral pH and it is therefore provided in an acidic solution.

Polypeptides with activity at both the amylin and calcitonin receptor and the amylin receptor may be advantageous; however increased half-life of amylin and calcitonin receptor agonists would highly increase the usability and convenience for the use as a medicament in treating the above mentioned diseases. A further drawback of 5 the currently known pool of calcitonin and amylin peptides is that they are only chemically stable in solution when handled in a narrow acidic pH range, which makes them bothersome to handle under circumstances where a broader range of pH is desired. Thus polypeptides which are amylin and/or calcitonin receptor agonists with more flexible solubility profiles would increase the usability in medicinal products.

10 **SUMMARY**

The invention relates to peptides comprising an amino acid sequence SEQ ID NO: 1 (EASELSTAALGRLSAELHELATLPRTETGPESP), analogues and derivatives thereof and pharmaceutical compositions comprising SEQ ID NO: 1, analogues or derivatives thereof.

15 Further this invention relates to derivatives, pharmaceutical formulations, co-formulations and co-treatments of such mimylin peptides or derivatives in combination with GLP-1 compounds and the use thereof as medicaments in the treatment of diabetes, overweight, obesity or neuropathic pain.

In some embodiments the present invention relates to a mimylin peptide 20 comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises up to 11 amino acid modifications relative to SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises up to 11 amino acid modifications in one or more of the positions 1, 2, 3, 4, 5, 6, 8, 9, 10, 12, 14, 15, 16, 17, 18, 19, 20, 25 21, 23, 24, 25, 27, 28, 30, 31, 32 relative to SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

In some embodiments the present invention relates to a mimylin peptide comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and c-terminal amide group.

30 In some embodiments the present invention relates to a mimylin peptide comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and no disulfide bridge. In some embodiments the present invention relates to a mimylin peptide comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and comprises no cysteins in certain positions, preferably no cysteins in position 2 and/or 8, 35 wherein the amino acid numbering corresponds to SEQ ID NO: 1.

In some embodiments the mimylin peptides of the present invention have less than 60% sequence identity to known amylin and calcitonin receptor agonists. However, the inventors surprisingly found that mimylin peptides are agonists to the amylin and calcitonin receptors and show a favourable solubility profile throughout the complete pH 5 scale, especially at neutral pH and above, i.e. from about pH 6.0 and above, preferably from about pH 7.0 and above. Further the peptides of the present invention are very stable peptides and thus potentially very useful for use in medicaments. Furthermore mimylin has a low Immunogenicity Risk Score (IRS). It was surprisingly found that the mimylin compounds of this invention are able to be combined with GLP-1 compounds in 10 co-formulations wherein both remain stable. It was surprisingly found that the mimylin compounds of this invention are able to be combined with GLP-1 compounds in formulations at pH between about 7.0 and 8.5 wherein both remain stable. It was further surprisingly found that co-administration in DIO rats of a compound according to this 15 invention and liraglutide enhanced the weightloss achieved by the liraglutide treatment alone, surpassing an add-on effect. Further studies are ongoing. It was surprisingly found that compounds of this invention do not affect the PK profile of liraglutide, and liraglutide does surprisingly not affect the PK profile of compounds of this invention when administered as co-formulations to LYD pigs. It was surprisingly found that Ex. compound 20 2 or 46 of this invention do not affect the PK profile of liraglutide and liraglutide does surprisingly not affect the PK profile of Ex. compound 2 or 46 of this invention when administered as co-formulations to LYD pigs.

The invention may also solve further problems that will be apparent from the disclosure of the exemplary embodiments and aspects.

BRIEF DESCRIPTION OF THE DRAWINGS

25 Fig. 1 shows relative body weight (% of initial) in DIO rats during the treatment period with liraglutide (QD) and Compound of Ex. #2. Data are mean \pm SEM, n=10.

DESCRIPTION

The invention relates to mimylin peptides comprising an amino acid sequence which is a mimylin analogue (EASELSTAALGRLSAELHELATLPRTEGPESP) or analogues or 30 derivatives thereof which all show agonist effects on the amylin receptor. Further this invention relates to derivatives, pharmaceutical compositions comprising of such mimylin peptides and the use of such mimylin peptides as medicaments.

In some embodiments the mimylin peptides of the present invention are agonists to the calcitonin receptor. In some embodiments the mimylin peptide of the present

invention agonises the human amylin and human calcitonin receptors and shows solubility throughout the complete pH scale, preferably neutral pH and above.

In some embodiments a mimylin peptide according to the present invention comprises up to 11 amino acid modifications relative to SEQ ID NO: 1. In some 5 embodiments a mimylin peptide according to the present invention comprises up to 11 amino acid modifications relative to SEQ ID NO: 1, wherein in one or more of the positions 1, 2, 3, 4, 5, 6, 8, 9, 10, 12, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 30, 31, 32, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

In some embodiments the present invention relates to a mimylin peptide 10 comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and a c-terminal amide group.

In some embodiments the present invention relates to a mimylin peptide comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and no disulfide bridge. In some embodiments the present invention relates to a mimylin peptide 15 comprising a sequence having at least 66% sequence identity to SEQ ID NO: 1 and comprises no cysteins, preferably in position 2 and/or 8, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of 20 about 50pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 20pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 19pM or less. In some embodiments a mimylin peptide 25 according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 18pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 17pM or less. In some embodiments a mimylin peptide 30 according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 16pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 15pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 14pM or less. In some embodiments a mimylin peptide 35 according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as

disclosed in Assay IIb) of about 13pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 12pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin 5 receptor functional assay (tested as disclosed in Assay IIb) of about 11pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 10pM or less. In some embodiments a mimylin peptide according to the present invention has an EC₅₀ in a human amylin receptor functional assay (tested as disclosed in Assay IIb) of about 5pM or less. 10

In some embodiments a mimylin peptide according to the present invention is a peptide comprising SEQ ID NO: 1A;

X(-1)-X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-X32-X33-X34 (SEQ ID NO: 1A),

15 wherein X represents amino acids and wherein

X(-1) is E or no amino acid,

X1 is selected from the group consisting of E or A or no amino acid,

X2 is selected from the group consisting of L, A or P,

X3 is selected from the group consisting of S or P

20 X4 is selected from the group consisting of E, P, K, Q or G

X5 is selected from the group consisting of L, V, or I,

X6 is S, T or H,

X7 is T,

X8 is selected from the group consisting of L or A,

25 X9 is selected from the group consisting of A, V, I, S or T,

X10 is selected from the group consisting of L, A, I, H or V,

X11 is G,

X12 is selected from the group consisting of R, H or K,

X13 is L,

30 X14 is selected from the group consisting of S, T or E,

X15 is selected from the group consisting of A, Q, E, e or T,

X16 is selected from the group consisting of R, E, K or Q,

X17 is selected from the group consisting of L or I,

X18 is selected from the group consisting of H or A,

35 X19 is selected from the group consisting of E, R or K,

X20 is selected from the group consisting of L, I or V,

X21 is selected from the group consisting of A, Q, S, E or T,
X22 is T,
X23 is selected from the group consisting of T, Y or L,
X24 is P,

5 X25 is selected from the group consisting of R, P, H or K,
X26 is T,
X27 is selected from the group consisting of E, Q, G or K,
X28 is selected from the group consisting of T or P,
X29 is G,

10 X30 is selected from the group consisting of P, S or T,
X31 is selected from the group consisting of E, Q, G, A, P or K,
X32 is selected from the group consisting of T, S, H, P or A and
X33 is P, Y, H, F, L, S, G or A and
X34 is G or no amino acid

15 In some embodiments a mimylin peptide according to the present invention is a peptide comprising SEQ ID NO: 1B;
X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-X32-X33-X34-X35-X36 (SEQ ID NO: 1B)
wherein X represents amino acids and wherein

20 X1 is selected from the group consisting of E or A or no amino acid,
X2 is selected from the group consisting of L, A or P,
X3 is selected from the group consisting of S or P
X4 is selected from the group consisting of E, P, K, Q or G
X5 is selected from the group consisting of L, V, or I,

25 X6 is S, T or H,
X7 is T,
X8 is selected from the group consisting of L or A,
X9 is selected from the group consisting of A, V, I, S or T,
X10 is selected from the group consisting of L, A, I, H or V,

30 X11 is G,
X12 is selected from the group consisting of R, H or K,
X13 is L,
X14 is selected from the group consisting of S, T or E,
X15 is selected from the group consisting of A, Q, E, e or T,

35 X16 is selected from the group consisting of R, E, K or Q,
X17 is selected from the group consisting of L or I,

X18 is selected from the group consisting of H or A,
X19 is selected from the group consisting of E, R or K,
X20 is selected from the group consisting of L, I or V,
X21 is selected from the group consisting of A, Q, S, E or T,
5 X22 is T,
X23 is selected from the group consisting of T, Y or L,
X24 is P,
X25 is selected from the group consisting of R, P, H or K,
X26 is T,
10 X27 is selected from the group consisting of E, Q, G or K,
X28 is selected from the group consisting of T or P,
X29 is G,
X30 is selected from the group consisting of P, S or T,
X31 is selected from the group consisting of E, Q, G, A, P or K,
15 X32 is selected from the group consisting of T, S, H, P or A,
X33 is P, Y, H, F, L, S, G or A
X34 is G or no amino acid
X35 is T or no amino acid and
X36 is Y or no amino acid.

20 In some embodiments a mimylin peptide according to the present invention is a peptide comprising SEQ ID NO: 1C;
X1-X2-X3-X4-X5-X6-T-X8-X9-X10-G-X12-L-X14-X15-X16-X17-X18-X19-X20-X21-T-X23-
P-X25-T-X27-X28-G-X30-X31-X32-X33 (SEQ ID NO: 1C),
wherein X represents amino acids and wherein

25 X1 is selected from the group consisting of E or A or no amino acid,
X2 is selected from the group consisting of L, A or P,
X3 is selected from the group consisting of S or P
X4 is selected from the group consisting of E, P, K, Q or G
X5 is selected from the group consisting of L, V, or I,
30 X6 is S, T or H,
X8 is selected from the group consisting of L or A,
X9 is selected from the group consisting of A, V, I, S or T,
X10 is selected from the group consisting of L, A, I, H or V,
X12 is selected from the group consisting of R, H or K,
35 X14 is selected from the group consisting of S, T or E,
X15 is selected from the group consisting of A, Q, E, e or T,

X16 is selected from the group consisting of R, E, K or Q,
X17 is selected from the group consisting of L or I,
X18 is selected from the group consisting of H or A,
X19 is selected from the group consisting of E, R or K,
5 X20 is selected from the group consisting of L, I or V,
X21 is selected from the group consisting of A, Q, S, E or T,
X23 is selected from the group consisting of T, Y or L,
X25 is selected from the group consisting of R, P, H or K,
X27 is selected from the group consisting of E, Q, G or K,
10 X28 is selected from the group consisting of T or P,
X30 is selected from the group consisting of P, S or T,
X31 is selected from the group consisting of E, Q, G, A, P or K,
X32 is selected from the group consisting of T, S, H, P or A and
X33 is P, Y, H, F, L, S, G or A.

15 In some embodiments a mimylin peptide according to this invention can be a peptide SEQ ID NO: 1A, 1B or 1C, wherein an additional amino acid is added to the N-terminal. In some embodiments a mimylin peptide according to this invention can be a peptide SEQ ID NO: 1A, 1B or 1C, wherein an additional amino acid is added to the N-terminal, wherein said additional amino acid is E.

20 In some embodiments a mimylin peptide according to this invention can be described according to any one of the SEQ ID NO: 1A, 1B or 1C, wherein said mimylin peptide is derivatised with a side chain in the alpha amino group of the N-terminal amino acid, wherein said side chain comprises a protracting moiety as defined in the present invention and optionally comprises a linker.

25 For some embodiments, the mimylin peptide has a substituent on one amino acid residue, which amino acid residue is either the amino acid residue in the N-terminal residue or the amino acid residue is a Lysine, wherein said lysine can be at any of the positions 1-33 according to the numbering of SEQ ID NO: 1.

For some embodiments, the mimylin peptide has a substituent on the N-terminal 30 amino acid residue bound via the α (alpha)-amino group of the N-terminal amino acid residue.

For some embodiments, the N-terminal amino acid residue is Lysine and the mimylin peptide has a substituent on the N-terminal amino acid residue bound via the ϵ (epsilon)-amino group of the lysine amino residue.

For some embodiments, the mimylin peptide is extended by addition of a Lysine residue at the N-terminal and the mimylin peptide has a substituent on the N-terminal amino acid residue bound via the ϵ -amino group of the lysine amino residue.

For some embodiments, the mimylin peptide is extended by addition of a 5 Glutamic acid residue at the N-terminal and the mimylin peptide has a substituent on the N-terminal amino acid residue bound via the α -amino group of the lysine amino residue.

For some embodiments, the mimylin peptide is extended by addition of an amino acid residue at the N-terminal and the mimylin peptide has a substituent on the N-terminal amino acid residue bound via the α -amino group of the N-terminal amino acid residue.

10 In some embodiments an amylin derivative is produced by derivatising a mimylin peptide with a side chain attached in the N-terminal of said mimylin peptide. In some embodiments an amylin derivative is produced by derivatising a mimylin peptide with a side chain attached at a K (Lys) within the sequence of said mimylin peptide. In some embodiments such attachment at a K (Lys) can be in position 4, 12, 16, 23, 18, 27 or 34.

15 In some embodiments SEQ ID NO: 1A, 1B or 1C are analogues of SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 11 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 11, 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1, preferably 1, 2 or 3, more preferably 4, 3 or 5 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 5 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 4 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 3 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is up to 2 amino acids different from SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is 1 amino acid different from SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 22 amino acids identical with SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a

5 sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 23 amino acids identical with SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 24 amino acids identical with SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 25 amino acids identical with SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 26 amino acids identical with SEQ ID NO: 1.

15 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 27 amino acids identical with SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 28 amino acids identical with SEQ ID NO: 1.

20 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 29 amino acids identical with SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 30 amino acids identical with SEQ ID NO: 1. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 31 amino acids identical with SEQ ID NO: 1.

25 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 32 amino acids identical with SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein the sequence is at least 32

30 amino acids identical with SEQ ID NO: 1.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C and a c-terminal amide group. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is E. In some 35 embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is E and the mimylin peptide is

derivatised with a side chain attached to the mimylin peptide at the N-terminal. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is E and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal, wherein
5 said side chain comprises a protracting moiety and a linker. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is E and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal, wherein said side chain comprises a protracting moiety and no linker.

10 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is A and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal. In some
15 embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is A and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal, wherein said side chain comprises a protracting moiety and a linker.

20 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is any amino acid except E. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is any amino acid except E and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal. In some embodiments a mimylin
25 peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X1 is any amino acid except E and the mimylin peptide is derivatised with a side chain attached to the mimylin peptide at the N-terminal, wherein said side chain comprises a protracting moiety and a linker. In particular embodiments, the side chain and/or the protracting moiety are lipophilic, and/or negatively charged at
30 physiological pH (pH about 7.4).

25 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X2 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X2 is A. In some embodiments a mimylin
30 peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X2 is P.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X3 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X3 is P.

5 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X4 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X4 is A.

10 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X5 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X5 is I. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X5 is V.

15 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X7 is T.

20 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X8 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X8 is A.

25 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is V. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is I. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is T.

30 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X9 is L.

35 In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X10 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X10 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to

SEQ ID NO: 1A, 1B or 1C, wherein X10 is V. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X10 is I.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X12 is R. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X12 is H. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X12 is K.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X15 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X15 is Q. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X15 is E. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X15 is e, wherein e is the d-isoform of Glutamic acid. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X15 is T.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X19 is E. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X19 is R. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X19 is K.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X20 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X20 is I. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X20 is V.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X21 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X21 is Q. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to

SEQ ID NO: 1A, 1B or 1C, wherein X21 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X21 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein 5 X21 is E. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X21 is T.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X23 is Y. In some 10 embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X23 is L.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X27 is E. In some 15 embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X27 is Q. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X27 is G. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X27 is K.

In some embodiments a mimylin peptide according to the present invention 20 comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X30 is P. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X20 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X30 is T.

In some embodiments a mimylin peptide according to the present invention 25 comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X31 is E. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X31 is Q. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to 30 SEQ ID NO: 1A, 1B or 1C, wherein X31 is G. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X31 is A. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X31 is P. In some embodiments a mimylin peptide according to the present invention 35 comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X31 is K.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X32 is T. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X32 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X32 is H. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X32 is P. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X32 is A.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is Y. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X16 is H. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is F. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X16 is L. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is S. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is G. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X33 is A.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A or 1B, wherein X34 is R. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A or 1B, wherein X34 is deleted.

In some embodiments the mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein one or all of X5, X10, X13, X17, X20 and X23 are L. In some embodiments the mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein at least four of X5, X10, X13, X17, X20 and X23 are L. In some embodiments the mimylin peptide according to the present invention comprises a sequence according

to SEQ ID NO: 1A, 1B or 1C, wherein at least three of X5, X10, X13, X17, X20 and X23 are L.

In some embodiments the mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein X12 and/or X25 is

5 R. In some embodiments the mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, wherein one or all of X5, X10, X13, X17, X20 and X23 are L and wherein X12 and/or X25 is R.

In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, which does not comprise

10 any N. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, which does not comprise any Q. In some embodiments a mimylin peptide according to the present invention comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, which does not comprise any C. In some embodiments a mimylin peptide according to the present invention 15 comprises a sequence according to SEQ ID NO: 1A, 1B or 1C, which does not comprise any disulfide bridges.

In some embodiments a mimylin derivative according to this invention is represented by the compounds listed in Table 1. The compound names as used herein are listed in Table

1 indicating the modifications relative to SEQ ID NO: 1 (also designated mimylin herein) 20 and the side chain as well as the site of attachment of the side chain to the mimylin peptide. Table 1 discloses the compound number (EX. #) and the compound name. Table 2 indicates the modifications relative to mimylin in the mimylin peptides, i.e. the mimylin peptides, which are derivatised with a side chain to the mimylin derivatives listed in Table 1. Ex. #1 in Table 1 is SEQ ID NO: 1 and is not derivatised as also indicated by the 25 name.

Table 1- mimylin derivatives (Example compounds)

Ex. #	Compound name
1	mimylin
2	[N-terminal(C18 diacid)]mimylin
3	[N-terminal(C16 diacid)]mimylin
4	[N-terminal(C14 diacid)]mimylin
5	[N-terminal(C14 diacid-2xGlu-4xOEG)]mimylin
6	[N-terminal(C12 diacid)]mimylin
7	[N-terminal(C16)]mimylin
8	[N-terminal(C18 diacid), 5I]mimylin
9	[N-terminal(C18 diacid), 9V]mimylin
10	[N-terminal(C18 diacid), 9I]mimylin
11	[N-terminal(C18 diacid), 17I]mimylin

Ex. #	Compound name
12	[N-terminal(C18 diacid), 20I]mimylin
13	[N-terminal(C18 diacid), 18A]mimylin
14	[N-terminal(C18 diacid), 9L]mimylin
15	[N-terminal(C18 diacid), 8L]mimylin
16	[N-terminal(C18 diacid), 6H]mimylin
17	[N-terminal(C18 diacid), 5H]mimylin
18	[N-terminal(C18 diacid), 32H]mimylin
19	[N-terminal(C14 diacid-gGlu), des1]mimylin
20	[N-terminal(C18 diacid), 23Y]mimylin
21	[N-terminal(C18 diacid), 30S, 31G]mimylin
22	[N-terminal(C20 diacid), 30S, 31G]mimylin
23	[N-terminal(C18 diacid-gGlu), des1, 30S]mimylin
24	[N-terminal(C18 diacid), 5V, 9V]mimylin
25	[N-terminal(C18 diacid), 5I, 9I]mimylin
26	[N-terminal(C18 diacid), 9V, 10I]mimylin
27	[N-terminal(C18 diacid), 9L, 10A]mimylin
28	[N-terminal(C18 diacid), 2P, 9V]mimylin
29	[N-terminal(C18 diacid), 3P, 9V]mimylin
30	[N-terminal(C18 diacid), 4P, 9V]mimylin
31	[N-terminal(C18 diacid), 9V, 25P]mimylin
32	[N-terminal(C18 diacid), 9V, 28P]mimylin
33	[N-terminal(C18 diacid), 9V, 18A]mimylin
34	[N-terminal(C20 diacid-gGlu), 23Y, 30S, 31G]mimylin
35	[N-terminal(C18 diacid-gGlu), des1, 30S, 31P]mimylin
36	[N-terminal(C18 diacid), 5V, 9V, 20V]mimylin
37	[N-terminal(C18 diacid), 5I, 9I, 10I]mimylin
38	[N-terminal(C18 diacid), 3P, 4P, 9V]mimylin
39	[N-terminal(C18 diacid), 9V, 12K, 25K]mimylin
40	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G]mimylin
41	[N-terminal(C20 diacid-gGlu-OEG), des1, 30S, 31G]mimylin
42	[N-terminal(C20 diacid-gGlu-2xOEG), des1, 30S, 31G]mimylin
43	[N-terminal(C20 diacid-gGlu-3xOEG), des1, 30S, 31G]mimylin
44	[N-terminal(C20 diacid-gGlu-4xOEG), des1, 30S, 31G]mimylin
45	[N-terminal(C20 diacid-gGlu-5xOEG), des1, 30S, 31G]mimylin
46	[N-terminal(C18 diacid-gGlu), des1, 30S, 31G]mimylin
47	[N-terminal(C16 diacid-gGlu), des1, 30S, 31G]mimylin
48	[N-terminal(C18 diacid), des1, 30S, 31G]mimylin
49	[N-terminal(C16 diacid), des1, 30S, 31G]mimylin
50	[N-terminal(C14 diacid-gGlu), des1, 30S, 31G]mimylin
51	[N-terminal(C14 diacid), des1, 30S, 31G]mimylin
52	[des1, 4K(C20 diacid-gGlu), 30S, 31G]mimylin
53	[des1, 16K(C20 diacid-gGlu), 30S, 31G]mimylin
54	[des1, 19K(C20 diacid-gGlu), 30S, 31G]mimylin
55	[des1, 27K(C20 diacid-gGlu), 30S, 31G]mimylin

Ex. #	Compound name
56	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G]mimylin
57	[N-terminal(C20 diacid-gGlu), 1A, 23Y, 30S, 31G]mimylin
58	[N-terminal(C18 diacid-gGlu), des1, 23Y, 30S, 31G]mimylin
59	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33Y]mimylin
60	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33H]mimylin
61	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33F]mimylin
62	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33L]mimylin
63	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33S]mimylin
64	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33G]mimylin
65	[N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33A]mimylin
66	[N-terminal(C20 diacid-gGlu), des1, 15E, 30S, 31G]mimylin
67	[N-terminal(C20 diacid-gGlu), des1, 15e, 30S, 31G]mimylin
68	[N-terminal(acetyl), des1, 4K(C20 diacid-gGlu), 30S, 31G]mimylin
69	[N-terminal(acetyl), des1, 16K(C20 diacid-gGlu), 30S, 31G]mimylin
70	[N-terminal(acetyl), des1, 19K(C20 diacid-gGlu), 30S, 31G]mimylin
71	[N-terminal(acetyl), des1, 27K(C20 diacid-gGlu), 30S, 31G]mimylin
72	[N-terminal(C20 diacid-gGlu), des1, 12H, 30S, 31G]mimylin
73	[N-terminal(C20 diacid-gGlu), des1, 25H, 30S, 31G]mimylin
74	[N-terminal(C20 diacid-gGlu), des1, 30T, 31G, 32T]mimylin
75	[N-terminal(C18 diacid-gGlu), des1, 30S, 31G, 32P]mimylin
76	[N-terminal(C18 diacid-gGlu), des1, 9V, 30S, 31G]mimylin
77	[N-terminal(C18 diacid), 5I, 9I, 10I, 20I]mimylin
78	[N-terminal(C18 diacid-gGlu), des1, 4Q, 30S, 31G]mimylin
79	[N-terminal(C20 diacid-gGlu), des1, 4G, 23Y, 30S, 31G]mimylin
80	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 33Y]mimylin
81	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 32A]mimylin
82	[N-terminal(C20 diacid-gGlu), des1, 21S, 23Y, 30S, 31G]mimylin
83	[N-terminal(C20 diacid-gGlu), -1E, 1A, 23Y, 30S, 31G]mimylin
84	[N-terminal(C20 diacid-gGlu), des1, 12H, 25H, 30S, 31G]mimylin
85	[N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30S, 31G]mimylin
86	[N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 30S, 31G]mimylin
87	[N-terminal(C18 diacid-gGlu), des1, 4Q, 16Q, 30S, 31G]mimylin
88	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 33Y, C-terminal(-)]mimylin
89	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 34G, C-terminal(-)]mimylin
90	[N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 34K, C-terminal(-)]mimylin
91	[N-terminal(C20 diacid-gGlu), des1, 9S, 23Y, 30S, 31G, 33Y]mimylin
92	[N-terminal(C20 diacid-gGlu), des1, 9T, 21S, 23Y, 30S, 31G]mimylin
93	[N-terminal(C20 diacid-gGlu), des1, 12H, 25H, 30T, 31G, 32T]mimylin
94	[N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30S, 31G, 32T]mimylin
95	[N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30T, 31G, 32T]mimylin
96	[N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 10V, 30S, 31G]mimylin
97	[N-terminal(C20 diacid-gGlu), des1, 21S, 23Y, 30S, 31G, 33Y]mimylin
98	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 23Y, 30S, 31G, 32T]mimylin
99	[N-terminal(C20 diacid-gGlu), des1, 9T, 21S, 23Y, 30S, 31G, 33Y]mimylin

Ex. #	Compound name
100	[N-terminal(C20 diacid-gGlu), des1, 9S, 21S, 23Y, 30S, 31G, 33Y]mimylin
101	[N-terminal(C20 diacid-gGlu), des1, 12K, 23Y, 25K, 30S, 31G, 33Y]mimylin
102	[N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 10V, 20V, 30S, 31G]mimylin
103	[N-terminal(C20 diacid-gGlu), 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
104	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 23Y, 30S, 31G, 32T, 33Y]mimylin
105	[N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 14T, 21E, 30T, 31G, 32T]mimylin
106	[N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 14E, 21T, 30T, 31G, 32T]mimylin
107	[des1, 4G, 15Q, 21Q, 23Y, 30S, 31K(C20 diacid-gGlu), 32T, 33Y]mimylin
108	[N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin
109	[N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin
110	[N-terminal(C18 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
111	[N-terminal(C20 diacid), des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
112	[N-terminal(C20 diacid-gGlu), des1, 4G, 15T, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin
113	[N-terminal(C20 diacid-gGlu), des1, 4G, 15E, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
114	[N-terminal(C20 diacid-gGlu), des1, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
115	[N-terminal(C20 diacid-gGlu), 4Q, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y]mimylin
116	[N-terminal(C20 diacid-gGlu), des1, 4Q, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin
117	[N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 25H, 30S, 31G, 32T, 33Y]mimylin
118	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
119	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin
120	[N-terminal(C20 diacid-gGlu-2xOEG), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
121	[N-terminal(C18 diacid-gGlu-2xOEG), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
122	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31A, 32T, 33Y]mimylin
123	[N-terminal(C20 diacid-gGlu), des1, 2L, 4G, 9V, 21S, 23Y, 30S, 31G, 32T, 33Y]mimylin
124	[N-terminal(C20 diacid-gGlu), des1, 4G, 9T, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin
125	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 25P, 30S, 31Q, 32T, 33Y]mimylin
126	[N-terminal(C20 diacid-gGlu), des1, 4G, 8L, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin
127	[N-terminal(C20 diacid-gGlu), des1, 2L, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin
128	[N-terminal(C20 diacid-gGlu), des1, 4G, 9T, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin
129	[N-terminal(C20 diacid-gGlu), 2L, 4G, 8L, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G,

Ex. #	Compound name
	32T, 33Y]mimylin
130	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23aQ, 23bT, 23cY, 30S, 31Q, 32T, 33Y]mimylin
131	[N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 12K, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin
132	[N-terminal(C20 diacid-gGlu), des1, 4Q, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin
133	[N-terminal(C20 diacid-gGlu), des1, 2L, 4Q, 8L, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin
134	[N-terminal(C18 diacid),C-terminal(-)]mimylin
135	[C-terminal(-)]mimylin

In some embodiments a mimylin peptide according to this invention is represented by the compounds listed in Table 2, wherein Table 2 indicates the amino acid modifications relative to SEQ ID NO: 1, also designated mimylin. Table 2 indicates the modifications relative to mimylin in the mimylin peptides, i.e. the mimylin peptides, which are derivatised with a side chain to form the mimylin derivatives listed in Table 1. Table 2 represents the mimylin analogues which have been derivatised, resulting in the corresponding mimylin derivative represented in Table 1. Thus the compound in EX. #8 in Table 1 or 3, respectively is a derivative of a mimylin analogue which has been modified with the amino acids as indicated in Table 2 or 4 as Ex. #8bb

10 **Table 2- mimylin peptides (backbones)**

Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)	Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)
1bb	N/A	68bb	des1, 4K, 30S, 31G
2bb	N/A	69bb	des1, 16K, 30S, 31G
3bb	N/A	70bb	des1, 19K, 30S, 31G
4bb	N/A	71bb	des1, 27K, 30S, 31G
5bb	N/A	72bb	des1, 12H, 30S, 31G
6bb	N/A	73bb	des1, 25H, 30S, 31G
7bb	N/A	74bb	des1, 30T, 31G, 32T
8bb	5I	75bb	des1, 30S, 31G, 32P
9bb	9V	76bb	des1, 9V, 30S, 31G
10bb	9I	77bb	5I, 9I, 10I, 20I
11bb	17I	78bb	des1, 4Q, 30S, 31G
12bb	20I	79bb	des1, 4G, 23Y, 30S, 31G
13bb	18A	80bb	des1, 23Y, 30S, 31G, 33Y
14bb	9L	81bb	des1, 23Y, 30S, 31G, 32A

Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)	Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)
15bb	8L	82bb	des1, 21S, 23Y, 30S, 31G
16bb	6H	83bb	-1E, 1A, 23Y, 30S, 31G
17bb	5H	84bb	des1, 12H, 25H, 30S, 31G
18bb	32H	85bb	des1, 6T, 9V, 30S, 31G
19bb	des1	86bb	des1, 5V, 9V, 30S, 31G
20bb	23Y	87bb	des1, 4Q, 16Q, 30S, 31G
21bb	30S, 31G	88bb	des1, 23Y, 30S, 31G, 33Y
22bb	30S, 31G	89bb	des1, 23Y, 30S, 31G, 34G
23bb	des1, 30S	90bb	des1, 23Y, 30S, 31G, 34K
24bb	5V, 9V	91bb	des1, 9S, 23Y, 30S, 31G, 33Y
25bb	5I, 9I	92bb	des1, 9T, 21S, 23Y, 30S, 31G
26bb	9V, 10I	93bb	des1, 12H, 25H, 30T, 31G, 32T
27bb	9L, 10A	94bb	des1, 6T, 9V, 30S, 31G, 32T
28bb	2P, 9V	95bb	des1, 6T, 9V, 30T, 31G, 32T
29bb	3P, 9V	96bb	des1, 5V, 9V, 10V, 30S, 31G
30bb	4P, 9V	97bb	des1, 21S, 23Y, 30S, 31G, 33Y
31bb	9V, 25P	98bb	des1, 4G, 9V, 23Y, 30S, 31G, 32T
32bb	9V, 28P	99bb	des1, 9T, 21S, 23Y, 30S, 31G, 33Y
33bb	9V, 18A	100bb	des1, 9S, 21S, 23Y, 30S, 31G, 33Y
34bb	23Y, 30S, 31G	101bb	des1, 12K, 23Y, 25K, 30S, 31G, 33Y
35bb	des1, 30S, 31P	102bb	des1, 5V, 9V, 10V, 20V, 30S, 31G
36bb	5V, 9V, 20V	103bb	4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
37bb	5I, 9I, 10I	104bb	des1, 4G, 9V, 23Y, 30S, 31G, 32T, 33Y
38bb	3P, 4P, 9V	104bb	des1, 4G, 9V, 23Y, 30S, 31G, 32T, 33Y
39bb	9V, 12K, 25K	105bb	des1, 6T, 9V, 14T, 21E, 30T, 31G, 32T
40bb	des1, 30S, 31G	106bb	des1, 6T, 9V, 14E, 21T, 30T, 31G, 32T
41bb	des1, 30S, 31G	107bb	des1, 4G, 15Q, 21Q, 23Y, 30S, 31K, 32T, 33Y
42bb	des1, 30S, 31G	108bb	des1, 4G, 15Q, 21E, 23Y, 30S, 31G, 32T, 33Y

Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)	Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)
43bb	des1, 30S, 31G	109bb	des1, 4G, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y
44bb	des1, 30S, 31G	110bb	des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
45bb	des1, 30S, 31G	111bb	des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
46bb	des1, 30S, 31G	112bb	des1, 4G, 15T, 21E, 23Y, 30S, 31G, 32T, 33Y
47bb	des1, 30S, 31G	113bb	des1, 4G, 15E, 21Q, 23Y, 30S, 31G, 32T, 33Y
48bb	des1, 30S, 31G	114bb	des1, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
49bb	des1, 30S, 31G	115bb	4Q, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y
50bb	des1, 30S, 31G	116bb	des1, 4Q, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y
51bb	des1, 30S, 31G	117bb	des1, 4G, 15Q, 21Q, 23Y, 25H, 30S, 31G, 32T, 33Y
52bb	des1, 4K, 30S, 31G	118bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
53bb	des1, 16K, 30S, 31G	119bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y
54bb	des1, 19K, 30S, 31G	120bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
55bb	des1, 27K, 30S, 31G	121bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
56bb	des1, 23Y, 30S, 31G	122bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31A, 32T, 33Y
57bb	1A, 23Y, 30S, 31G	123bb	des1, 2L, 4G, 9V, 21S, 23Y, 30S, 31G, 32T, 33Y
58bb	des1, 23Y, 30S, 31G	124bb	des1, 4G, 9T, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y
59bb	des1, 30S, 31G, 33Y	125bb	des1, 4G, 9V, 15Q, 21Q, 23Y, 25P, 30S, 31Q, 32T, 33Y
60bb	des1, 30S, 31G, 33H	126bb	des1, 4G, 8L, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y
61bb	des1, 30S, 31G, 33F	127bb	des1, 2L, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y
62bb	des1, 30S, 31G, 33L	128bb	des1, 4G, 9T, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y

Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)	Ex. #	Amino acid modifications relative to mimylin (SEQ ID NO: 1)
63bb	des1, 30S, 31G, 33S	129bb	2L, 4G, 8L, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y
64bb	des1, 30S, 31G, 33G	130bb	des1, 4G, 9V, 15Q, 21Q, 23aQ, 23bT, 23cY, 30S, 31Q, 32T, 33Y
65bb	des1, 30S, 31G, 33A	131bb	des1, 4G, 9V, 12K, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y
66bb	des1, 15E, 30S, 31G	132bb	des1, 4Q, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y
67bb	des1, 15e, 30S, 31G	133bb	des1, 2L, 4Q, 8L, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y

In some embodiments a mimylin derivative comprising a mimylin peptide with up to 11 amino acid modifications relative to SEQ ID NO: 1 (mimylin) according to this invention is represented by the compounds listed in Table 3. Table 2 and 4 respectively, represent 5 the mimylin analogues which have been derivatised, resulting in the corresponding mimylin derivative represented in Table 1 or 3 respectively. Thus the compound in EX. #8 in Table 1 or 3, respectively is a derivative of a mimylin analogue which has been modified with the amino acids as indicated in Table 2 or 4 as Ex. #8bb.

Table 3- mimylin derivatives (mimylin compounds) comprising mimylin backbones with up to 11 amino acid modifications relative to SEQ ID NO: 1

Ex. #	1	19	37	55	73	91	109
2	20	38	56	74	92	110	
3	21	39	57	75	93	111	
4	22	40	58	76	94	112	
5	23	41	59	77	95	113	
6	24	42	60	78	96	114	
7	25	43	61	79	97	115	
8	26	44	62	80	98	116	
9	27	45	63	81	99	117	
10	28	46	64	82	100	118	
11	29	47	65	83	101	119	
12	30	48	66	84	102	120	
13	31	49	67	85	103	121	
14	32	50	68	86	104	122	
15	33	51	69	87	105	123	

Ex. #						
16	34	52	70	88	106	124
17	35	53	71	89	107	-
18	36	54	72	90	108	-

In some embodiments a mimylin peptide with up to 11 amino acid modifications relative to SEQ ID NO: 1 (mimylin) according to this invention is represented by the compounds listed in Table 4. Thus the compound in Ex. #8 in Table 1 or 3, respectively is a derivative of a mimylin analogue which has been modified with the amino acids as 5 indicated in Table 2 or 4 as Ex. #8bb.

Table 4- mimylin peptides (backbones (bb)) with up to 11 amino acid modifications relative to SEQ ID NO: 1

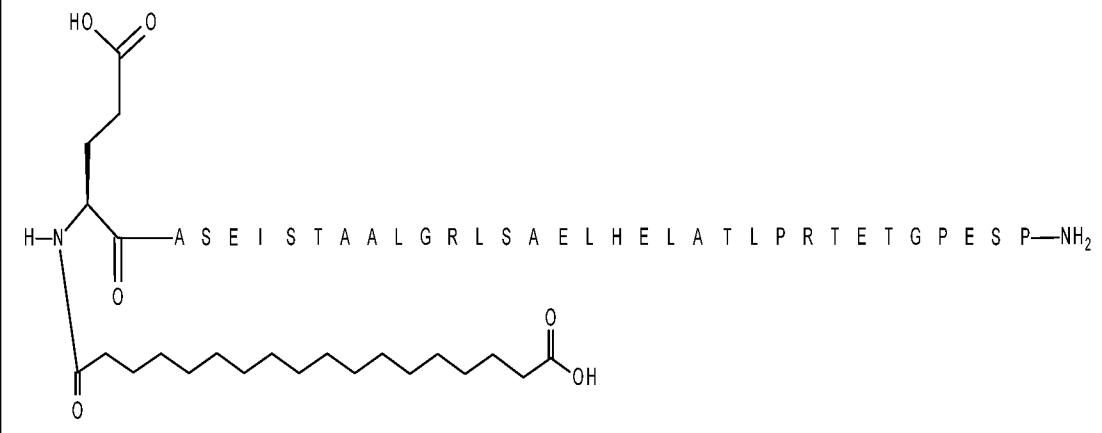
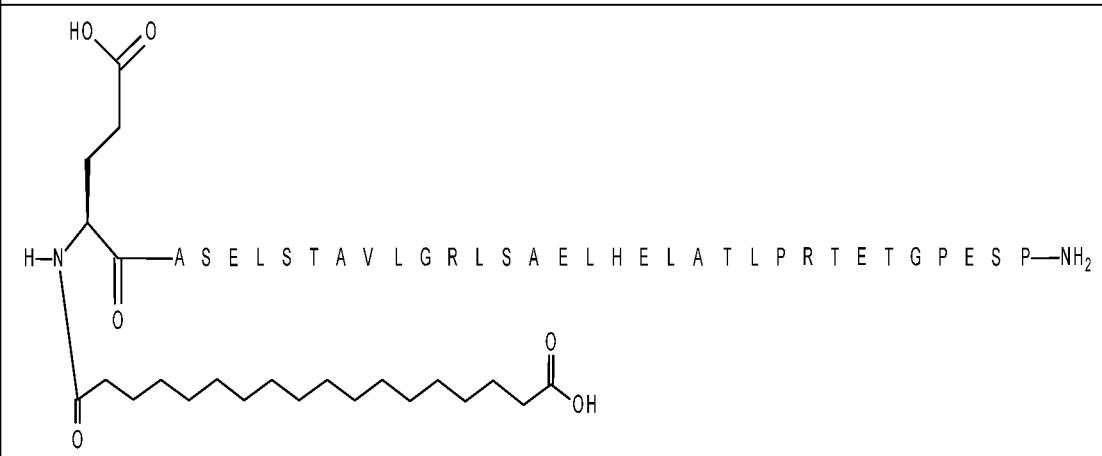
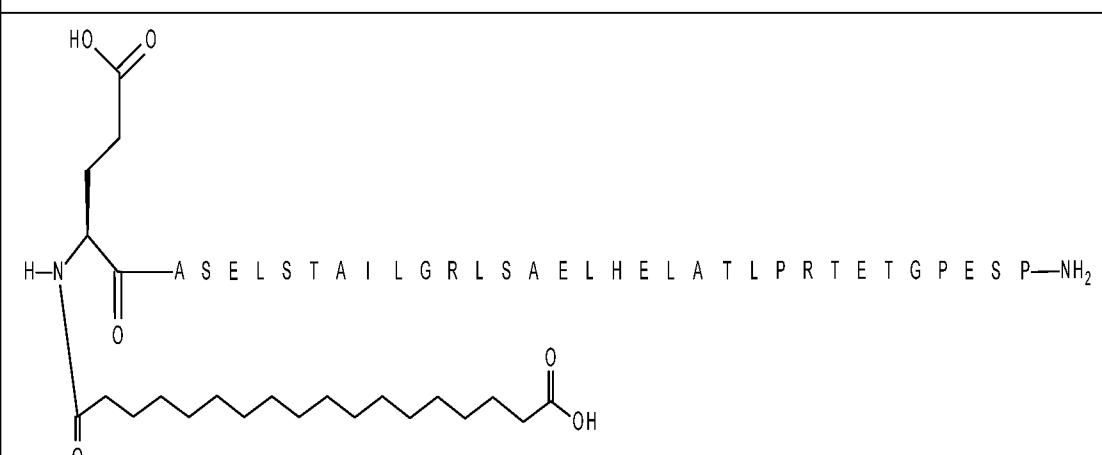
Ex. #							
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3bb	20bb	37bb	54bb	71bb	88bb	105bb	122bb
4bb	21bb	38bb	55bb	72bb	89bb	106bb	123bb
5bb	22bb	39bb	56bb	73bb	90bb	107bb	124bb
6bb	23bb	40bb	57bb	74bb	91bb	108bb	125bb
7bb	24bb	41bb	58bb	75bb	92bb	109bb	126bb
8bb	25bb	42bb	59bb	76bb	93bb	110bb	127bb
9bb	26bb	43bb	60bb	77bb	94bb	111bb	-
10bb	27bb	44bb	61bb	78bb	95bb	112bb	-
11bb	28bb	45bb	62bb	79bb	96bb	113bb	-
12bb	29bb	46bb	63bb	80bb	97bb	114bb	-
13bb	30bb	47bb	64bb	81bb	98bb	115bb	-
14bb	31bb	48bb	65bb	82bb	99bb	116bb	-
15bb	32bb	49bb	66bb	83bb	100bb	117bb	-
16bb	33bb	50bb	67bb	84bb	101bb	118bb	-
17bb	34bb	51bb	68bb	85bb	102bb	119bb	-

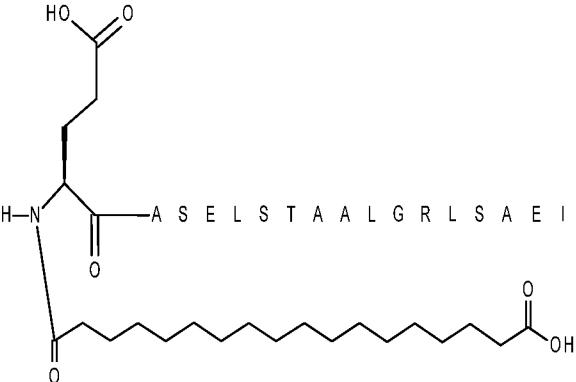
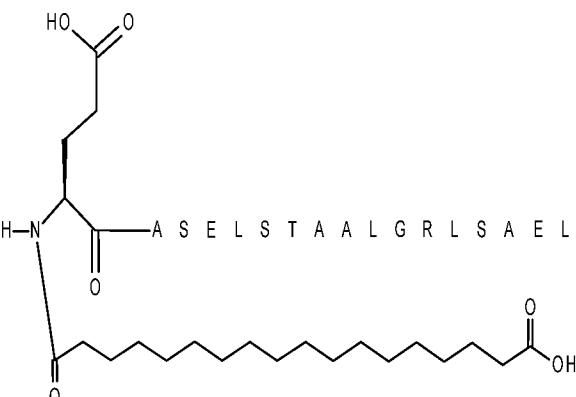
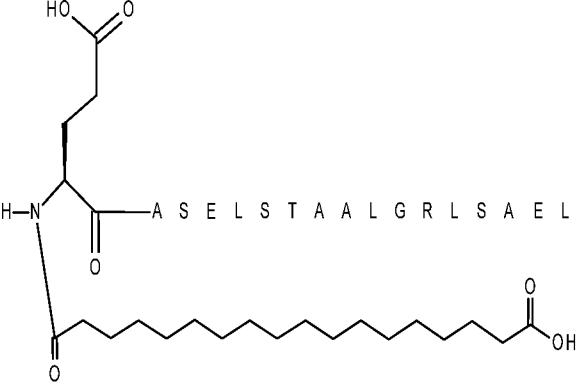
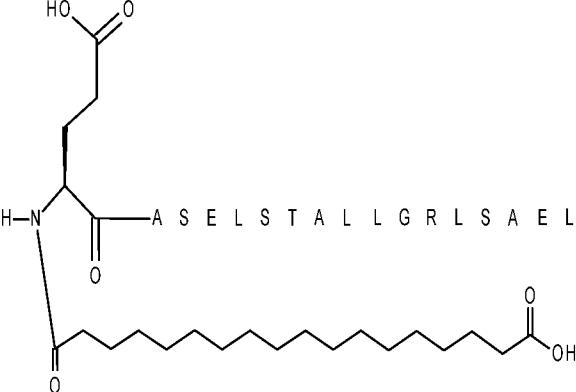
10 I one embodiment the mimylin derivatives of this invention can be presented by their structure formula as presented in Table 5.

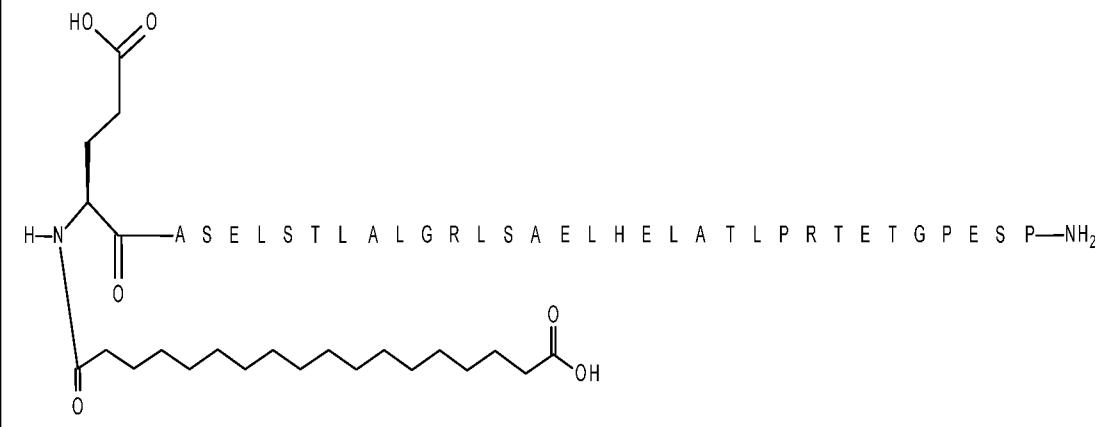
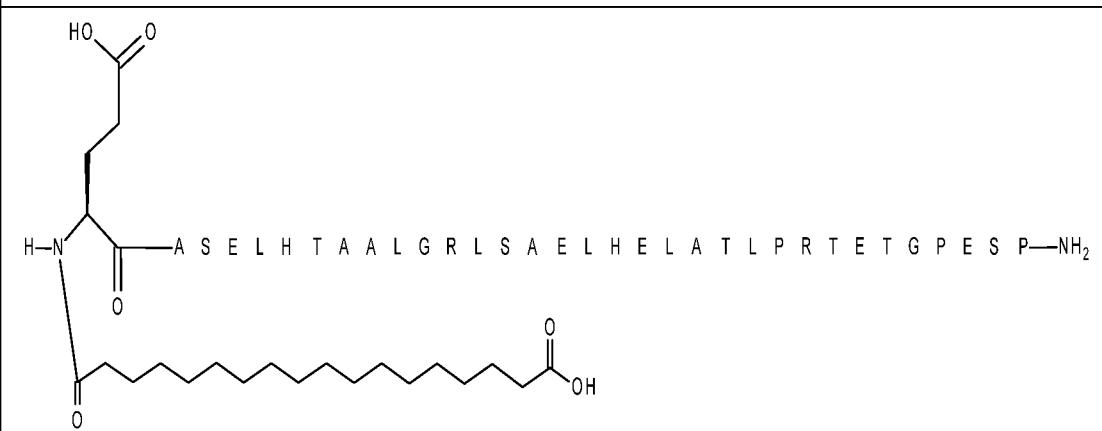
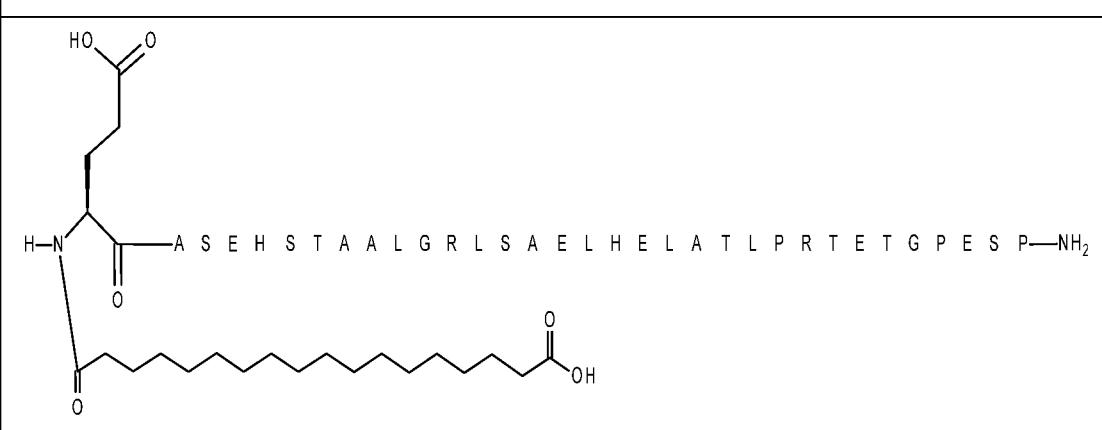
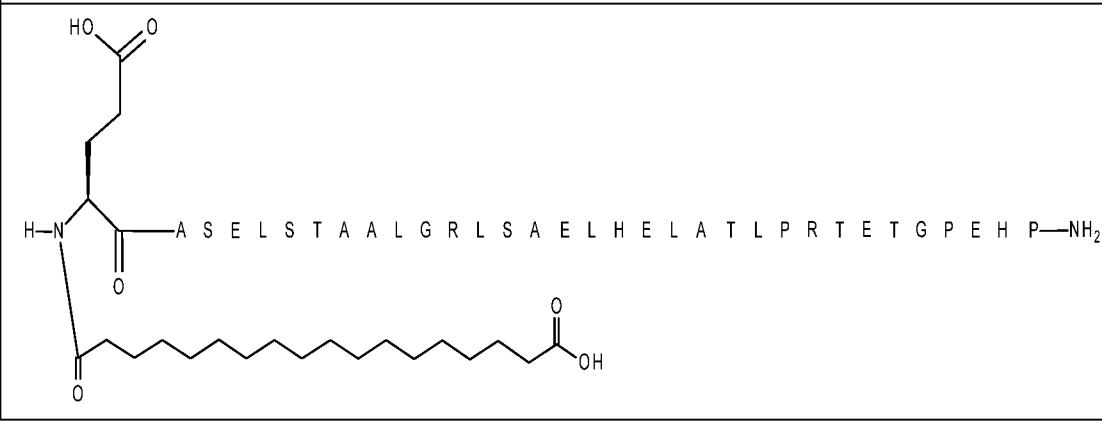
Table 5- Structure formulas of mimylin derivatives (mimylin compounds)

Ex#	Structure of compound
1	H—E A S E L S T A A L G R L S A E L H E L A T L P R T E T G P E S P—NH ₂
2	
3	
4	

Ex#	Structure of compound
5	
6	
7	

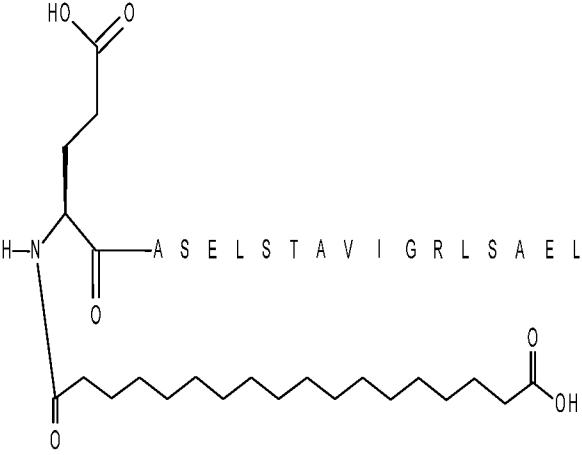
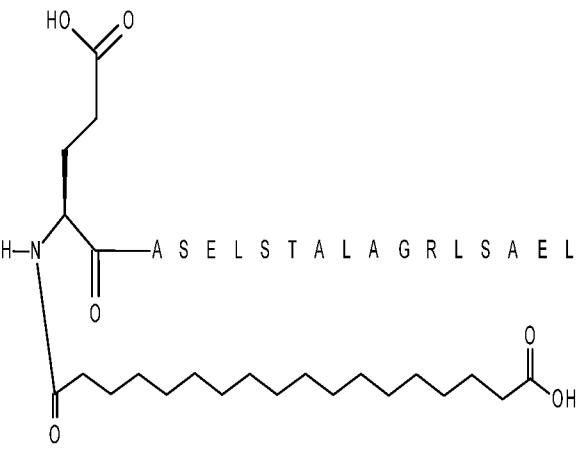
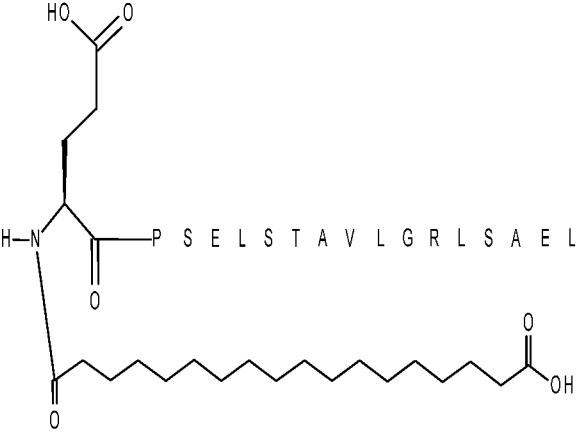
Ex#	Structure of compound
8	
9	
10	

Ex#	Structure of compound
10	
12	
13	
14	

Ex#	Structure of compound
15	
16	
17	
18	

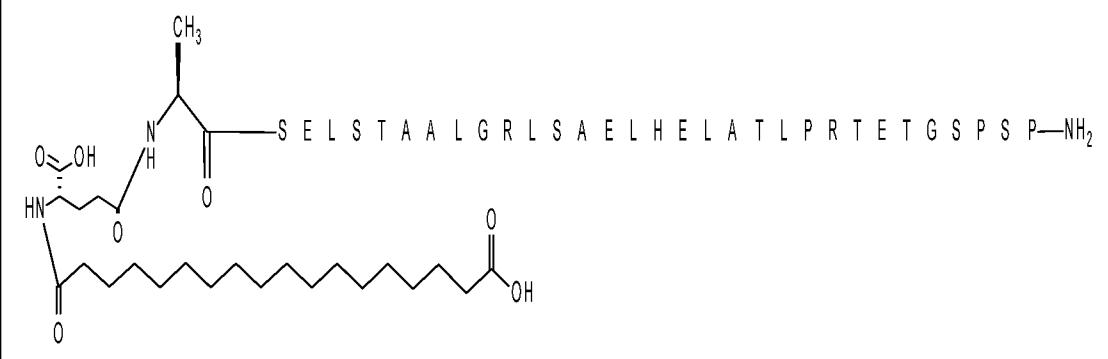
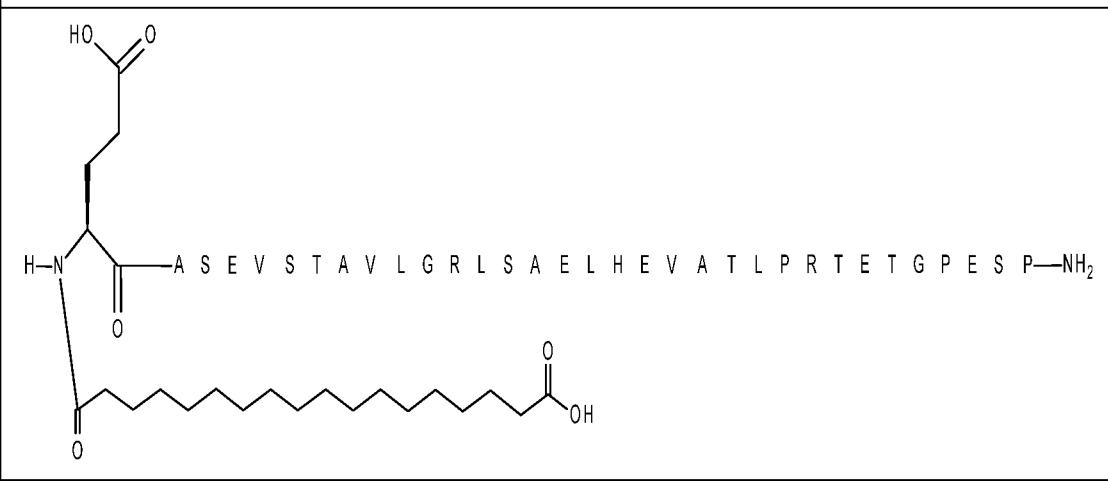
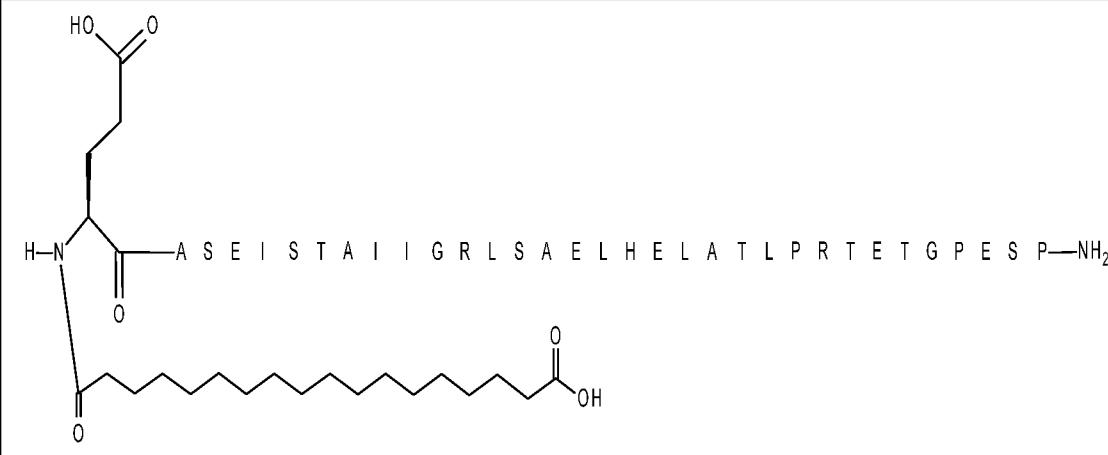
Ex#	Structure of compound
19	<p>Chemical structure of compound 19: A peptide chain with a C-terminal amide group (NH₂). The sequence is SELSTAALGRLSAELHELATLPRTEVGPESP-NH₂. The chain features a thioether linkage (-S-), a cyclohexyl group, and a long hydrocarbon tail ending in a carboxylic acid group (OH).</p>
20	<p>Chemical structure of compound 20: A peptide chain with a C-terminal amide group (NH₂). The sequence is ASELSSTAALGRLSAELHELATYPRTEVGPESP-NH₂. The chain features a cyclohexyl group and a long hydrocarbon tail ending in a carboxylic acid group (OH).</p>
21	<p>Chemical structure of compound 21: A peptide chain with a C-terminal amide group (NH₂). The sequence is ASELSSTAALGRLSAELHELATLPRTEVGSGSP-NH₂. The chain features a cyclohexyl group and a long hydrocarbon tail ending in a carboxylic acid group (OH).</p>
22	<p>Chemical structure of compound 22: A peptide chain with a C-terminal amide group (NH₂). The sequence is ASELSSTAALGRLSAELHELATLPRTEVGSGSP-NH₂. The chain features a cyclohexyl group and a long hydrocarbon tail ending in a carboxylic acid group (OH).</p>

Ex#	Structure of compound
23	
24	
25	

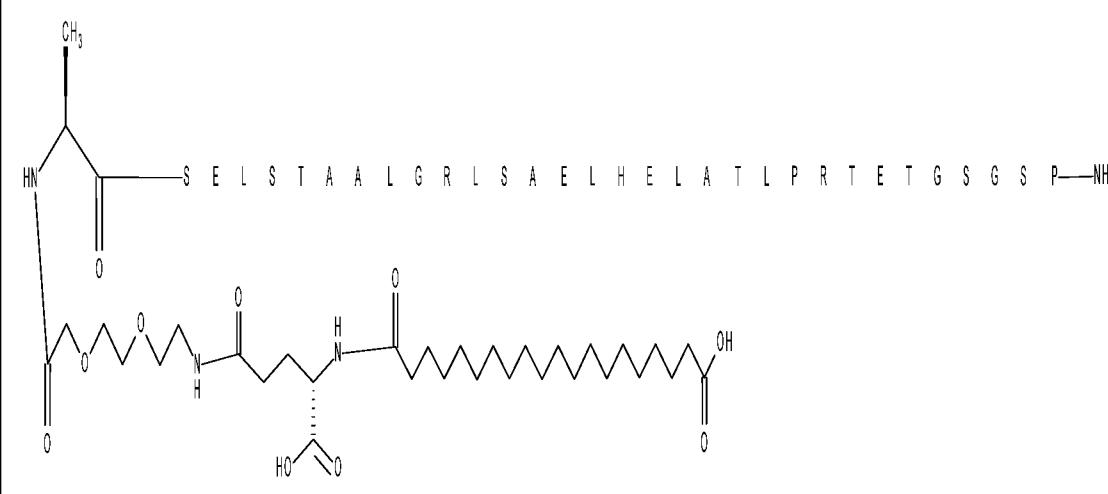
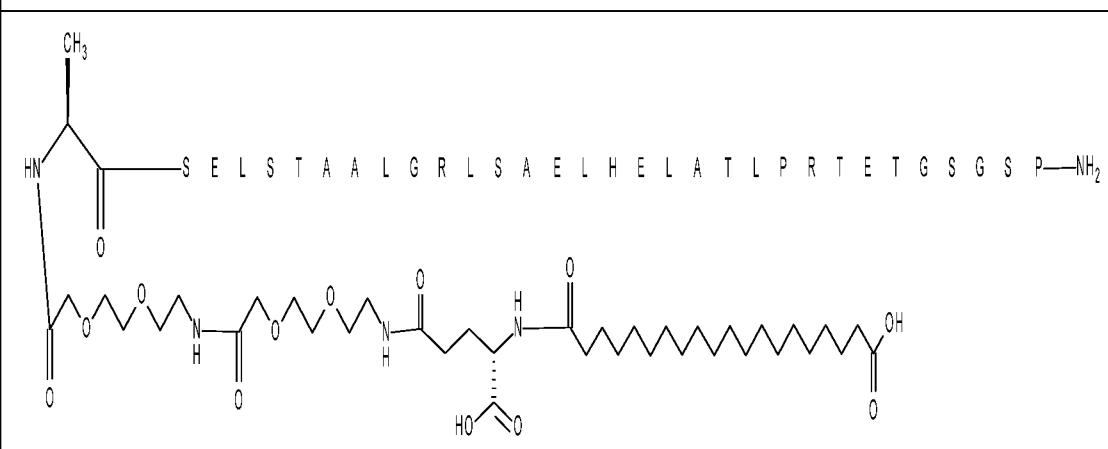
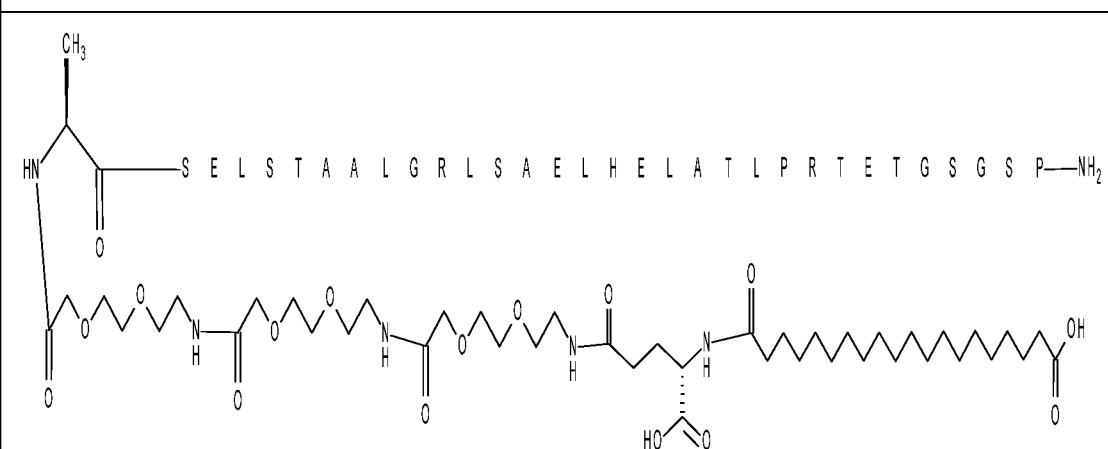
Ex#	Structure of compound
26	
27	
28	

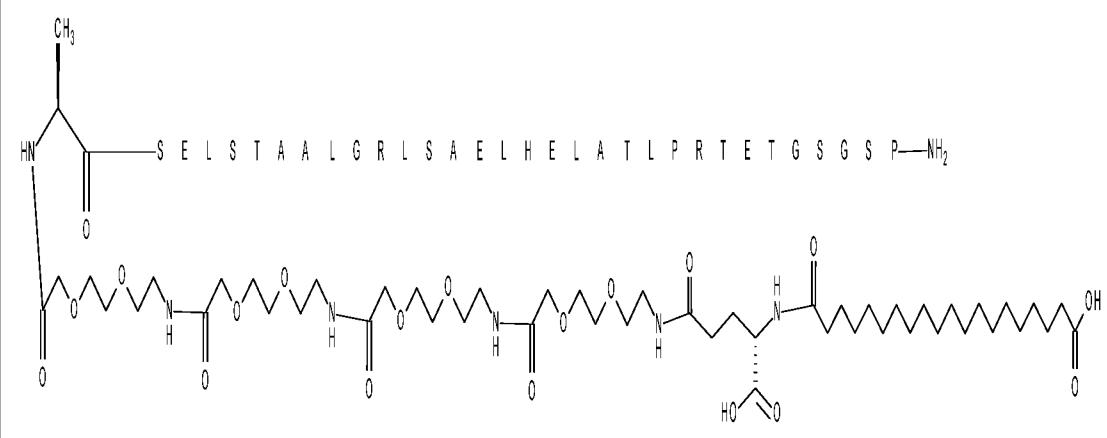
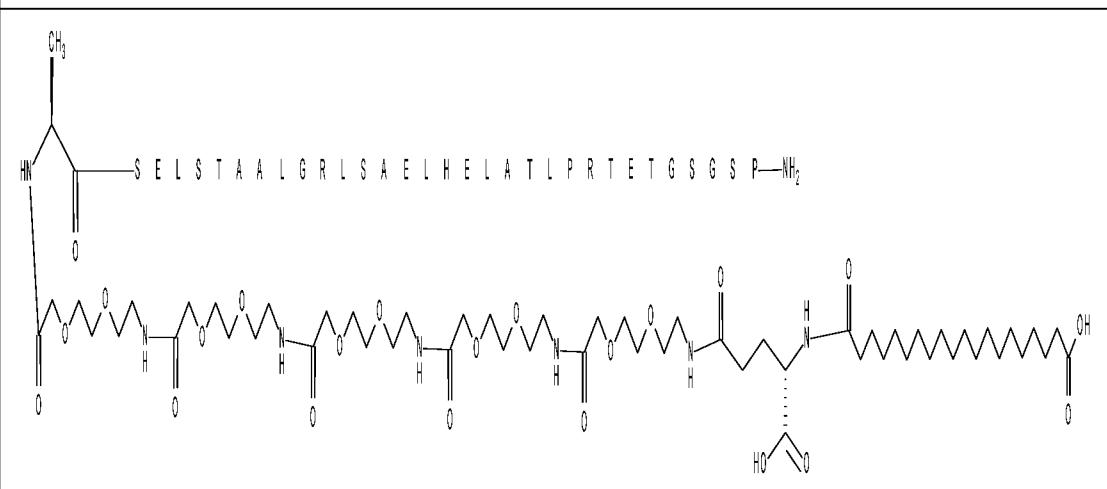
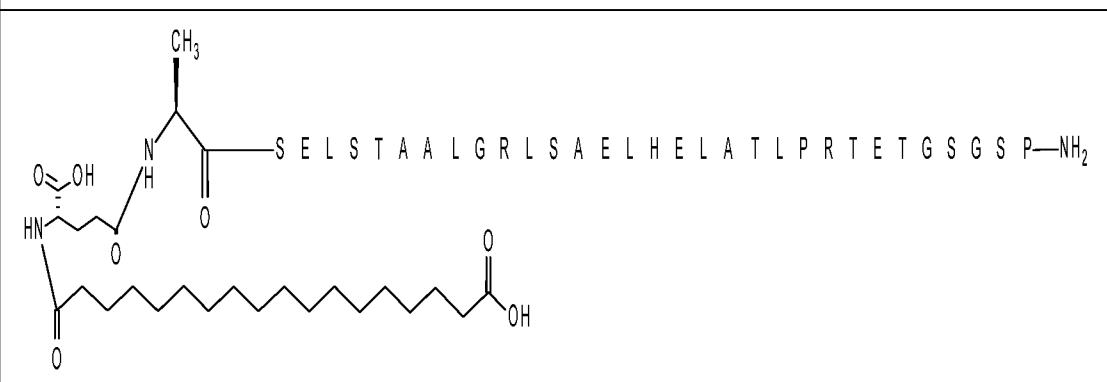
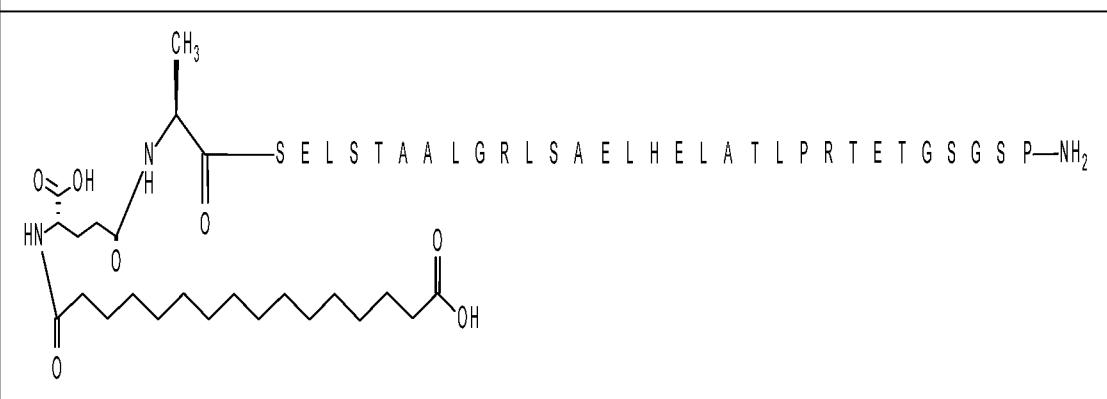
Ex#	Structure of compound
29	
30	
31	

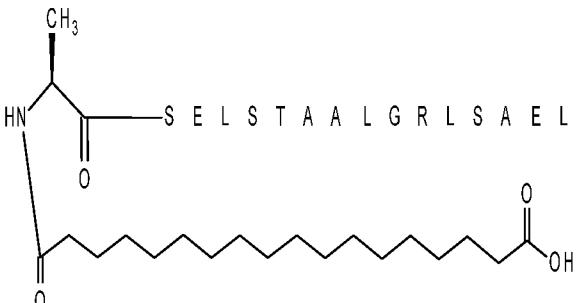
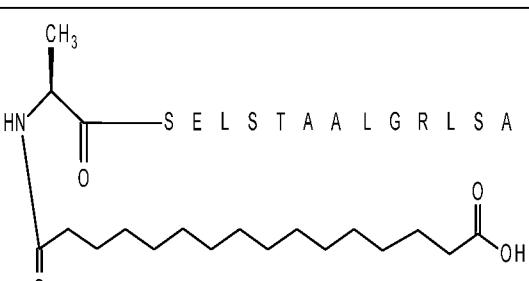
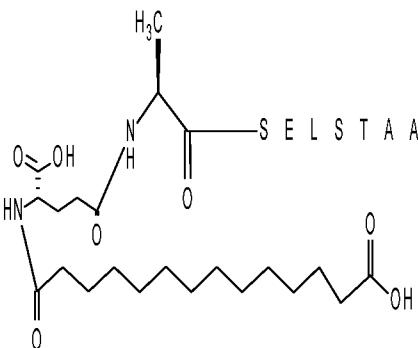
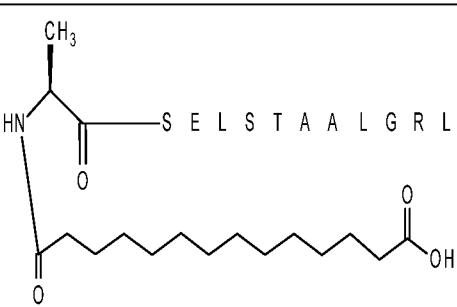
Ex#	Structure of compound
32	
33	
34	

Ex#	Structure of compound
35	
36	
37	

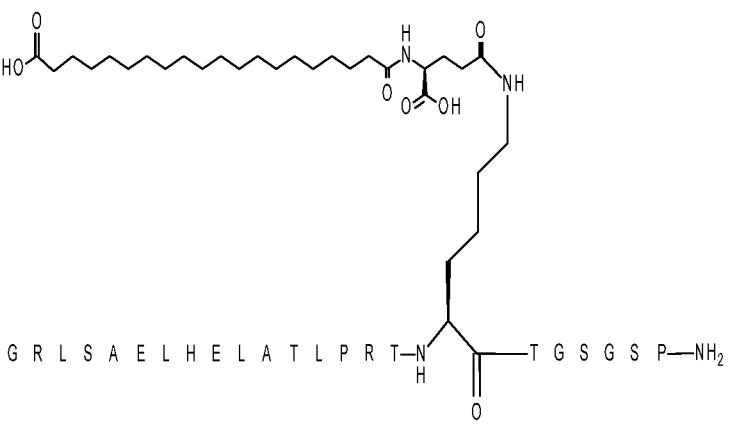
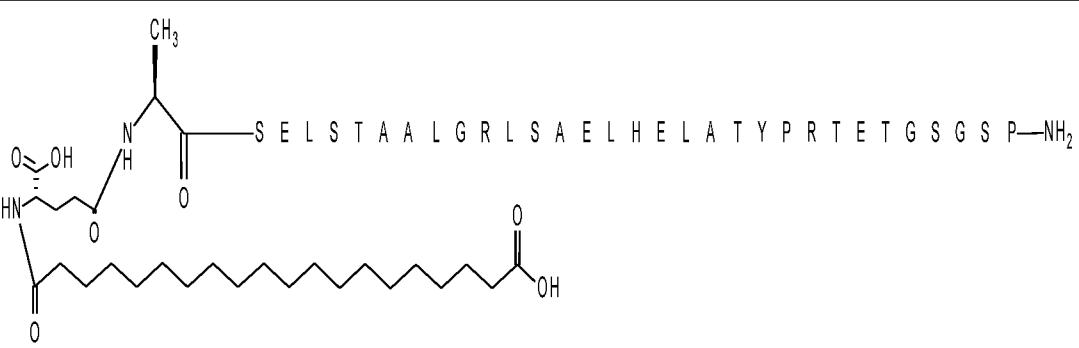
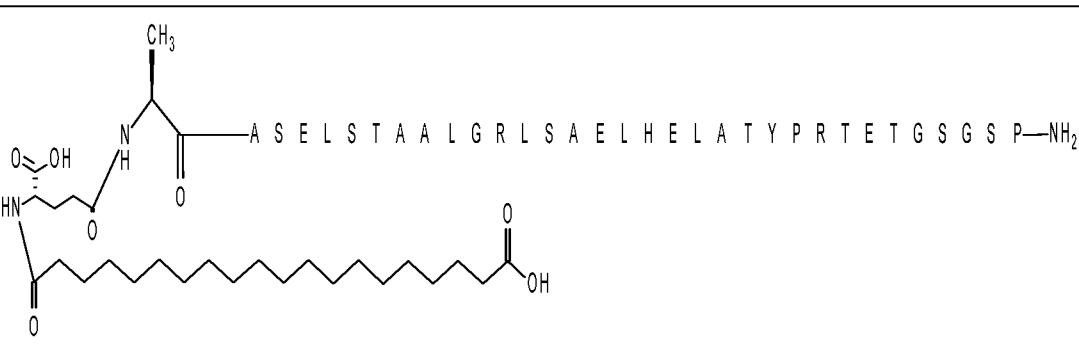
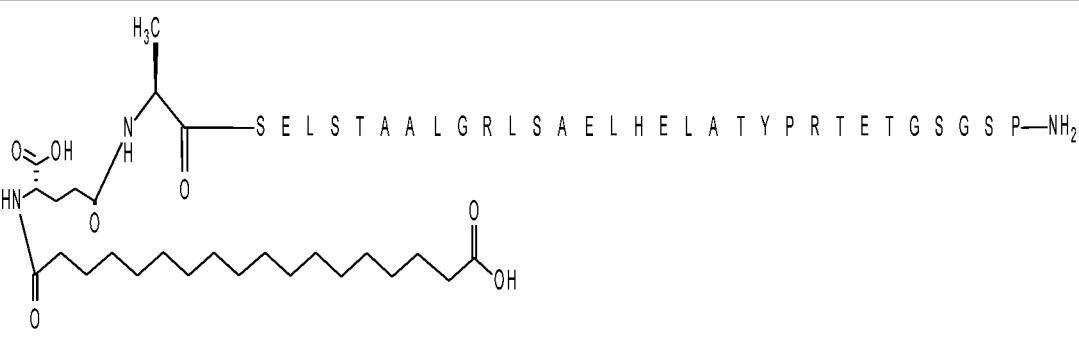
Ex#	Structure of compound
38	
39	
40	

Ex#	Structure of compound
41	
42	
43	

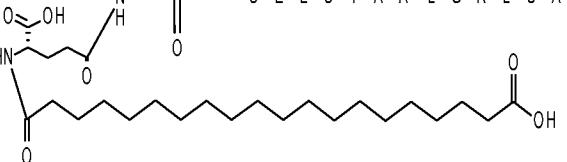
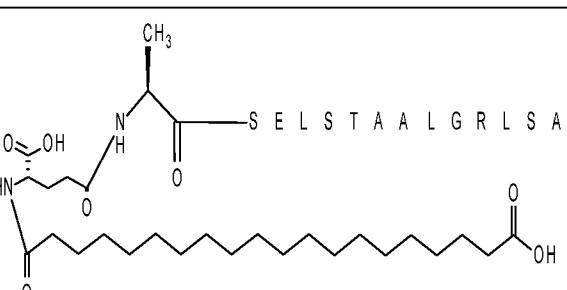
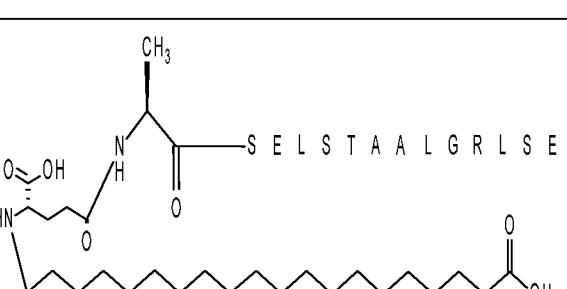
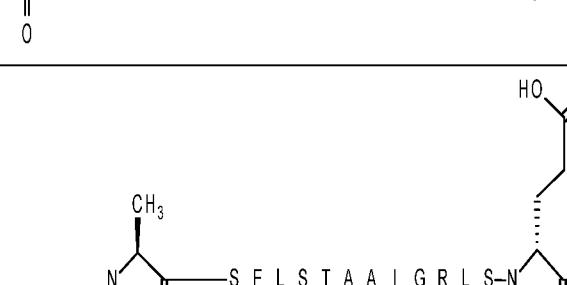
Ex#	Structure of compound
44	
45	
46	
47	

Ex#	Structure of compound
48	
49	
50	
51	

Ex#	Structure of compound
52	<p>Chemical structure of compound 52: A peptide chain starting with a cysteine residue (CYS) linked to a thioether group. The sequence is SELSTAALGRLSAELH- (underlined). The chain continues with a proline residue (PRO) linked to a dipeptide side chain: (R)-[D,L]-Glycyl-L-Histidyl. The side chain ends with a carboxylic acid group (-COOH).</p>
53	<p>Chemical structure of compound 53: A peptide chain starting with a cysteine residue (CYS) linked to a thioether group. The sequence is SELSTAALGRLSA- (underlined). The chain continues with a proline residue (PRO) linked to a dipeptide side chain: (R)-[D,L]-Glycyl-L-Histidyl. The side chain ends with a carboxylic acid group (-COOH).</p>
54	<p>Chemical structure of compound 54: A peptide chain starting with a cysteine residue (CYS) linked to a thioether group. The sequence is SELSTAALGRLSAELH- (underlined). The chain continues with a proline residue (PRO) linked to a dipeptide side chain: (R)-[D,L]-Glycyl-L-Histidyl. The side chain ends with a carboxylic acid group (-COOH).</p>

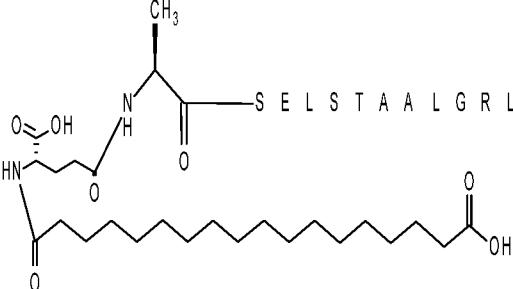
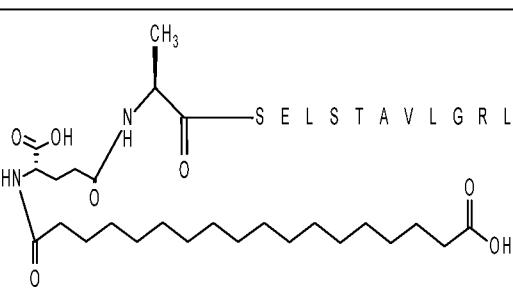
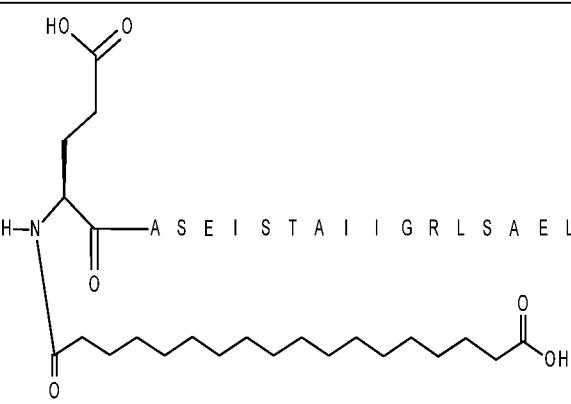
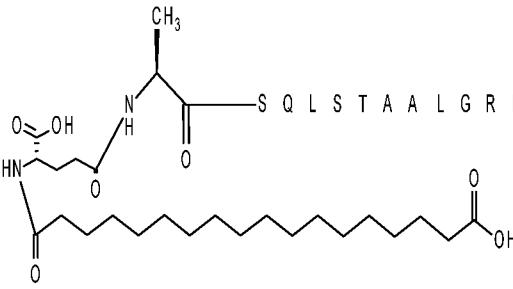
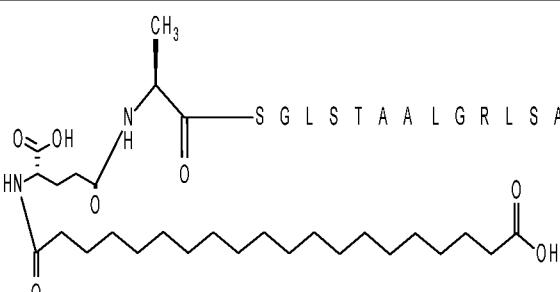
Ex#	Structure of compound
55	
56	
57	
58	

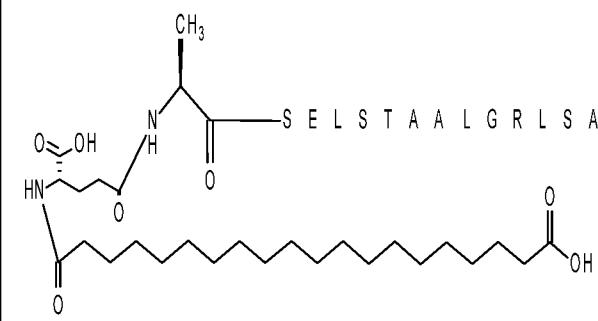
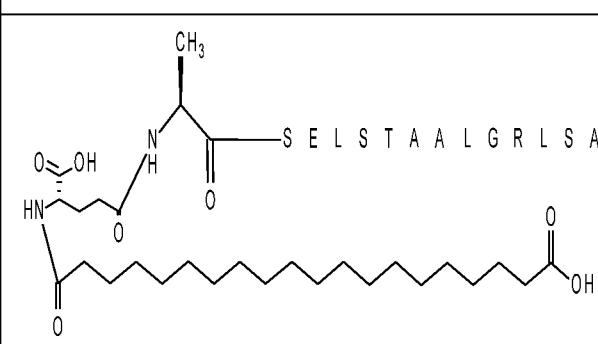
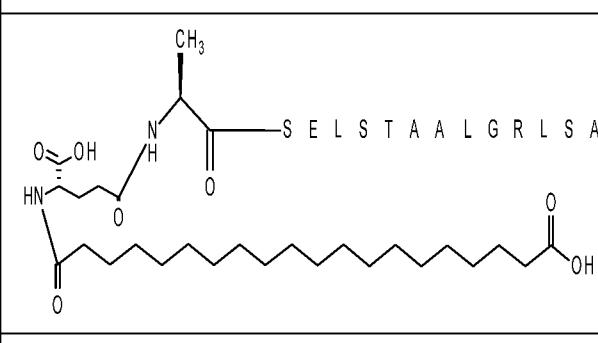
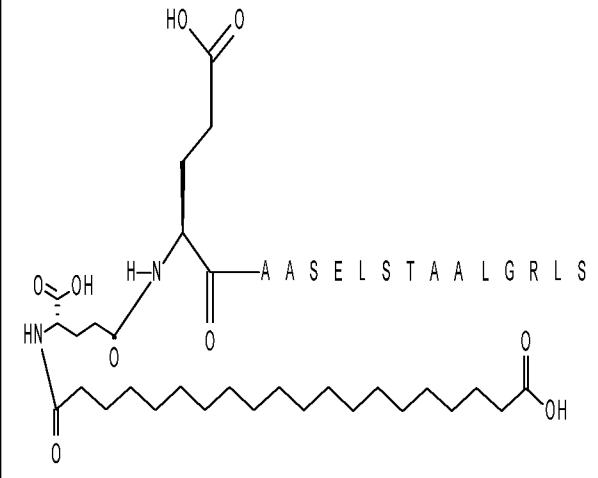
Ex#	Structure of compound
59	<p>SELSTAALGRLSAELHELATLPRTE TGS GS Y-NH₂</p>
60	<p>SELSTAALGRLSAELHELATLPRTE TGS GS H-NH₂</p>
61	<p>SELSTAALGRLSAELHELATLPRTE TGS GS F-NH₂</p>
62	<p>SELSTAALGRLSAELHELATLPRTE TGS GS L-NH₂</p>
63	<p>SELSTAALGRLSAELHELATLPRTE TGS GS S-NH₂</p>

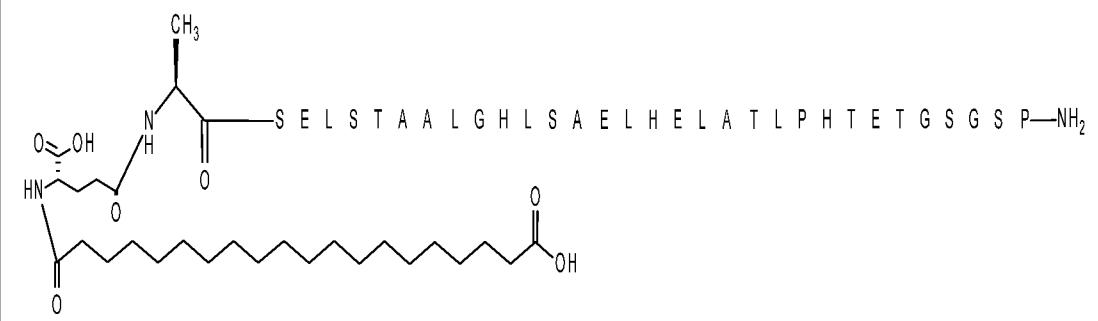
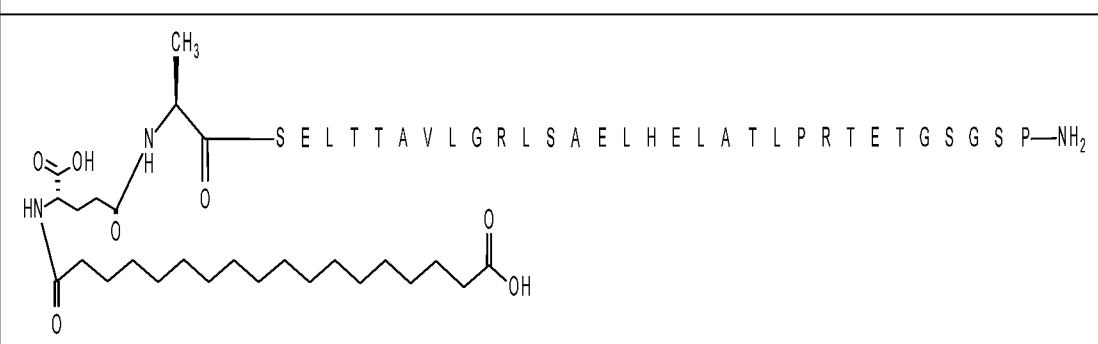
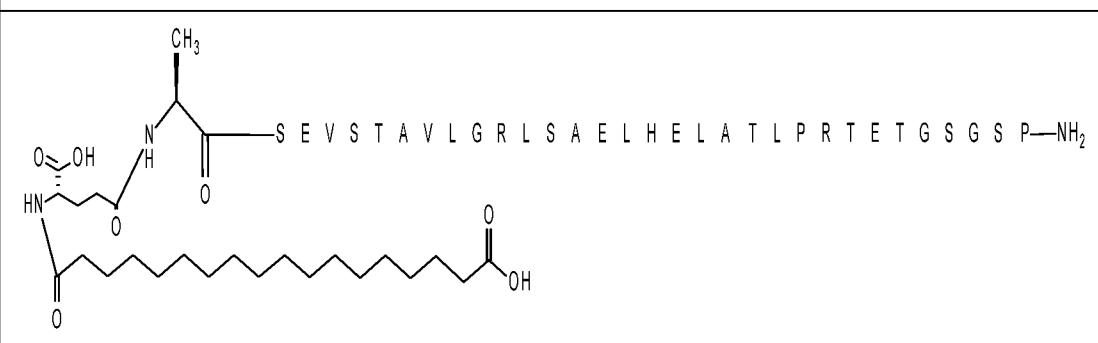
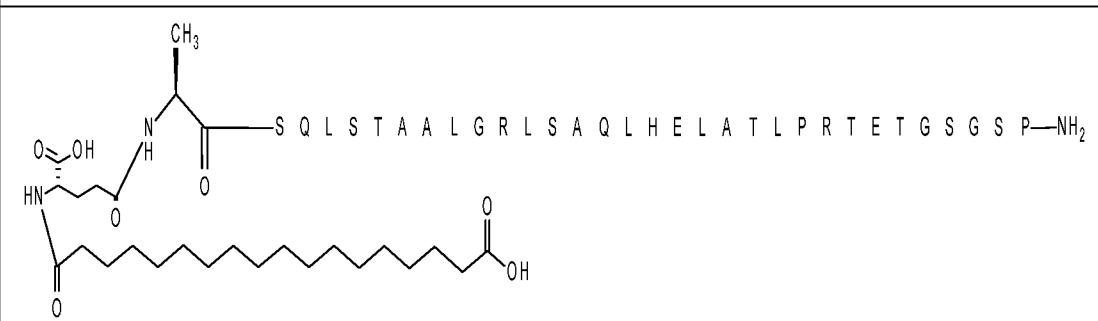
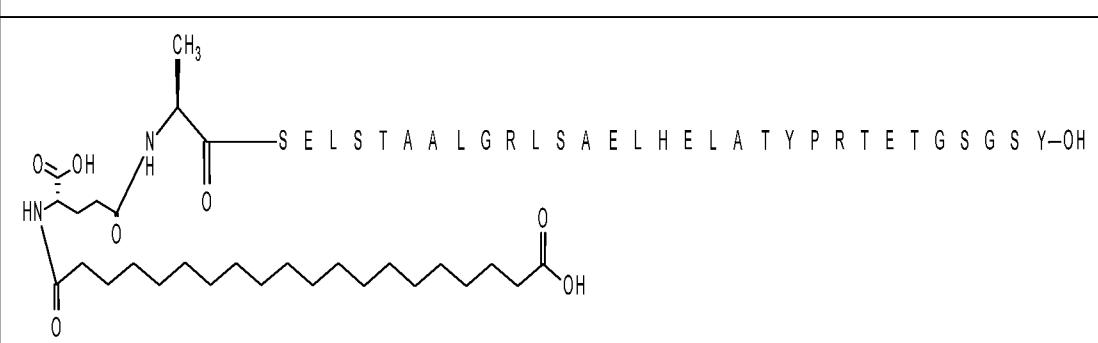
Ex#	Structure of compound
64	
64	
66	
67	

Ex#	Structure of compound
68	<p>Chemical structure of compound 68: A peptide chain starting with a C-terminal carboxylic acid (NH₂-LEDTA-CH₂-CH₂-CH₂-CH₂-COOH). The chain continues with a methionine residue (Met), followed by a thioether linkage (-S-), and then the sequence SELSTAALGRLSAELH-.</p>
69	<p>Chemical structure of compound 69: A peptide chain starting with a C-terminal carboxylic acid (NH₂-LEDTA-CH₂-CH₂-CH₂-CH₂-COOH). The chain continues with a methionine residue (Met), followed by a thioether linkage (-S-), and then the sequence SELSTAALGRLSA-NH-.</p>
70	<p>Chemical structure of compound 70: A peptide chain starting with a C-terminal carboxylic acid (NH₂-LEDTA-CH₂-CH₂-CH₂-CH₂-COOH). The chain continues with a methionine residue (Met), followed by a thioether linkage (-S-), and then the sequence SELSTAALGRLSAELH-NH-.</p>

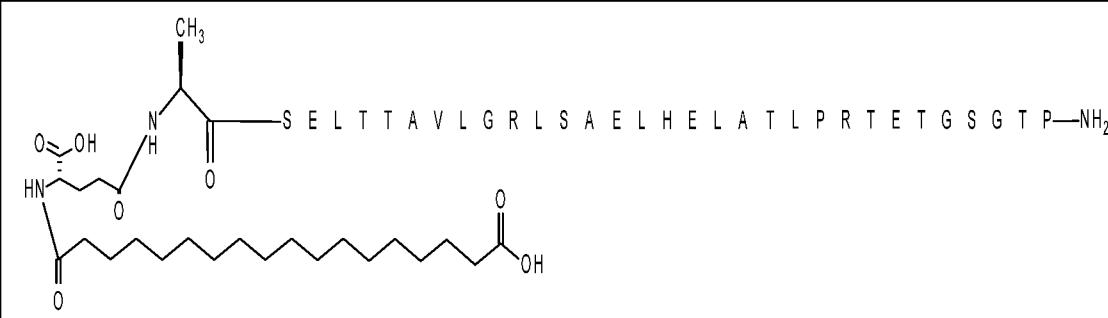
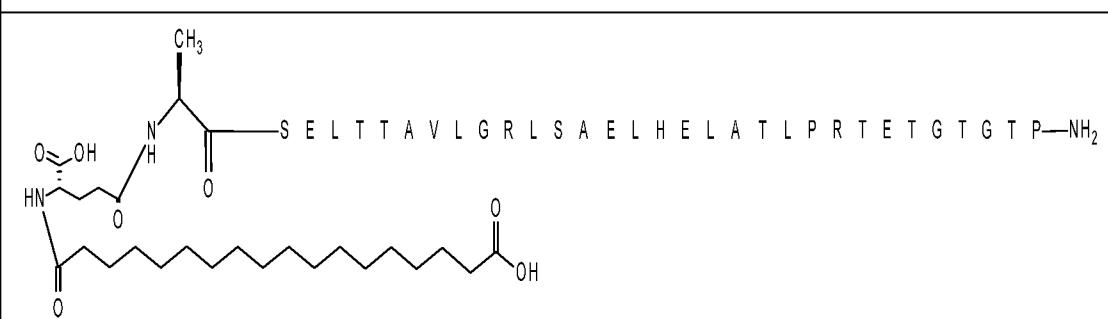
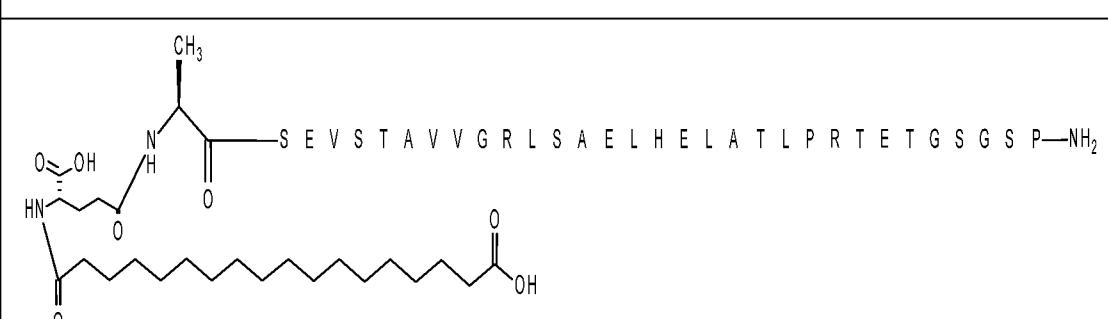
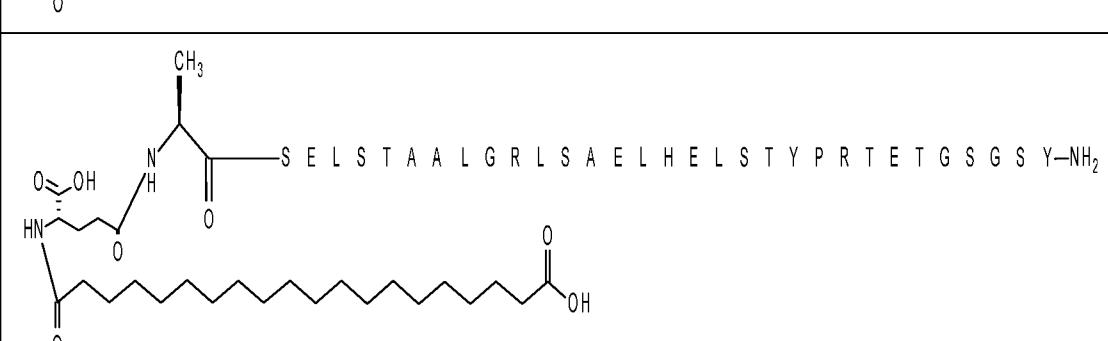
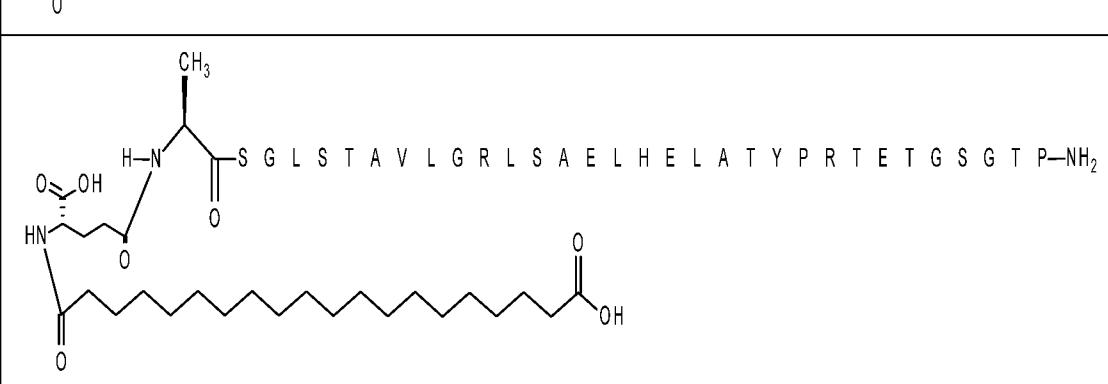
Ex#	Structure of compound
71	
72	
73	
74	

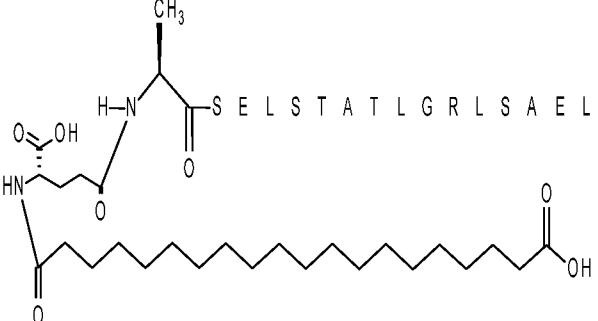
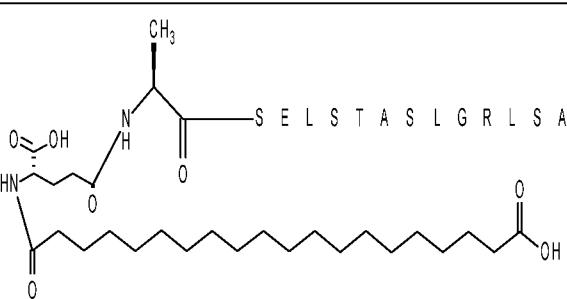
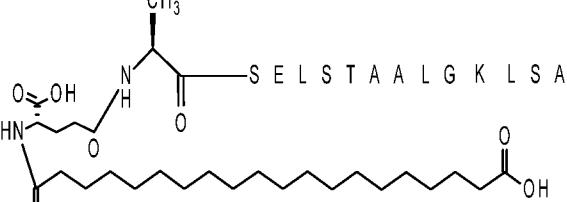
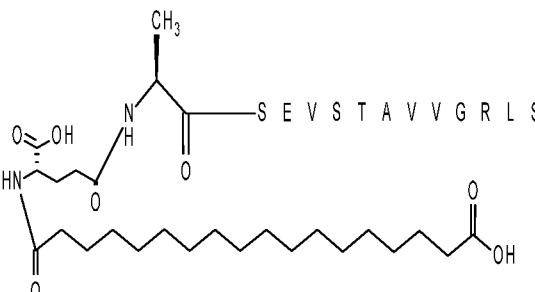
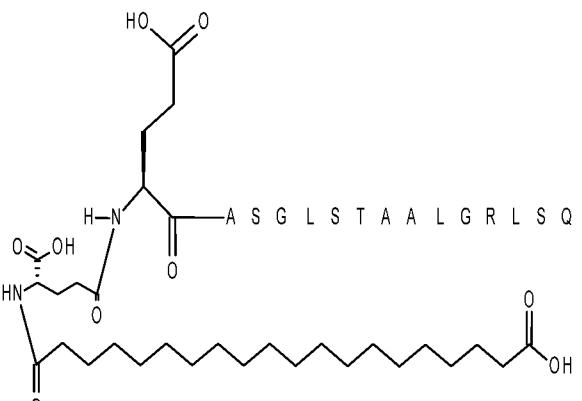
Ex#	Structure of compound
75	 <p>Sequence: SELSTAALGRLSAELHELATLPRTEETGSGGPP-NH₂</p>
76	 <p>Sequence: SELSTAVALGRLSAELHELATLPRTEETGSGGSP-NH₂</p>
77	 <p>Sequence: ASEISTAIIGRLSAELHEIATLPRTEETGPESP-NH₂</p>
78	 <p>Sequence: SQLSTAALGRLSAELHELATLPRTEETGSGGSP-NH₂</p>
79	 <p>Sequence: SGLSTAALGRLSAELHELATYPRTEETGSGGSP-NH₂</p>

Ex#	Structure of compound
80	
81	
82	
83	

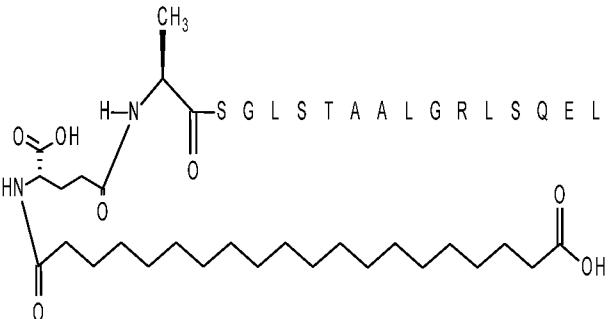
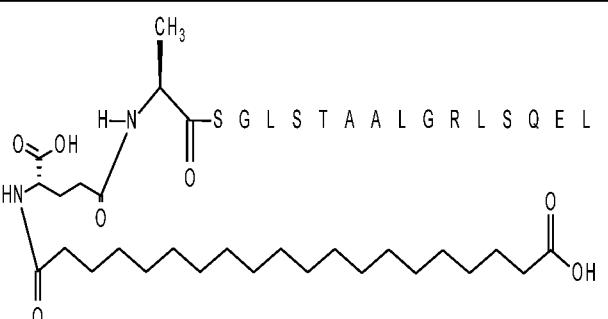
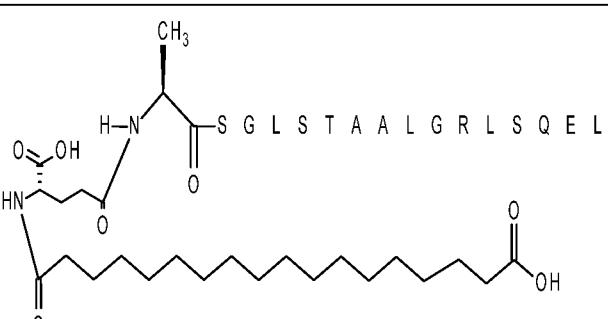
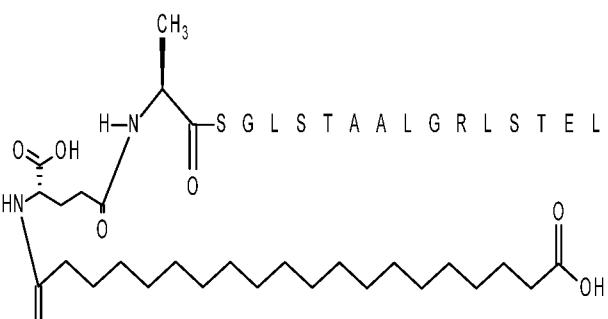
Ex#	Structure of compound
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85	
86	
87	
88	

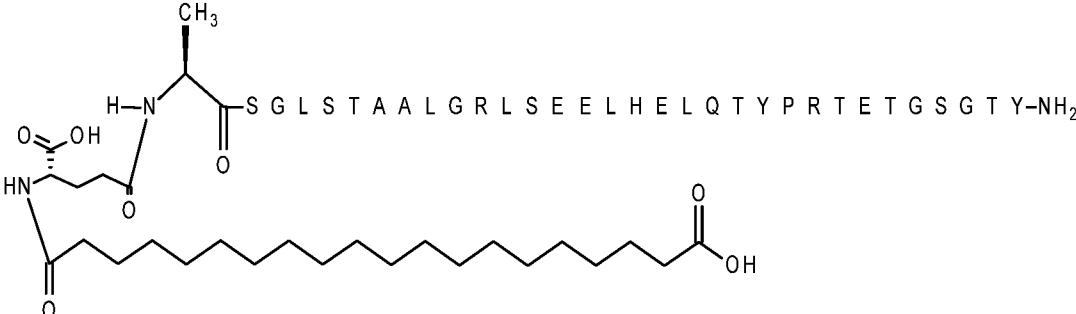
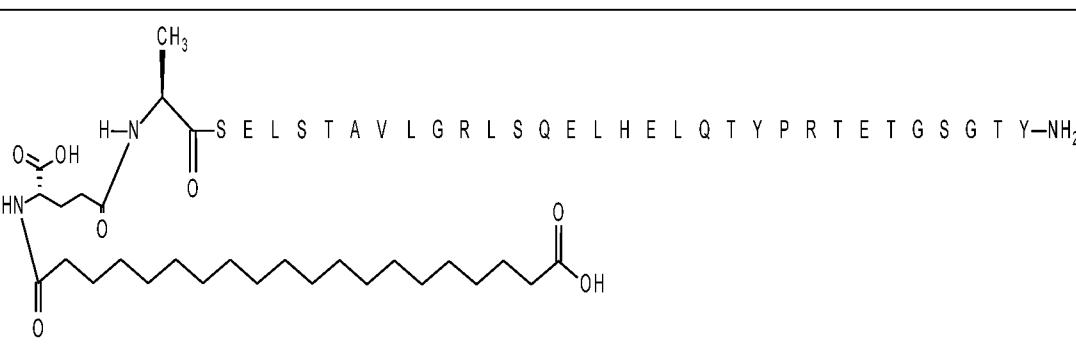
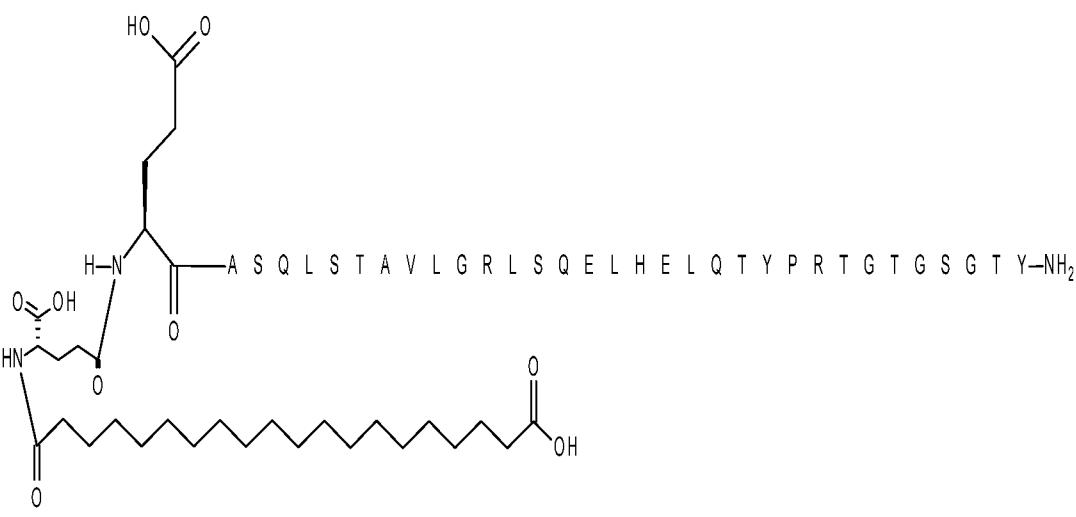
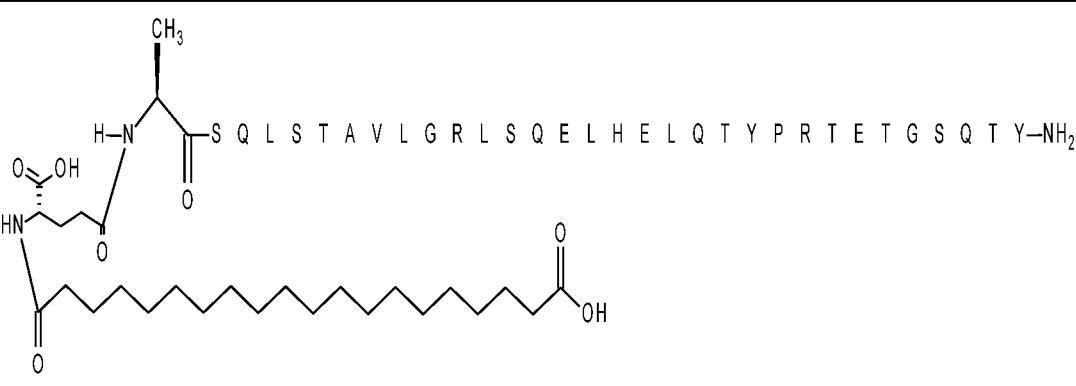
Ex#	Structure of compound
89	<p>SELSTAALGRLSAELHELATYPRTEETGSGSPPG-OH</p>
90	<p>SELSTAALGRLSAELHELATYPRTEETGSGSPPK-OH</p>
91	<p>SELSTASLGRRLSAELHELATYPRTEETGSGSYY-NH₂</p>
92	<p>SELSTATLGRRLSAELHELSTYPRTEETGSGSPP-NH₂</p>
93	<p>SELSTAALGHLSAELHELATLPHTEETGTGTP-NH₂</p>

Ex#	Structure of compound
94	
95	
96	
97	
98	

Ex#	Structure of compound
99	 <p>SELSTATLGRLSAELHELSTYPRTEGSGSY-NH₂</p>
100	 <p>SELSTASLGRLSAELHELSTYPRTEGSGSY-NH₂</p>
101	 <p>SELSTAALGKLSAELHELATYPKTETGSGSY-NH₂</p>
102	 <p>SEVSTA VV GRL S A E L H E V A T L P R T E T G S G S P-NH₂</p>
103	 <p>ASGLSTAALGRLSQELHELQTYPRTEGSGTYS-NH₂</p>

Ex#	Structure of compound
104	
105	
106	
107	

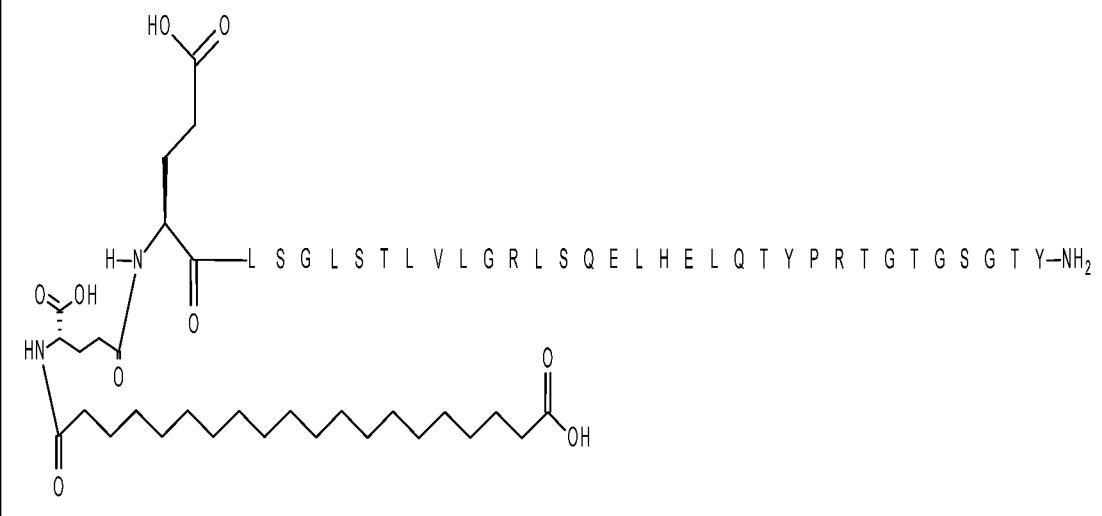
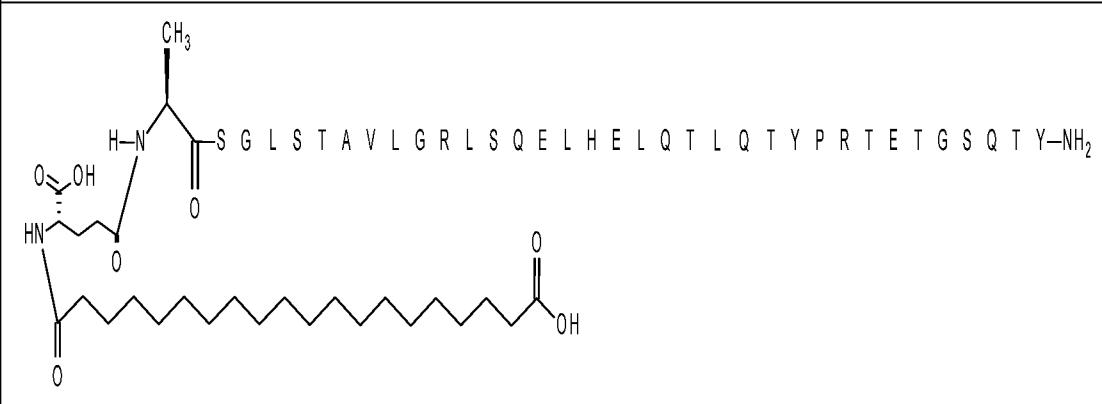
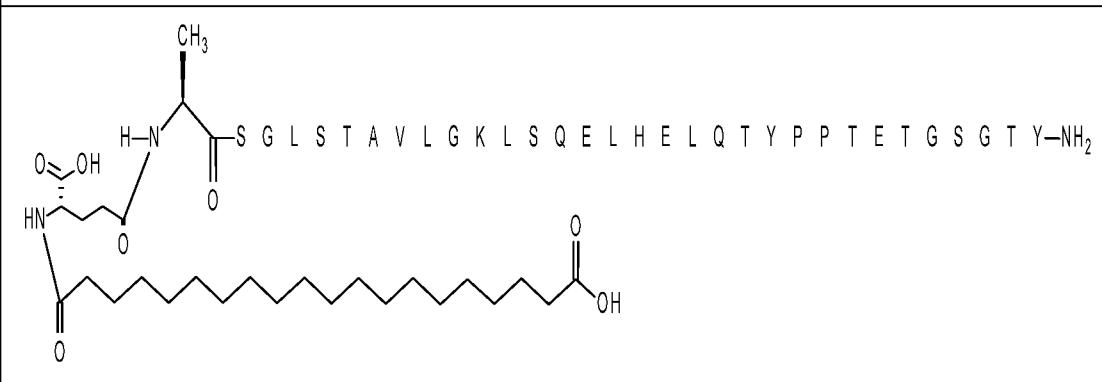
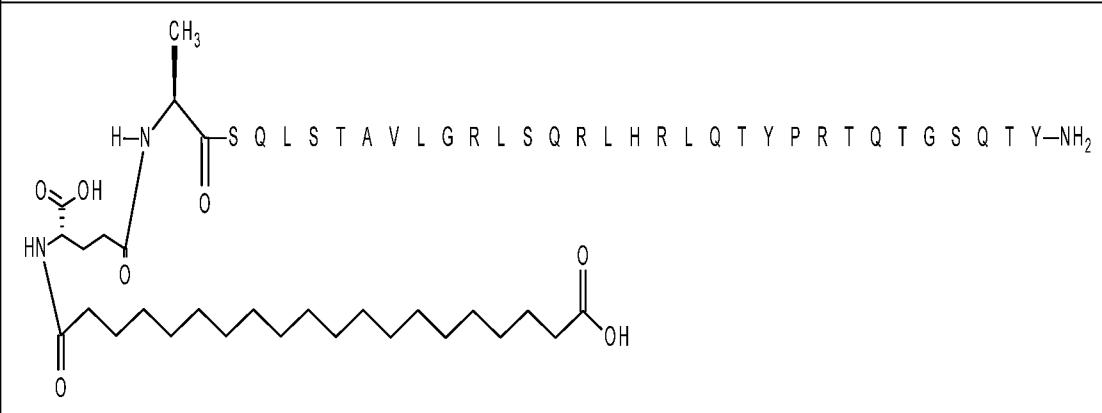
Ex#	Structure of compound
108	
109	
110	
111	
112	

Ex#	Structure of compound
113	 <p>Sequence: SGLSTAALGR</p>
114	 <p>Sequence: SELSTAVALGR</p>
115	 <p>Sequence: ASQLSTAVALGR</p>
116	 <p>Sequence: SQLSTAVALGR</p>

Ex#	Structure of compound
117	
118	
119	
120	

Ex#	Structure of compound
121	
122	
123	
124	

Ex#	Structure of compound
125	<p>Sequence: S G L S T A V L G R L S Q E L H E L Q T Y P P T E T G S Q T Y-NH₂</p>
126	<p>Sequence: S G L S T L V L G R L S Q E L H E L Q T Y P R T E T G S Q T Y-NH₂</p>
127	<p>Sequence: S G L S T A V L G R L S Q E L H E L Q T Y P R T E T G S Q T Y-NH₂</p>
128	<p>Sequence: S G L S T A T L G R L S Q E L H E L Q T Y P P T E T G S G T Y-NH₂</p>

Ex#	Structure of compound
129	
130	
131	
132	

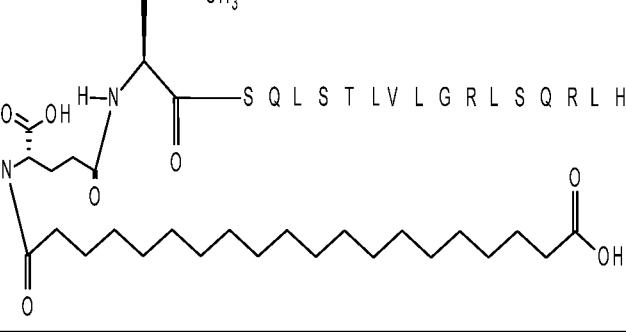
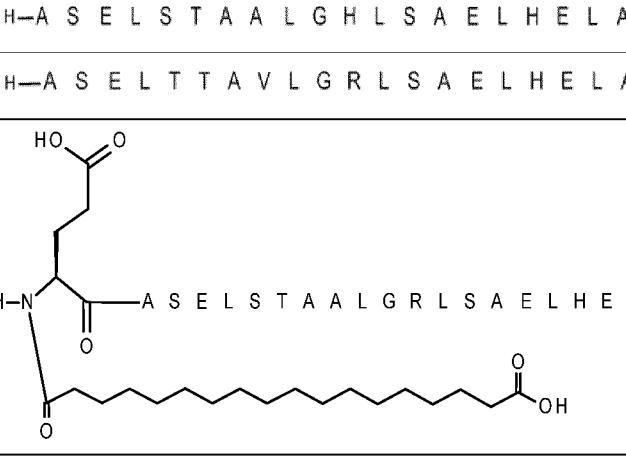
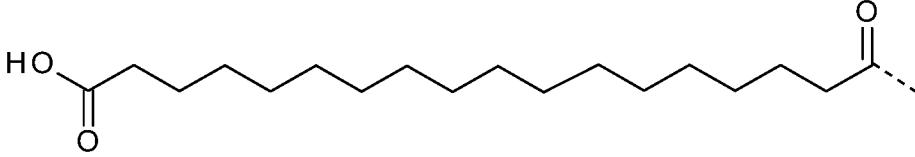
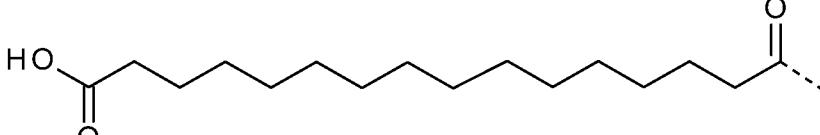
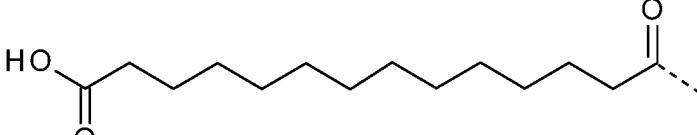
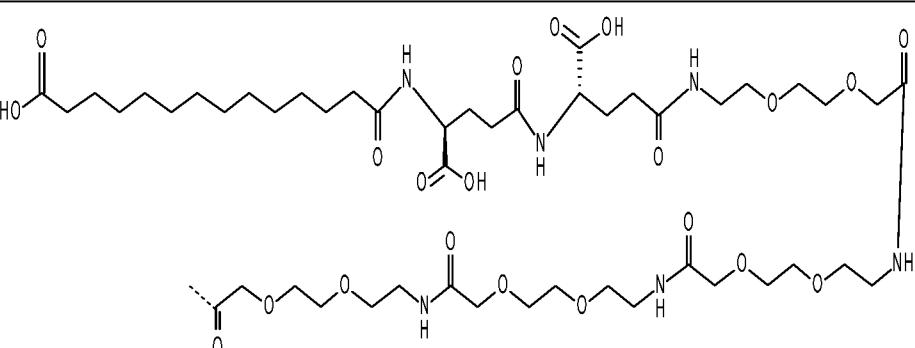
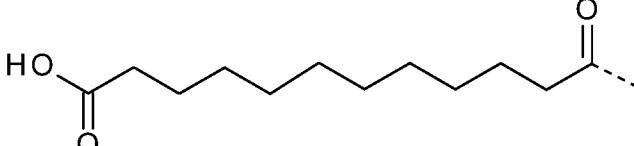
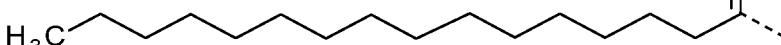
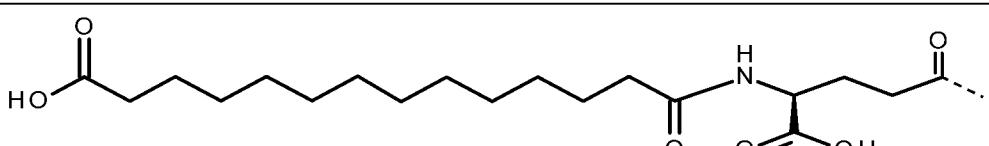
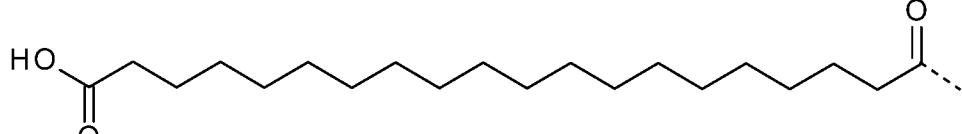
Ex#	Structure of compound
133	 <p>Chemical structure of a peptide with a branched side chain. The side chain is a 16-carbon chain with a 2-methylpropyl group at position 8. The peptide sequence is SQQLSTLVLGRLSQRLHRLQTYPRTTQTGSGSQTY-NH₂.</p>
72 bb	H-A S E L S T A A L G H L S A E L H E L A T L P R T E T G S G S P—NH ₂
95 bb	H-A S E L T T A V L G R L S A E L H E L A T L P R T E T G T G T P—NH ₂
134	 <p>Chemical structure of a peptide with a branched side chain. The side chain is a 16-carbon chain with a 2-hydroxypropyl group at position 8. The peptide sequence is AS E L S T A A L G R L S A E L H E L A T L P R T E T G P E S P—OH.</p>
127 bb	H—L S G L S T A V L G R L S Q E L H E L Q T Y P R T E T G S Q T Y-NH ₂
22 bb	H-E A S E L S T A A L G R L S A E L H E L A T L P R T E T G S G S P—NH ₂
86 bb	H-A S E V S T A V L G R L S A E L H E L A T L P R T E T G S G S P—NH ₂
106 bb	H-A S E L T T A V L G R L E A E L H E L T T L P R T E T G T G T P—NH ₂
135	 <p>Chemical structure of a peptide with a branched side chain. The side chain is a 16-carbon chain with a 2-(cyclopentylmethyl)propyl group at position 8. The peptide sequence is H-E A S E L S T A A L G R L S A E L H E L A T L P R T E T G P E S N.</p>

Table 6- side chain names and structure

Side chain name	Side chain structure
-----------------	----------------------

Side chain name	Side chain structure
C18diacid	
C16diacid	
C14diacid	
C14diacid-2xgGlu-4xOEG	
C12diacid	
C16	
C14diacid-gGlu	
C20diacid	

Side chain name	Side chain structure
C18diacid-gGlu	
C20diacid-gGlu	
C20diacid-gGlu-OEG	
C20diacid-gGlu-2xOEG	
C20diacid-gGlu-3xOEG	
C20diacid-gGlu-4xOEG	

Side chain name	Side chain structure
C20diacid-gGlu-5xOEG	
C16diacid-gGlu	

In some embodiments the invention relates to a method for weight management making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered aspects of this

5 invention. In some embodiments the invention relates to a method for reduction of appetite making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered aspects of this invention. In some embodiments the invention relates to a method for reduction of food intake making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered aspects of this

10 invention.

In some embodiments the invention relates to a method for treatment or prevention of obesity making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered

15 aspects of this invention. In some embodiments the invention relates to use of a mimylin peptide or derivative or a pharmaceutical formulation, co-formulation or co-treatment according to the non-limiting numbered aspects of this invention for treatment or prevention of obesity. In some embodiments the subject suffering from obesity is human, such as an adult human or a paediatric human (including infants, children, and

20 adolescents). A human subject suffering from obesity may have a BMI of ≥ 30 ; this subject may also be referred to as obese. In some embodiments the human subject suffering from obesity may have a BMI of ≥ 35 or a BMI in the range of ≥ 30 to < 40 . In some embodiments the obesity is severe obesity or morbid obesity, wherein the human subject may have a BMI of ≥ 40 .

In some embodiments the invention relates to a method for treatment or prevention of overweight making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered aspects of this invention, optionally in the presence of at least one weight-related 5 comorbidity. In some embodiments the invention relates to use of the a mimylin peptide or derivative or a pharmaceutical formulations, co-formulation or co-treatment according to the non-limiting numbered aspects of this invention for treatment or prevention of overweight, optionally in the presence of at least one weight-related comorbidity. In some embodiments the subject suffering from overweight is human, such as an adult 10 human or a paediatric human (including infants, children, and adolescents). In some embodiments a human subject suffering from overweight may have a BMI of ≥ 25 , such as a BMI of ≥ 27 . In some embodiments a human subject suffering from overweight has a BMI in the range of 25 to <30 or in the range of 27 to <30 . In some embodiments the 15 weight-related comorbidity is selected from the group consisting of hypertension, diabetes (such as type 2 diabetes), dyslipidaemia, high cholesterol, and obstructive sleep apnoea.

In some embodiments the invention relates to a method for reduction of body weight making use of a mimylin peptide or derivative a pharmaceutical formulation, co-formulation or co-treatment of any one of the non-limiting numbered aspects of this 20 invention. In some embodiments the invention relates to use of a mimylin peptide or derivative or a pharmaceutical formulations according to the non-limiting numbered aspects of this invention for reduction of body weight. A human to be subjected to reduction of body weight according to the present invention may have a BMI of ≥ 25 , such as a BMI of ≥ 27 or a BMI of ≥ 30 . In some embodiments the human to be subjected 25 to reduction of body weight according to the present invention may have a BMI of ≥ 35 or a BMI of ≥ 40 . The term "reduction of body weight" may include treatment or prevention of obesity and/or overweight.

Non-limiting aspect of the invention

- 30 1. A mimylin peptide comprising a sequence with at least 54% sequence identity to SEQ ID NO: 1;
EASELSTAALGRLSAELHELATLPRTETGPESP (SEQ ID NO: 1)
2. A mimylin peptide having at least 66% sequence identity to SEQ ID NO: 1;
3. The mimylin peptide according to any one of the preceding aspects, wherein said 35 mimylin peptide more than about 66% sequence identity to SEQ ID NO:1;

4. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 69% sequence identity to SEQ ID NO:1;
5. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 72% sequence identity to SEQ ID NO:1;
- 5 6. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 75% sequence identity to SEQ ID NO:1;
7. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 78% sequence identity to SEQ ID NO:1;
- 10 8. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 81% sequence identity to SEQ ID NO:1;
9. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 84% sequence identity to SEQ ID NO:1;
- 10 10. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 87% sequence identity to SEQ ID NO:1;
- 15 11. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 90% sequence identity to SEQ ID NO:1;
12. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has at least about 93% sequence identity to SEQ ID NO:1;
13. The mimylin peptide according to any one of the preceding aspects, wherein said 20 mimylin peptide has at least about 96% sequence identity to SEQ ID NO:1;
14. The mimylin peptide according to any one of the preceding aspects, having ≤ about 70% sequence identity with salmon calcitonin;
15. The mimylin peptide according to any one of the preceding aspects, having having ≤ about 70% sequence identity with eel calcitonin;
- 25 16. The mimylin peptide according to any one of the preceding aspects, having having ≤ about 70% sequence identity with any calcitonin variant;
17. The mimylin peptide according to any one of the preceding aspects, having ≤ about 66% sequence identity with salmon calcitonin;
18. The mimylin peptide according to any one of the preceding aspects, having 30 having ≤ about 66% sequence identity with eel calcitonin;
19. The mimylin peptide according to any one of the preceding aspects, having having ≤ about 66% sequence identity with any calcitonin variant;
20. The mimylin peptide according to any one of the preceding aspects, having ≤ about 60% sequence identity with salmon calcitonin;
- 35 21. The mimylin peptide according to any one of the preceding aspects, having having ≤ about 60% sequence identity with eel calcitonin;

22. The mimylin peptide according to any one of the preceding aspects, having having \leq about 60% sequence identity with any calcitonin variant;
23. The mimylin peptide according to any one of the preceding aspects wherein up to 11 amino acids have been modified by means of substitutions or deletions of one or 5 more of amino acids relative to SEQ ID NO: 1;
24. The mimylin peptide according to any one of the preceding aspects wherein up to 10 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
25. The mimylin peptide according to any one of the preceding aspects wherein up 10 to 9 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
26. The mimylin peptide according to any one of the preceding aspects wherein up to 8 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
27. The mimylin peptide according to any one of the preceding aspects wherein up 15 to 7 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
28. The mimylin peptide according to any one of the preceding aspects wherein up 20 to 6 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
29. The mimylin peptide according to any one of the preceding aspects wherein up to 5 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
30. The mimylin peptide according to any one of the preceding aspects wherein up 25 to 4 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
31. The mimylin peptide according to any one of the preceding aspects wherein up to 3 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
32. The mimylin peptide according to any one of the preceding aspects wherein up 30 to 2 amino acids have been modified by means of substitutions or deletions of one or more of amino acids relative to SEQ ID NO: 1;
33. The mimylin peptide according to any one of the preceding aspects wherein 1 amino acid has been modified by means of substitution or deletion of one amino acid 35 relative to SEQ ID NO: 1;

34. A mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a c-terminal amide group;
35. A mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises an amide group in its c-terminal;
- 5 36. A mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a c-terminal acid;
37. A mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide does not comprise a c-terminal acid;
- 10 38. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide does not comprise any disulfide bridge;
39. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide does not comprise a disulfide bridge between the amino acids in positions 2 and 8, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 15 40. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide does not comprise cystein residues in one or both positions 2 and 8, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
41. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises up to one cystein residue;
- 20 42. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide does not comprise any cysteins;
43. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in one, more or all of the positions selected from 5, 10, 13, 17, 20 and 23, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 25 44. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 5, 10 and 13, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
45. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 5, 10, 13 and 17, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 30 46. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 5, 10, 13, 17 and 20, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
47. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 10, 13, 17 and 20, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 35

48. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 10, 13, 17, 20 and 23, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
49. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises L in positions 5, 10, 13, 17, 20 and 23, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
50. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises R in one or more of the positions 12 or 25, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 10 51. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises R in both positions 12 and 25, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
52. The mimylin peptide according to any one of the preceding aspects 35-41 further comprising R in one or both of the positions 12 or 25, wherein the amino acid 15 numbering corresponds to SEQ ID NO: 1;
53. The mimylin peptide according to any one of the aspects 35-41 further comprising R in both positions 12 and 25, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
54. The mimylin peptide according to any one of the preceding aspects, wherein said 20 mimylin peptide comprises a P, Y, H, F, L, S, G or A in position 33, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
55. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a P, Y, H, F, L, S or A in position 33, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
- 25 56. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a P, Y, H or F in position 33, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
57. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a P, Y or F in position 33, wherein the amino acid 30 numbering corresponds to SEQ ID NO: 1;
58. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises a P or Y in position 33, wherein the amino acid numbering corresponds to SEQ ID NO: 1;
59. The mimylin peptide according to any one of the preceding aspects, wherein said 35 mimylin peptide comprises a P or in position 33, wherein the amino acid numbering corresponds to SEQ ID NO: 1;

60. The mimylin peptide according to any one of the preceding aspects, wherein said peptide does not comprise any N;

61. The mimylin peptide according to any one of the preceding aspects, wherein said peptide does not comprise N in position 4 or position 27

5 62. The mimylin peptide according to any one of the preceding aspects, wherein said peptide does not comprise any Q;

63. The mimylin peptide according to any one of the preceding aspects, wherein said peptide only comprises one Q;

64. The mimylin peptide according to any one of the preceding aspects, wherein said 10 peptide only comprises up to 2 Q; The mimylin peptide according to any one of the preceding aspects, wherein said peptide does not comprise any K;

65. The mimylin peptide according to any one of the preceding aspects, wherein said peptide does not comprises one or more K;

66. The mimylin peptide according to any one of the preceding aspects, wherein said 15 mimylin peptide does not comprise any aromatic amino acids;

67. The mimylin peptide according to any one of the preceding aspects 1-65, wherein said mimylin peptide comprises at least one of the following amino acids or modifications relative to SEQ ID NO: 1:

20 a. E or no amino acid in position -1,

b. E, A or no amino acid in position 1,

c. A, L or P in position 2,

d. S or P in position 3,

e. E, P, K, Q or G in position 4,

f. L, V, I or H in position 5,

25 g. S, T or H in position 6,

h. T in position 7,

i. L or A in position 8,

j. A, V, I, S or T in position 9,

k. L, A, I, H or V in position 10,

30 l. G in position 11,

m. R, H or K in position 12,

n. L in position 13 ,

o. S, T or E in position 14,

p. A, Q, E, e or T in position 15,

35 q. E, R, K or Q in position 16,

r. L or I in position 17,

- s. H or A in position 18,
- t. E, R or K in position 19,
- u. L, I or V in position 20,
- v. A, Q, S, E or T in position 21,
- 5 w. T in position 22,
- x. L or Y in position 23,
- y. P in position 24,
- z. R, P, H or K in position 25,
- aa. T in position 26,
- 10 bb. E, Q, G or K in position 27,
- cc. T or P in position 28,
- dd. G in position 29,
- ee. P, S or T in position 30,
- ff. E, Q, G, A, P or K in position 31,
- 15 gg. T, S, H, P or A in position 32,
- hh. P, Y, H, F, L, S, G or A in position 33,
- ii. G or K in position 34.

68. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises at least one of the following amino acids or 20 modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. P in position 3,
- 25 e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- g. T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 30 j. A, I, S or T in position 9,
- k. A, I, H or V in position 10,
- l. R, H in position 12,
- m. T or E in position 14,
- n. A, E, e or T in position 15,
- 35 o. R, K or Q in position 16,
- p. I in position 17,

- q. A in position 18,
- r. E or R in position 19,
- s. A, S, E or T in position 21,
- t. L in position 23,
- 5 u. R, P, H or K in position 25,
- v. E, Q, G or K in position 27,
- w. P in position 28,
- x. P, S or T in position 30,
- y. E, Q, G, A, P or K in position 31,
- 10 z. S, H, P or A in position 32,
- aa. Y, H, F, L, S, G or A in position 33,
- bb. G or K in position 34.

69. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises at least one of the following amino acids or 15 modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- 20 e. E, Q, G or P in position 4,
- f. L, V, I or H in position 5,
- g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 25 j. A, I, S or T in position 9,
- k. R, H in position 12,
- l. A, E, e or T in position 15,
- m. E or R in position 19,
- n. A, S, E or T in position 21,
- 30 o. L in position 23,
- p. E, Q, G or K in position 27,
- q. P, S or T in position 30,
- r. E, Q, G, A, P or K in position 31,
- s. S, H, P or A in position 32,
- 35 t. Y, H, F, L, S, G or A in position 33,
- u. G or K in position 34.

70. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises any one of the following amino acids or modifications relative to SEQ ID NO: 1:

- 5 a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- 10 g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- j. A, V, I, S or T in position 9,
- k. L, A, I, H or V in position 10,
- 15 l. G in position 11,
- m. R, H or K in position 12,
- n. L in position 13,
- o. S, T or E in position 14,
- p. A, Q, E, e or T in position 15,
- 20 q. R, E, K or Q in position 16,
- r. L or I in position 17,
- s. H or A in position 18,
- t. E, R or K in position 19,
- u. L, I or V in position 20,
- 25 v. A, Q, S, E or T in position 21,
- w. T in position 22,
- x. Y or L in position 23,
- y. P in position 24,
- z. R, P, H or K in position 25,
- 30 aa. T in position 26,
- bb. E, Q, G or K in position 27,
- cc. T or P in position 28,
- dd. G in position 29,
- ee. P, S or T in position 30,
- 35 ff. E, Q, G, A, P or K in position 31,
- gg. T, S, H, P or A in position 32,

hh. P, Y, H, F, L, S, G or A in position 33,
ii. G or K in position 34.

71. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises any one of the following amino acids or 5 modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. P in position 3,
- 10 e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- g. T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 15 j. A, I, S or T in position 9,
- k. A, I, H or V in position 10,
- l. R or H in position 12,
- m. T or E in position 14,
- n. A, E, e or T in position 15,
- 20 o. R, K or Q in position 16,
- p. I in position 17,
- q. A in position 18,
- r. E or R in position 19,
- s. A, S, E or T in position 21,
- 25 t. L in position 23,
- u. R, P, H or K in position 25,
- v. E, Q, G or K in position 27,
- w. P in position 28,
- x. P, S or T in position 30,
- 30 y. E, Q, G, A, P or K in position 31,
- z. S, H, P or A in position 32,
- aa. Y, H, F, L, S, G or A in position 33,
- bb. G or K in position 34.

72. The mimylin peptide according to any one of the preceding aspects 1-67, 35 wherein said mimylin peptide comprises any one of the following amino acids or modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- 5 e. E, Q, G or P in position 4,
- f. L, V, I or H in position 5,
- g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 10 j. A, I, S or T in position 9,
- k. R or H in position 12,
- l. A, E, e or T in position 15,
- m. E or R in position 19,
- n. A, S, E or T in position 21,
- 15 o. L in position 23,
- p. E, Q, G or K in position 27,
- q. P, S or T in position 30,
- r. E, Q, G, A, P or K in position 31,
- s. S, H, P or A in position 32,
- 20 t. Y, H, F, L, S, G or A in position 33,
- u. G or K in position 34.

73. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ

25 ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- 30 e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 35 j. A, V, I, S or T in position 9,
- k. L, A, I, H or V in position 10,

- I. G in position 11,
- m. R, H or K in position 12,
- n. L in position 13,
- o. S, T or E in position 14,
- 5 p. A, Q, E, e or T in position 15,
- q. R, E, K or Q in position 16,
- r. L or I in position 17,
- s. H or A in position 18,
- t. E, R or K in position 19,
- 10 u. L, I or V in position 20,
- v. A, Q, S, E or T in position 21,
- w. T in position 22,
- x. Y or L in position 23,
- y. P in position 24,
- 15 z. R, P, H or K in position 25,
- aa. T in position 26,
- bb. E, Q, G or K in position 27,
- cc. T or P in position 28,
- dd. G in position 29,
- 20 ee. P, S or T in position 30,
- ff. E, Q, G, A, P or K in position 31,
- gg. T, S, H, P or A in position 32,
- hh. P, Y, H, F, L, S, G or A in position 33,
- ii. G or K in position 34.

25 74. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1, 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. P in position 3,
- e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- 30 g. T or H in position 6,
- h. T in position 7,

- i. L or A in position 8,
- j. A, I, S or T in position 9,
- k. A, I, H or V in position 10,
- l. R or H in position 12,
- 5 m. T or E in position 14,
- n. A, E, e or T in position 15,
- o. R, K or Q in position 16,
- p. I in position 17,
- q. A in position 18,
- 10 r. E or R in position 19,
- s. A, S, E or T in position 21,
- t. L in position 23,
- u. R, P, H or K in position 25,
- v. E, Q, G or K in position 27,
- 15 w. P in position 28,
- x. P, S or T in position 30,
- y. E, Q, G, A, P or K in position 31,
- z. S, H, P or A in position 32,
- aa. Y, H, F, L, S, G or A in position 33,
- 20 bb. G or K in position 34.

75. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1, 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- 25 a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- e. E, Q, G or P in position 4,
- 30 f. L, V, I or H in position 5,
- g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- j. A, I, S or T in position 9,
- 35 k. R or H in position 12,
- l. A, E, e or T in position 15,

- m. E or R in position 19,
- n. A, S, E or T in position 21,
- o. L in position 23,
- p. E, Q, G or K in position 27,
- 5 q. P, S or T in position 30,
- r. E, Q, G, A, P or K in position 31,
- s. S, H, P or A in position 32,
- t. Y, H, F, L, S, G or A in position 33,
- u. G or K in position 34.

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76. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- 15 a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1, preferably E,
- c. A, L or P in position 2,
- d. S or P in position 3,
- e. E, P, K, Q or G in position 4,
- 20 f. L, V, I or H in position 5,
- g. S, T or H in position 6, preferably S,
- h. T in position 7,
- i. L or A in position 8, preferably A,
- j. A, V, I, S or T in position 9, preferably A or V or I,
- 25 k. L, A, I, H or V in position 10, preferably L or I,
- l. G in position 11,
- m. R, H or K in position 12,
- n. L in position 13,
- o. S, T or E in position 14,
- 30 p. A, Q, E, e or T in position 15, preferably A,
- q. E, R, K or Q in position 16, preferably E,
- r. L or I in position 17,
- s. H or A in position 18,
- t. E, R or K in position 19, preferably E,
- 35 u. L, I or V in position 20, preferably L,
- v. A, Q, S, E or T in position 21, preferably A,

- w. T in position 22,
- x. L or Y in position 23,
- y. P in position 24,
- z. R, P, H or K in position 25, preferably R,
- 5 aa. T in position 26,
- bb. E, Q, G or K in position 27, preferably E,
- cc. T or P in position 28,
- dd. G in position 29,
- ee. P, S or T in position 30,
- 10 ff. E, Q, G, A, P or K in position 31, preferably E or G,
- gg. T, S, H, P or A in position 32, preferably S or T,
- hh. P, Y, H, F, L, S, G or A in position 33 preferably P or Y,
- ii. G or K in position 34, preferably P or Y.

77. The mimylin peptide according to any one of the preceding aspects 1-67,

15 wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1, preferably E,
- 20 c. L, A or P in position 2,
- d. P in position 3,
- e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- g. T or H in position 6,
- 25 h. T in position 7,
- i. L or A in position 8, preferably A,
- j. A, I, S or T in position 9, preferably A or I,
- k. A, I, H or V in position 10, preferably I,
- l. R, H in position 12,
- 30 m. T or E in position 14,
- n. A, E, e or T in position 15, preferably A,
- o. R, K or Q in position 16,
- p. I in position 17,
- q. A in position 18,
- 35 r. E or R in position 19, preferably E,
- s. A, S, E or T in position 21,

- t. L in position 23,
- u. R, P, H or K in position 25, preferably R,
- v. E, Q, G or K in position 27, preferably E,
- w. P in position 28,
- 5 x. P, S or T in position 30,
- y. E, Q, G, A, P or K in position 31, preferably E or G,
- z. S, H, P or A in position 32 preferably S,
- aa. Y, H, F, L, S, G or A in position 33, preferably Y,
- bb. G or K in position 34.

10 78. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- 15 b. E, A or no amino acid in position 1, preferably E,
- c. L, A or P in position 2,
- d. S or P in position 3,
- e. E, Q, G or P in position 4,
- f. L, V, I or H in position 5,
- 20 g. S, T or H in position 6, preferably S,
- h. T in position 7,
- i. L or A in position 8, preferably A,
- j. A, I, S or T in position 9, preferably A or V or I,
- k. R, H in position 12,
- 25 l. A, E, e or T in position 15, preferably A,
- m. E or R in position 19, preferably E,
- n. A, S, E or T in position 21, preferably E,
- o. L in position 23,
- p. E, Q, G or K in position 27, preferably E,
- 30 q. P, S or T in position 30,
- r. E, Q, G, A, P or K in position 31, preferably E or G,
- s. S, H, P or A in position 32 preferably S or G,
- t. Y, H, F, L, S, G or A in position 33, preferably P or Y,
- u. G or K in position 34.

35 79. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most

preferably 1 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ

ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1, preferably E,
- c. A, L or P in position 2,
- d. S or P in position 3,
- e. E, P, K, Q or G in position 4,
- f. L, V, I or H in position 5,
- g. S, T or H in position 6, preferably S,
- h. T in position 7,
- i. L or A in position 8, preferably A,
- j. A, V, I, S or T in position 9, preferably A or V or I,
- k. L, A, I, H or V in position 10, preferably L or I,
- l. G in position 11,
- m. R, H or K in position 12,
- n. L in position 13,
- o. S, T or E in position 14,
- p. A, Q, E, e or T in position 15, preferably A,
- q. E, R, K or Q in position 16, preferably E,
- r. L or I in position 17,
- s. H or A in position 18,
- t. E, R or K in position 19, preferably E,
- u. L, I or V in position 20, preferably L,
- v. A, Q, S, E or T in position 21, preferably A,
- w. T in position 22,
- x. L or Y in position 23,
- y. P in position 24,
- z. R, P, H or K in position 25, preferably R,
- aa. T in position 26,
- bb. E, Q, G or K in position 27, preferably E,
- cc. T or P in position 28,
- dd. G in position 29,
- ee. P, S or T in position 30,
- ff. E, Q, G, A, P or K in position 31, preferably E or G,
- gg. T, S, H, P or A in position 32, preferably S or T,
- hh. P, Y, H, F, L, S, G or A in position 33 preferably P or Y,

ii. G or K in position 34, preferably P or Y.

80. The mimylin peptide according to any one of the preceding aspects 1-67, wherein said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1, 2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ

5 ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1, preferably E,
- c. L, A or P in position 2,
- d. P in position 3,
- 10 e. E, Q, G or P in position 4,
- f. V, I or H in position 5,
- g. T or H in position 6,
- h. T in position 7,
- i. L or A in position 8, preferably A,
- 15 j. A, I, S or T in position 9, preferably A or I,
- k. A, I, H or V in position 10, preferably I,
- l. R, H in position 12,
- m. T or E in position 14,
- n. A, E, e or T in position 15, preferably A,
- 20 o. R, K or Q in position 16,
- p. I in position 17,
- q. A in position 18,
- r. E or R in position 19, preferably E,
- s. A, S, E or T in position 21,
- 25 t. L in position 23,
- u. R, P, H or K in position 25, preferably R,
- v. E, Q, G or K in position 27, preferably E,
- w. P in position 28,
- x. P, S or T in position 30,
- 30 y. E, Q, G, A, P or K in position 31, preferably E or G,
- z. S, H, P or A in position 32 preferably S,
- aa. Y, H, F, L, S, G or A in position 33, preferably Y,
- bb. G or K in position 34.

81. The mimylin peptide according to any one of the preceding aspects 65, wherein
35 said mimylin peptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, most preferably 1,
2, 3, 4 or 5 of the following amino acids or modifications relative to SEQ ID NO: 1:

- a. E or no amino acid in position -1,
- b. E, A or no amino acid in position 1,
- c. L, A or P in position 2,
- d. S or P in position 3,
- 5 e. E, Q, G or P in position 4,
- f. L, V, I or H in position 5,
- g. S, T or H in position 6,
- h. T in position 7,
- i. L or A in position 8,
- 10 j. A, I, S or T in position 9,
- k. R or H in position 12,
- l. A, E, e or T in position 15,
- m. E or R in position 19,
- n. A, S, E or T in position 21,
- 15 o. L in position 23,
- p. E, Q, G or K in position 27,
- q. P, S or T in position 30,
- r. E, Q, G, A, P or K in position 31,
- s. S, H, P or A in position 32,
- 20 t. Y, H, F, L, S, G or A in position 33,
- u. G or K in position 34.

82. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

83. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29, wherein position 33 remains P or is modified to Y, F, H, S, G or A, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

84. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29, wherein position 33 remains P, Y or F, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

85. The mimylin peptide according to any one of the preceding, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

5 86. The mimylin peptide according to any one of the any one of the preceding, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29 , wherein position 33 remains P, Y, F, H, S, G or A, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

10 87. The mimylin peptide according to any one of the any one of the preceding, wherein said mimylin peptide comprises T in position 7, G in position 11, L in position 13, T in position 22, P in position 24, T in position 26 and G in position 29 , wherein position 33 remains P, Y or F, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

15 88. The mimylin peptide according to any one of the preceding aspects wherein an E is added in the position -1 , wherein the amino acid numbering corresponds to SEQ ID NO: 1.

89. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 2, 3, 4, 5, 6, 8, 20 9, 10, 12, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 30, 31, 32 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

25 90. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in up to 11, up to 10, up to 9, up to 8, up to 7, up to 6, preferably up to 5, up to 4, up to 3, up to 2 or 1 of the positions selected from the group consisting of: 1, 2, 3, 4, 5, 6, 8, 9, 10, 12, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 30, 31, 32 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

91. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 2, 4, 8, 9, 15, 30 21, 23, 25, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

92. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in up to 11 of the positions 1, 2, 4, 8, 9, 15, 21, 23, 25, 27, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

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93. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 11 of the positions 1, 2, 4, 8, 9, 15, 21, 23, 25, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

5 94. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 2, 4, 8, 9, 15, 21, 23, 25, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

10 E in said position 1 is absent,
position 2 can be modified to L,
position 4 can be modified to G,
position 8 can be modified to L,
position 9 can be modified to V or T,

15 position 15 can be modified to Q,
position 21 can be modified to Q,
position 23 can be modified to Y,
position 25 can be modified to P,
position 30 can be modified to S,

20 position 31 can be modified to G or Q,
position 32 can be modified to T,
position 33 can be modified to Y, H, F, L, S, G or A, preferably Y.

95. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 9, 15, 21, 23, 25, 27, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

25 96. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 10 of the positions 1, 4, 9, 15, 21, 23, 25, 27, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

30 97. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 10 of the positions 1, 4, 9, 15, 21, 23, 25, 27, 30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

35 98. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the 1, 4, 9, 15, 21, 23, 25, 27,

30, 31, 32, 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

- E in said position 1 is absent,
- 5 position 4 can be modified to G or Q,
- position 9 can be modified to V or T,
- position 15 can be modified to Q,
- position 21 can be modified to Q,
- position 23 can be modified to Y,
- 10 position 25 can be modified to H or P,
- position 27 can be modified to G,
- position 30 can be modified to S,
- position 31 can be modified to G, Q or A,
- position 32 can be modified to T,
- 15 position 33 can be modified to Y.

99. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 15, 21, 23, 30, 32, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1

20 100. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 9 of the positions 1, 4, 15, 21, 23, 30, 32, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1

25 101. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 9 of the positions 1, 4, 15, 21, 23, 30, 32, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1

30 102. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the 1, 4, 15, 21, 23, 30, 32, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

- E in said position 1 is absent,
- position 4 can be modified to G,
- 35 position 9 can be modified to V,
- position 15 can be modified to Q, T or E,

position 21 can be modified to Q or E,
position 23 can be modified to Y,
position 30 can be modified to S,
position 31 can be modified to G, Q or K,
5 position 32 can be modified to T,
position 33 can be modified to Y.

103. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 6, 9, 14, 15, 21, 23, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

104. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 8 of the positions 1, 4, 6, 9, 14, 15, 21, 23, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

15 105. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 8 of the positions 1, 4, 6, 9, 14, 15, 21, 23, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

106. The mimylin peptide according to any one of the preceding aspects, wherein said 20 mimylin peptide has been modified in one or more of the positions 1, 4, 6, 9, 14, 15, 21, 23, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

25 E in said position 1 is absent,
position 4 can be modified to G,
position 6 can be modified to T,
position 9 can be modified to V,
position 14 can be modified to T or S,
position 15 can be modified to Q,
30 position 21 can be modified to Q, T or E,
position 23 can be modified to Y,
position 30 can be modified to S or T,
position 31 can be modified to G,
position 32 can be modified to T,
35 position 33 can be modified to Y.

107. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 5, 6, 9, 10, 12, 20, 21, 23, 25, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

5 108. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 7 of the positions 1, 4, 5, 6, 9, 10, 12, 20, 21, 23, 25, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

10 109. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 7 of the positions 1, 4, 5, 6, 9, 10, 12, 20, 21, 23, 25, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

15 110. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 5, 6, 9, 10, 12, 20, 21, 23, 25, 30, 31, 21 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

E in said position 1 is absent,
position 4 can be modified to G,
20 position 5 can be modified to V,
position 6 can be modified to T,
position 9 can be modified to V, T or S,
position 10 can be modified to V,
position 12 can be modified to K,
25 position 20 can be modified to V,
position 21 can be modified to S,
position 23 can be modified to Y,
position 25 can be modified to K,
position 30 can be modified to S,
30 position 31 can be modified to G,
position 32 can be modified to S,
position 33 can be modified to Y.

111. The mimylin peptide according to aspect 107 does not comprise K.

112. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 5, 6, 9, 10, 21,

23, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

113. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 6 of the positions 1, 5, 6, 9, 10, 21, 23, 30, 5 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

114. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 6 of the positions 1, 5, 6, 9, 10, 21, 23, 30, 31, 10 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

115. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the 1, 5, 6, 9, 10, 21, 23, 30, 15 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

E in said position 1 is absent,
position 5 can be modified to V,
position 6 can be modified to T,
position 9 can be modified to V, T or S,
20 position 10 can be modified to V,
position 21 can be modified to S,
position 23 can be modified to Y,
position 30 can be modified to S or T,
position 31 can be modified to G,
25 position 32 can be modified to T and
position 33 can be modified to Y.

116. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions -1, 1, 4, 5, 6, 9, 12, 16, 21, 23, 25, 30, 31, 32, 33 or 34 of SEQ ID NO: 1, wherein the amino acid 30 numbering corresponds to SEQ ID NO: 1.

117. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 5 of the positions -1, 1, 4, 5, 6, 9, 12, 16, 21, 23, 25, 30, 31, 32, 33 and 34 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

35 118. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 5 of the positions -1, 1, 4, 5, 6, 9, 12, 16, 21,

23, 25, 30, 31, 32, 33 and 34 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

119. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions -1, 1, 4, 5, 6, 9, 5 12, 16, 21, 23, 25, 30, 31, 32, 33 or 34 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

position -1 can be modified to E or is absent

position 1 can be modified to A or deleted,

10 position 4 can be modified to G,

position 5 can be modified to V,

position 6 can be modified to T,

position 9 can be modified to V,

position 12 can be modified to H,

15 position 21 can be modified to S,

position 23 can be modified to Y,

position 25 can be modified to H,

position 30 can be modified to S,

position 31 can be modified to G,

20 position 32 can be modified to A,

position 33 can be modified to Y and

position 34 can be modified to K.

120. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 5, 9, 12, 15, 25 16, 19, 20, 23, 25, 27, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

121. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 4 of the positions 1, 4, 5, 9, 12, 15, 16, 19, 20, 23, 25, 27, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid 30 numbering corresponds to SEQ ID NO: 1.

122. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 4 of the positions 1, 4, 5, 9, 12, 15, 16, 19, 20, 23, 25, 27, 30, 31, 32 and 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

35 123. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 4, 5, 9, 10 12,

15, 16, 19, 20, 23, 25, 27, 30, 31, 32 or 33 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

position 1 can be modified to A or deleted,

5 position 4 can be modified to K or Q,
position 5 can be modified to I,
position 9 can be modified to V or I,
position 10 can be modified to I,
position 12 can be modified to H,

10 position 15 can be modified to E or e,
position 20 can be modified to I,
position 23 can be modified to Y,
position 25 can be modified to H,
position 27 can be modified to K

15 position 30 can be modified to S,
position 31 can be modified to G,
position 32 can be modified to T or P, and
position 33 can be modified Y, H, F, L, S, A or G, preferably Y.

124. The mimylin peptide according to any one of the preceding aspects, wherein said
20 mimylin peptide has been modified in one or more of the positions 1, 3, 4, 5, 9,
10, 12, 20, 23, 25, 30 or 31 of SEQ ID NO: 1, wherein the amino acid numbering
corresponds to SEQ ID NO: 1.

125. The mimylin peptide according to any one of the preceding aspects, wherein said
25 mimylin peptide has been modified up to 3 of the positions 1, 3, 4, 5, 9, 10, 12, 20,
23, 25, 30 and 31, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

126. The mimylin peptide according to any one of the preceding aspects, wherein said
30 mimylin peptide has been modified in 3 of the positions 1, 3, 4, 5, 9, 10, 12, 20, 23,
25, 30 and 31, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

127. The mimylin peptide according to any one of the preceding aspects, wherein said
35 mimylin peptide has been modified in one or more of the positions 1, 3, 4, 5, 9, 10,
12, 20, 23, 25, 30 and 31 of SEQ ID NO: 1, wherein the amino acid numbering
corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected
from the list consisting of:

position 1 can be deleted,

35 position 3 can be modified to P,
position 4 can be modified to P,

position 5 can be modified to I,
position 9 can be modified to V or I,
position 10 can be modified to I,
position 12 can be modified to K,
5 position 20 can be modified to V,
position 23 can be modified to Y,
position 25 can be modified to K,
position 30 can be modified to S, and
position 31 can be modified to G.

10 128. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 2,3, 4, 5, 9, 10, 18, 25, 28, 30 or 31 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

15 129. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified up to 2 of the positions 1, 2,3, 4, 5, 9, 10, 18 25, 28, 30 and 31 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

20 130. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in 2 of the positions 1, 2,3, 4, 5, 9, 10, 18 25, 28, 30 and 31 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

25 131. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 2,3, 4, 5, 9, 10, 18, 25, 28, 30 and 31 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

30 position 1 can be deleted,
position 2 can be modified to P,
position 3 can be modified to P,
position 4 can be modified to P,
position 5 can be modified to I or V,
position 9 can be modified to V or I,
position 10 can be modified to I,
position 18 can be modified to A,
35 position 25 can be modified to P,
position 28 can be modified with P,

position 30 can be modified to S, and
position 31 can be modified to G.

132. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one of the positions 1, 5, 6, 8, 9, 17, 20, 23 or 5 32 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

133. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide has been modified in one or more of the positions 1, 5, 6, 8, 9, 17, 10 20, 23 and 32 of SEQ ID NO: 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1, wherein said one or more modifications are selected from the list consisting of:

position 1 can be deleted,
position 5 can be modified to H,
position 6 can be modified to H,
15 position 8 can be modified to L,
position 9 can be modified to L, V or I,
position 17 can be modified to I,
position 20 can be modified to I,
position 23 can be modified to Y,
20 position 28 can be modified with P, and
position 32 can be modified to H.

134. The mimylin peptide according to any one of the preceding aspects, wherein said mimylin peptide comprises an E in position 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

25 135. The mimylin peptide according to any one of the preceding aspects, wherein positions 10, 13, 17 and 20 are L, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

136. The mimylin peptide according to any one of the preceding aspects, wherein position 23 is L, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

30 137. The mimylin peptide according to any one of the preceding aspects, wherein position 9 is V, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

138. The mimylin peptide according to any one of the preceding aspects, wherein position 30 is S and/or position 31 is G, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

35 139. The mimylin peptide according to any one of the preceding aspects, wherein a G is added in position 34 and the amino acid numbering corresponds to SEQ ID NO: 1.

140. The mimylin peptide according to any one of the preceding aspects, wherein a G is added in position 34 and the amino acid numbering corresponds to SEQ ID NO: 1.
141. The mimylin peptide according to any one of the preceding aspects comprising the sequence EASELSTAALGRLSAELHELATLPRTEGPESP (SEQ ID NO: 1).
- 5 142. The mimylin peptide according to any one of the preceding aspects comprising the sequence EASELSTAALGRLSAELHELATLPRTEGSGSP (SEQ ID NO: 19).
143. The mimylin peptide according to any one of the preceding aspects comprising the sequence selected from the group consisting of the compounds listed in Table 2.
144. The mimylin peptide according to any one of the preceding aspects comprising 10 the sequence selected from the group consisting of the compounds listed in Table 4.
145. The mimylin peptide according to any one of the preceding aspects having the sequence EASELSTAALGRLSAELHELATLPRTEGPESP (SEQ ID NO: 1).
146. The mimylin peptide according to any one of the preceding aspects having the sequence EASELSTAALGRLSAELHELATLPRTEGSGSP (SEQ ID NO: 19).
- 15 147. The mimylin peptide according to any one of the preceding aspects having the sequence selected from the group consisting of the compounds listed in Table 4.
148. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #1bb to EX. #7bb.
149. The mimylin peptide according to any one of the preceding aspects, comprising a 20 sequence selected from the group consisting of EX. #8bb to EX. #20bb.
150. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #21bb to EX. #33bb
151. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #34bb to EX. #51bb
- 25 152. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #52bb to EX. #55bb and EX. #68bb to EX. #72bb.
153. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #56bb to EX. #67bb and EX. 30 #72bb to EX. #78bb and EX. #107bb.
154. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #79bb to EX. #90bb.
155. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #91bb to EX. #97bb.
- 35 156. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #98bb to EX. #102bb.

157. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #103bb to EX. #106bb.
158. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #8bb to EX. #20bb.
- 5 159. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #107bb to EX. #114bb.
160. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #115bb to EX. #124bb.
- 10 161. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #125bb to EX. #127bb.
162. The mimylin peptide according to any one of the preceding aspects, comprising a sequence selected from the group consisting of EX. #128bb to EX. #133bb.
163. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: mimylin.
- 15 164. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V]mimylin.
165. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5I]mimylin.
166. The mimylin peptide according to any one of the preceding aspects 1-162, 20 comprising sequence: [9I]mimylin.
167. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [17I]mimylin.
168. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [20I]mimylin.
- 25 169. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [18A]mimylin.
170. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9L]mimylin.
171. The mimylin peptide according to any one of the preceding aspects 1-162, 30 comprising sequence: [8L]mimylin.
172. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [6H]mimylin.
173. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5H]mimylin.
- 35 174. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [32H]mimylin.

175. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1]mimylin.
176. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [23Y]mimylin.
- 5 177. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [30S, 31G]mimylin.
178. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [30S, 31G]mimylin.
- 10 179. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S]mimylin.
180. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5V, 9V]mimylin.
181. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5I, 9I]mimylin.
- 15 182. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V, 10I]mimylin.
183. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9L, 10A]mimylin.
184. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [2P, 9V]mimylin.
- 20 185. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [3P, 9V]mimylin.
186. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [4P, 9V]mimylin.
- 25 187. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V, 25P]mimylin.
188. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V, 28P]mimylin.
189. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V, 18A]mimylin.
- 30 190. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [23Y, 30S, 31G]mimylin.
191. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31P]mimylin.
- 35 192. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5V, 9V, 20V]mimylin.

193. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5I, 9I, 10I]mimylin.
194. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [3P, 4P, 9V]mimylin.
- 5 195. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [9V, 12K, 25K]mimylin.
196. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
197. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
- 10 198. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
199. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
- 15 200. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
201. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
202. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
- 20 203. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
204. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
- 25 205. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 30S, 31G]mimylin.
206. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G]mimylin.
207. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 30S, 31G]mimylin.
- 30 208. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4K, 30S, 31G]mimylin.
209. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 16K, 30S, 31G]mimylin.
- 35 210. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 19K, 30S, 31G]mimylin.

211. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 27K, 30S, 31G]mimylin.
212. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 23Y, 30S, 31G]mimylin.
- 5 213. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [1A, 23Y, 30S, 31G]mimylin.
214. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 23Y, 30S, 31G]mimylin.
215. The mimylin peptide according to any one of the preceding aspects 1-162, 10 comprising sequence: [des1, 30S, 31G, 33Y]mimylin.
216. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G, 33H]mimylin.
217. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G, 33F]mimylin.
- 15 218. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 30S, 31G, 33L]mimylin.
219. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G, 33S]mimylin.
220. The mimylin peptide according to any one of the preceding aspects 1-162, 20 comprising sequence: [des1, 30S, 31G, 33G]mimylin.
221. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G, 33A]mimylin.
222. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 15E, 30S, 31G]mimylin.
- 25 223. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 15e, 30S, 31G]mimylin.
224. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4K, 30S, 31G]mimylin.
225. The mimylin peptide according to any one of the preceding aspects 1-162, 30 comprising sequence: [des1, 16K, 30S, 31G]mimylin.
226. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 19K, 30S, 31G]mimylin.
227. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 27K, 30S, 31G]mimylin.
- 35 228. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 12H, 30S, 31G]mimylin.

229. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 25H, 30S, 31G]mimylin.

230. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30T, 31G, 32T]mimylin.

5 231. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 30S, 31G, 32P]mimylin.

232. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 9V, 30S, 31G]mimylin.

233. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [5I, 9I, 10I, 20I]mimylin.

10 234. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4Q, 30S, 31G]mimylin.

235. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 23Y, 30S, 31G]mimylin.

15 236. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 23Y, 30S, 31G, 33Y]mimylin.

237. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 23Y, 30S, 31G, 32A]mimylin.

238. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 21S, 23Y, 30S, 31G]mimylin.

20 239. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [-1E, 1A, 23Y, 30S, 31G]mimylin.

240. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 12H, 25H, 30S, 31G]mimylin.

25 241. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 6T, 9V, 30S, 31G]mimylin.

242. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 5V, 9V, 30S, 31G]mimylin.

243. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4Q, 16Q, 30S, 31G]mimylin.

30 244. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 23Y, 30S, 31G, 33Y]mimylin.

245. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 23Y, 30S, 31G, 34G]mimylin.

35 246. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 23Y, 30S, 31G, 34K]mimylin.

247. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 9S, 23Y, 30S, 31G, 33Y]mimylin.

248. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 9T, 21S, 23Y, 30S, 31G]mimylin.

5 249. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 12H, 25H, 30T, 31G, 32T]mimylin.

250. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 6T, 9V, 30S, 31G, 32T]mimylin.

251. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 6T, 9V, 30T, 31G, 32T]mimylin.

10 252. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 5V, 9V, 10V, 30S, 31G]mimylin.

253. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 21S, 23Y, 30S, 31G, 33Y]mimylin.

15 254. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 23Y, 30S, 31G, 32T]mimylin.

255. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 9T, 21S, 23Y, 30S, 31G, 33Y]mimylin.

256. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 9S, 21S, 23Y, 30S, 31G, 33Y]mimylin.

20 257. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 12K, 23Y, 25K, 30S, 31G, 33Y]mimylin.

258. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 5V, 9V, 10V, 20V, 30S, 31G]mimylin.

25 259. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

260. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 23Y, 30S, 31G, 32T, 33Y]mimylin.

261. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 6T, 9V, 14T, 21E, 30T, 31G, 32T]mimylin.

30 262. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 6T, 9V, 14E, 21T, 30T, 31G, 32T]mimylin.

263. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21Q, 23Y, 30S, 31K, 32T, 33Y]mimylin.

35 264. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin.

265. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

266. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

5 267. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

268. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 4G, 15T, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin.

269. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15E, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

10 270. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

271. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [4Q, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y]mimylin.

15 272. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 4Q, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

273. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 15Q, 21Q, 23Y, 25H, 30S, 31G, 32T, 33Y]mimylin.

274. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

20 275. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

276. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

25 277. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

278. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31A, 32T, 33Y]mimylin.

279. The mimylin peptide according to any one of the preceding aspects, comprising sequence: [des1, 2L, 4G, 9V, 21S, 23Y, 30S, 31G, 32T, 33Y]mimylin.

30 280. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9T, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

281. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23Y, 25P, 30S, 31Q, 32T, 33Y]mimylin.

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282. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 8L, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

283. The mimylin peptide according to any one of the preceding aspects 1-162, 5 comprising sequence: [des1, 2L, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

284. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9T, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin.

10 285. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [2L, 4G, 8L, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y]mimylin.

286. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 15Q, 21Q, 23aQ, 23bT, 23cY, 30S, 31Q, 32T, 15 33Y]mimylin.

287. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 4G, 9V, 12K, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin.

288. The mimylin peptide according to any one of the preceding aspects 1-162, 20 comprising sequence: [des1, 4Q, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin.

289. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [des1, 2L, 4Q, 8L, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin.

25 290. The mimylin peptide according to any one of the preceding aspects 1-162, comprising sequence: [N-terminal(C18 diacid),C-terminal(-)]mimylin.

291. A mimylin derivative, wherein a mimylin peptide according to any one of the preceding aspects 1-162 is derivatised with a side chain.

292. The mimylin derivative according to aspect 280, wherein said mimylin peptide 30 according to any one of the aspects 1-162 is derivatised by bonding, in particular covalent bonding of a side chain to said mimylin peptide.

293. The mimylin derivative according to any one of the preceding aspects 163-292, wherein said derivatisation is performed by acylation chemistry.

294. The mimylin derivative according to any one of the preceding aspects 163-293, 35 wherein a mimylin peptide is derivatised in the N-terminal.

295. The mimylin derivative according to any one of the preceding aspects 163-295, wherein a mimylin peptide is derivatised in the alpha-amino group of the N-terminal amino acid.

296. The mimylin derivative according to any one of the preceding aspects 163-296, 5 wherein said fatty acid or diacid is directly attached to the N-terminal, wherein the N-terminal amino acid is E in position 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

297. The mimylin derivative according to any one of the preceding aspects 163-297, 10 wherein said mimylin peptide is derivatised at E in position 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

298. The mimylin derivative according to any one of the preceding aspects 163-298, wherein said mimylin peptide is derivatised at any K in the mimylin peptide sequence of any one of the mimylin peptides according to aspect 1-163.

299. The mimylin derivative according to aspect 298, wherein such K can be in 15 position, 4, 12, 16, 23, 18, 27 or 34, wherein the amino acid numbering is relative to SEQ ID NO: 1.

300. The mimylin derivative according to any one of the preceding aspects 163-299, wherein said fatty acid or diacid is covalently bonded to the alpha-amino group of the N-terminal amino residue, wherein the N-terminal amino acid is E in position 1 and 20 wherein the amino acid numbering is relative to SEQ ID NO: 1.

301. The mimylin derivative according to any one of the preceding aspects 163-300, wherein said fatty acid or diacid is covalently bonded to the alpha-amino group of the N-terminal amino residue, wherein any amino acid in position 1 is not an E and wherein the amino acid numbering is relative to SEQ ID NO: 1.

302. The mimylin derivative according to any one of the preceding aspects 163-301, 25 wherein said fatty acid or diacid is covalently bonded to the alpha-amino group of the N-terminal amino residue, wherein any amino acid in position 1 is any other amino acid than E and wherein the amino acid numbering is relative to SEQ ID NO: 1.

303. The mimylin derivative according to any one of the preceding aspects 163-302, 30 wherein said fatty acid or diacid is covalently bonded to the alpha-amino group of the N-terminal amino residue, wherein any amino acid in position 1 is any other amino acid than E, Q and/or N and wherein the amino acid numbering is relative to SEQ ID NO: 1.

304. The mimylin derivative according to any one of the aspects 163-303, comprising 35 a side chain, wherein said side chain comprises a protracting moiety.

305. The mimylin derivative according to any one of the aspects 163-304, comprising a side chain, wherein said side chain comprises a protracting moiety which is a fatty acid or diacid.

306. The mimylin derivative according to any one of the aspects 163-305, aspects 5 comprising a protracting moiety which is a fatty diacid.

307. The mimylin derivative according to any one of the aspects 163-306, wherein said fatty diacid comprises 14-20 carbon atoms.

308. The mimylin derivative according to any one of the aspects 163-307, wherein said fatty diacid comprises 14, 16, 18 or 20 carbon atoms.

10 309. The mimylin derivative according to any one of the aspects 163-308, wherein said fatty diacid comprises 18 carbon atoms.

310. The mimylin derivative according to any one of the aspects 163-309, wherein said fatty diacid comprises 20 carbon atoms.

15 311. The mimylin derivative according to any one of the aspects 163-310, wherein said fatty acid or diacid is directly attached to the N-terminal.

312. The mimylin derivative according to any one of the aspects 163-311, wherein said fatty acid or diacid is covalently bonded to the alpha-amino group of the N-terminal amino residue.

20 313. The mimylin derivative according to any one of the aspects 163-312, wherein said fatty acid or diacid is directly attached to the N-terminal, wherein any amino acid in position 1 is not an E and wherein said diacid comprises 20 carbon acids.

314. The mimylin derivative according to any one of the aspects 163-313, wherein said fatty acid or diacid is directly attached to the N-terminal, wherein any amino acid in position 1 is an amino acid is different from Q, N and/or E and wherein said diacid 25 comprises 20 carbon acids.

315. The mimylin derivative according to any one of the aspects 163-314, wherein a mimylin peptide is derivatised at E in in position 1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

316. The mimylin derivative according to any one of the aspects 163-315, wherein a mimylin peptide is derivatised at E in said mimylin peptides in position -1, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

30 317. The mimylin derivative according to any one of the aspects 163-316, wherein a mimylin peptide is derivatised at E in position 2, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

318. The mimylin derivative according to any one of the preceding aspects 163-317-, wherein a mimylin peptide is derivatised with a side chain comprising a protracting moiety and a linker.

319. The mimylin derivative according to any one of the preceding aspects 163-318, 5 wherein a mimylin peptide is derivatised in the N-terminal and wherein said mimylin peptide is derivatised with a side chain comprising a protracting moiety and a linker.

320. The mimylin derivative according to any one of the preceding aspects 163-319, wherein a mimylin peptide is derivatised in the N-terminal and wherein said mimylin peptide is derivatised with a side chain comprising a protracting moiety and no linker.

10 321. The mimylin derivative according to any one of the preceding aspects 163-320, wherein a mimylin peptide is derivatised in the N-terminal and wherein said mimylin peptide is derivatised with a side chain without a linker.

322. The mimylin derivative according to any one of the preceding preceding aspects 163-321, wherein said fatty acid or diacid is attached to the N-terminal or E in position 15 1 via a linker and wherein the amino acid numbering is relative to SEQ ID NO: 1.

323. The mimylin derivative according to any one of the preceding aspects 163-322, wherein a mimylin peptide is derivatised at any K present in the sequense, preferably in any one of the position selected from positions 4K, 16K, 19K and 27K.

324. A mimylin derivative according to any one of the aspects 163-323, wherein said 20 mimylin derivative is a mimylin peptide according to any one of the aspects 1-162 which is derivatised with a side chain comprising fatty acid or diacid and a linker.

325. The mimylin derivative according aspect to any one of the aspects 163-324, wherein said linker is an gGlu, gGlu-OEG, gGlu-OEG-OEG, gGlu-OEG-OEG-OEG, gGlu- 25 OEG-OEG-OEG, gGlu-OEG-OEG-OEG-OEG-OEG.

326. The mimylin derivative according to aspect 325, wherein said linker is a gGlu.

327. The mimylin derivative according to aspect 325, wherein said linker is a gGlu-OEG.

328. The mimylin derivative according to aspect 325, wherein said linker is a gGlu-OEG-OEG.

30 329. The mimylin derivative according to aspect 325, wherein said linker is a gGlu-OEG-OEG-OEG.

330. The mimylin derivative according to aspect 325, wherein said linker is a gGlu-OEG-OEG-OEG-OEG.

331. The mimylin derivative according to aspect 325, wherein said linker is a gGlu- 35 OEG-OEG-OEG-OEG.

332. The mimylin derivative according to aspect 331, wherein the side chain is selected from Table 6.

333. The mimylin derivative according to any one of the preceding aspects 163-332, increasing the half-life of more than 3 hours, preferably more than 6 hours, most 5 preferably more than 12 hours after intravenous treatment in rats when measured with Assay (**X**).

334. The mimylin derivative according to any one of the preceding aspects 163-333, increasing the half-life of more than 3 hours, preferably more than 13 hours after subcutaneous treatment in rats when measured with Assay (**X**).

10 335. The mimylin derivative according to any one of the preceding aspects 163-334, increasing the half-life of the mimylin peptide in mini pig relative to the corresponding mimylin peptide without a side chain according to any one of the aspects 1-162, measured according to Assay (**IX**).

336. The mimylin derivative according to any one of the preceding aspects 163-335, 15 with a T_{1/2} of about 1-200 hours longer than the T_{1/2} of compound of Ex. #1 or salmon calcitonin measured according to Assay (**IX**).

337. The mimylin derivative according to any one of the preceding aspects 163-336, with a T_{1/2} of about 1-200 hours, preferably \geq about 1 hour, \geq about 2 hour, \geq about 17, \geq about 32, \geq about 86, \geq about 87, \geq about 88, \geq about 90, \geq about 108, \geq 20 about 118, \geq about 171 hours measured according to Assay (**IX**).

338. The mimylin derivative according to any one of the preceding aspects 163-337, with a T_{1/2} of about 85 hours measured according to Assay (**IX**).

339. The mimylin derivative according to any one of the preceding aspects 163-338, 25 with a T_{1/2} of about 50-70 in LYD-pigs, preferably about 64 hours intravenously and has a subcutaneous bioavailability of about 80-100%, preferably about 99%, measured according to Assay (**XVI**).

340. The mimylin derivative according to any one of the preceding aspects 163-339, with a T_{1/2} of about 80-110 in Beagle dogs, preferably about 95 hours intravenously and a subcutaneous bioavailability of about 80-100%, preferably about 99%, 30 measured according to Assay (**XVII**).

341. The mimylin derivative according to any one of the preceding aspects 163-340, increasing the half-life of the mimylin peptide in human relative to the corresponding mimylin peptide without a side chain according to any one of the aspects 1-162.

342. The mimylin derivative according to any one of the preceding aspects 163-341, 35 comprising a G in position 34, wherein said G in position 34 is converted in such a way

that the resulting mimylin peptide comprises an amino acid in position 33 with a c-terminal amide and wherein the amino acid numbering corresponds to SEQ ID NO: 1.

343. The mimylin derivative according to any one of the preceding aspects 163-342, comprising a G in position 34, wherein said G in position 34 is converted with PAM 5 enzymes in such a way that the resulting mimylin peptide comprises an amino acid in position 33 with a c-terminal amide and wherein the amino acid numbering corresponds to SEQ ID NO: 1.

344. The mimylin derivative according to any one of the preceding aspects 163-343 comprising V in position 9, wherein the amino acid numbering corresponds to SEQ ID 10 NO: 1.

345. The mimylin derivative according to any one of the preceding aspects 163-344, comprising S in position 30 and/or G in position 31, wherein the amino acid numbering corresponds to SEQ ID NO: 1.

346. The mimylin derivative according to any one of the preceding aspects 163-345, 15 wherein said mimylin derivative has a calculated pI value of between about 3.5 to about 5.5.

347. The mimylin derivative according to any one of the preceding aspects 163-346, wherein said mimylin peptide has a pI value of between about 3.5 to about 5.5, 20 wherein the calculated pI is estimated by solving the equation $Q(pI) = 0$, with Q designation the net charge found by summing the protonation fraction of all ionizable sites in the molecule, wherein natural amino acid residues tabulated pKa-values are used for free terminales and ionizable sites in the side chains, wherein pKa-values for non-natural amino acid residues are estimated by ACD/Labs Software ver. 12 package, wherein compounds with more than 255 atoms and comprising residues 25 containing pseudo atoms should not have their pI estimated according to this method.

348. The mimylin derivative according to any one of the preceding aspects 163-347, wherein said mimylin peptide has a calculated pI value of about 4 to about 5.

349. The mimylin derivative according to any one of the preceding aspects 163-348, wherein said mimylin peptide has a calculated pI value of 4,5 plus or minus 1 pI value.

350. The mimylin derivative according to any one of the preceding aspects 163-349, 30 wherein said mimylin peptide has a calculated pI value of 4,5 plus or minus 1 pH value.

351. The mimylin derivative according to any one of the preceding aspects 163-350, wherein said mimylin peptide is soluble in the complete pH range, preferably in the pH 35 range about 6.0 to about 8.0.

352. The mimylin derivative according to any one of the preceding aspects 163-351, wherein said mimylin peptide is completely soluble in the complete pH range, preferably in the pH range about 6.0 to about 8.0, wherein completely soluble means that the solubility score is of $\geq 200\mu\text{M}$ tested in Assay IV.

5 353. The mimylin derivative according to any one of the preceding aspects 163-352, wherein said mimylin peptide is highly soluble in the complete pH range, preferably in the pH range about 6.0 to about 8.0, wherein highly soluble means that the solubility score is of $\geq 100\mu\text{M}$ tested in Assay IV.

10 354. The mimylin derivative according to any one of the preceding aspects 163-353, wherein said mimylin derivative is soluble in the pH ranges below about pH 3 and above about 5, when tested at a concentration of $200\mu\text{M}$ in Assay IV.

355. The mimylin derivative according to any one of the preceding aspects 163-354, wherein said mimylin peptide is soluble in the pH ranges below about 3 and above about 6.

15 356. The mimylin derivative according to any one of the preceding aspects 163-355, wherein said mimylin peptide is soluble in the pH ranges below about 3 and above about 6.5.

357. The mimylin derivative according to any one of the preceding aspects 163-356, wherein said mimylin peptide is soluble above pH about 4.

20 358. The mimylin derivative according to any one of the preceding aspects 163-357, wherein said mimylin peptide is soluble above pH about 5.

359. The mimylin derivative according to any one of the preceding aspects 163-358, wherein said mimylin peptide is soluble at pH about 3, 4, 5, 6 7, 8 and 9.

360. The mimylin derivative according to any one of the preceding aspects 163-359, wherein said mimylin peptide is soluble at pH about 3, 4, 7, 8 and 9.

25 361. The mimylin derivative according to any one of the preceding aspects 163-360, wherein said mimylin peptide is soluble at pH about 3, 6, 7, 8 and 9.

362. The mimylin derivative according to any one of the aspects 163-361, wherein said mimylin derivative is soluble in the complete pH range or soluble in the complete pH range, preferably between about 6.0 to about 8.0 and decreasing in solubility in the pH range around the said mimylin peptides pI.

30 363. The mimylin derivative according to any one of the aspects 163-362, wherein said mimylin derivative is soluble in the complete pH range or soluble in the complete pH range, preferably in the pH range about 6.0 to about 8.0 and decreasing in solubility in the pH range in the pH range plus or minus 1 pH value from said mimylin peptides pI.

35

364. The mimylin derivative according to any one of the aspects 163-363, wherein said mimylin derivative is soluble in the complete pH range or soluble in the complete pH range and not soluble in the pH range around the said mimylin peptides pI.

5 365. The mimylin derivative according to any one of the aspects 163-364, wherein said mimylin derivative is soluble in the complete pH range or soluble in the complete pH range and not soluble in the pH range in the pH range plus or minus 1 pH value from said mimylin peptides pI.

366. The mimylin derivative according to any one of the preceding aspects 163-365, selected from the compounds listed in table 16.

10 367. The mimylin derivative according to any one of the preceding aspects 163-366, wherein said derivative has a solubility of $\geq 200\mu\text{M}$ in the complete pH range tested, preferably in the range between pH 6.0 to about 8.0, tested in Assay IV selected from the compounds listed in Table 16, preferably Ex #2-19, 21-85, 87-88, 91-99, 101-106, 108-110, 112-114, 116-117, 119-125, 126-128, 130-131, most preferably Ex 15 #2-19, 21-85, 87-88, 91-99, 101-106, 108-110, 112-114, 116-117, 119-125, 126-127.

368. The mimylin derivative according to any one of the preceding aspects 163-367, which is selected from the group consisting of any one of the example compounds of Ex #2 to Ex #7.

20 369. The mimylin derivative according to any one of the preceding aspects 163-368, which is selected from the group consisting of any one of the example compounds Ex #8 to Ex #19.

370. The mimylin derivative according to any one of the preceding aspects 163-369, which is selected from the group consisting of any one of the example compounds Ex 25 Ex #21 to Ex #33.

371. The mimylin derivative according to any one of the preceding aspects 163-370, which is selected from the group consisting of any one of the example compounds Ex #34 to Ex #1.

372. The mimylin derivative according to any one of the preceding aspects 163-371, which is selected from the group consisting of any one of the example compounds Ex 30 Ex #52 to Ex #55 and Ex #68 to Ex #72.

373. The mimylin derivative according to any one of the preceding aspects 162-372, which is selected from the group consisting of any one of the example compounds Ex #56 to Ex #67 and Ex #72 to Ex #78 and Ex #107.

374. The mimylin derivative according to any one of the preceding aspects 163-373, which is selected from the group consisting of any one of the example compounds Ex #79 to Ex #90.

5 The mimylin derivative according to any one of the preceding aspects 163-374, which is selected from the group consisting of any one of the example compounds Ex #91 to Ex #97.

375. The mimylin derivative according to any one of the preceding aspects 163-374, which is selected from the group consisting of any one of the example compounds Ex #103 to Ex #106.

10 376. The mimylin derivative according to any one of the preceding aspects 163-375, which is selected from the group consisting of any one of the example compounds Ex #108 to Ex #114.

15 377. The mimylin derivative according to any one of the preceding aspects 163-376, which is selected from the group consisting of any one of the example compounds Ex #115 to Ex #124.

378. The derivatised mimylin peptide or mimylin derivative according to any one of the preceding aspects 163-376, which is selected from the group consisting of any one of the example compounds Ex #125 to Ex #127.

20 379. The derivatised mimylin peptide or mimylin derivative according to any one of the preceding aspects 163-378, which is selected from the group consisting of any one of the example compounds Ex #2 to Ex #33.

380. The mimylin derivative according to any one of the preceding aspects 163-379, which is a derivatised mimylin peptide selected from the group consisting of any one of the example compounds Ex #2 to Ex #131.

25 381. The mimylin derivative according to any one of the preceding aspects 163-380, which is a derivatised mimylin peptide selected from the group consisting of any one of the example compounds Ex #2 to Ex #127.

30 382. The derivative according to any one of the preceding aspects 163-381, comprising the sequence selected from the group consisting of the compounds listed in Table 1.

383. The mimylin derivative according to any one of the preceding aspects 163-382, comprising the sequence selected from the group consisting of the compounds listed in Table 3.

35 384. The mimylin derivative according to any one of the preceding aspects 163-384, comprising the sequence selected from the group consisting of the compounds listed in Table 5.

385. The mimylin derivative according to any one of the preceding aspects 163-384, having the compound name [N-terminal(C18 diacid)]mimylin.

386. The mimylin derivative according to any one of the preceding aspects 163-385, having the compound name [N-terminal(C16 diacid)]mimylin.

5 387. The mimylin derivative according to any one of the preceding aspects 163-386, having the compound name [N-terminal(C14 diacid)]mimylin.

388. The mimylin derivative according to any one of the preceding aspects 163-387, having the compound name [N-terminal(C14 diacid-2xGlu-4xOEG)]mimylin.

389. The mimylin derivative according to any one of the preceding aspects 163-388,

10 having the compound name [N-terminal(C12 diacid)]mimylin.

390. The mimylin derivative according to any one of the preceding aspects 163-389, having the compound name [N-terminal(C16)]mimylin.

391. The mimylin derivative according to any one of the preceding aspects 163-390, having the compound name [N-terminal(C18 diacid), 5I]mimylin.

15 392. The mimylin derivative according to any one of the preceding aspects 163-391, having the compound name [N-terminal(C18 diacid), 9V]mimylin.

393. The mimylin derivative according to any one of the preceding aspects 163-392, having the compound name [N-terminal(C18 diacid), 9I]mimylin.

394. The mimylin derivative according to any one of the preceding aspects 163-393,

20 having the compound name [N-terminal(C18 diacid), 17I]mimylin.

395. The mimylin derivative according to any one of the preceding aspects 163-394, having the compound name [N-terminal(C18 diacid), 20I]mimylin.

396. The mimylin derivative according to any one of the preceding aspects 163-395, having the compound name [N-terminal(C18 diacid), 18A]mimylin.

25 397. The mimylin derivative according to any one of the preceding aspects 163-396, having the compound name [N-terminal(C18 diacid), 9L]mimylin.

398. The mimylin derivative according to any one of the preceding aspects 163-397, having the compound name [N-terminal(C18 diacid), 8L]mimylin.

399. The mimylin derivative according to any one of the preceding aspects 163-398,

30 having the compound name [N-terminal(C18 diacid), 6H]mimylin.

400. The mimylin derivative according to any one of the preceding aspects 163-399, having the compound name [N-terminal(C18 diacid), 5H]mimylin.

401. The mimylin derivative according to any one of the preceding aspects 163-400, having the compound name [N-terminal(C18 diacid), 32H]mimylin.

35 402. The mimylin derivative according to any one of the preceding aspects 163-401, having the compound name [N-terminal(C14 diacid-gGlu), des1]mimylin.

403. The mimylin derivative according to any one of the preceding aspects 163-402, having the compound name [N-terminal(C18 diacid), 23Y]mimylin.

404. The mimylin derivative according to any one of the preceding aspects 163-403, having the compound name [N-terminal(C18 diacid), 30S, 31G]mimylin.

5 405. The mimylin derivative according to any one of the preceding aspects 163-404, having the compound name [N-terminal(C20 diacid), 30S, 31G]mimylin.

406. The mimylin derivative according to any one of the preceding aspects 163-405, having the compound name [N-terminal(C18 diacid-gGlu), des1, 30S]mimylin.

407. The mimylin derivative according to any one of the preceding aspects 163-406, 10 having the compound name [N-terminal(C18 diacid), 5V, 9V]mimylin.

408. The mimylin derivative according to any one of the preceding aspects 163-407, having the compound name [N-terminal(C18 diacid), 5I, 9I]mimylin.

409. The mimylin derivative according to any one of the preceding aspects 163-408, having the compound name [N-terminal(C18 diacid), 9V, 10I]mimylin.

15 410. The mimylin derivative according to any one of the preceding aspects 163-409, having the compound name [N-terminal(C18 diacid), 9L, 10A]mimylin.

411. The mimylin derivative according to any one of the preceding aspects 163-410, having the compound name [N-terminal(C18 diacid), 2P, 9V]mimylin.

412. The mimylin derivative according to any one of the preceding aspects 163-411, 20 having the compound name [N-terminal(C18 diacid), 3P, 9V]mimylin.

413. The mimylin derivative according to any one of the preceding aspects 163-412, having the compound name [N-terminal(C18 diacid), 4P, 9V]mimylin.

414. The mimylin derivative according to any one of the preceding aspects 163-413, having the compound name [N-terminal(C18 diacid), 9V, 25P]mimylin.

25 415. The mimylin derivative according to any one of the preceding aspects 163-414, having the compound name [N-terminal(C18 diacid), 9V, 28P]mimylin.

416. The mimylin derivative according to any one of the preceding aspects 163-415, having the compound name [N-terminal(C18 diacid), 9V, 18A]mimylin.

417. The mimylin derivative according to any one of the preceding aspects 163-416, 30 having the compound name [N-terminal(C20 diacid-gGlu), 23Y, 30S, 31G]mimylin.

418. The mimylin derivative according to any one of the preceding aspects 163-417, having the compound name [N-terminal(C18 diacid-gGlu), des1, 30S, 31P]mimylin.

419. The mimylin derivative according to any one of the preceding aspects 163-418, having the compound name [N-terminal(C18 diacid), 5V, 9V, 20V]mimylin.

35 420. The mimylin derivative according to any one of the preceding aspects 163-419, having the compound name [N-terminal(C18 diacid), 5I, 9I, 10I]mimylin.

421. The mimylin derivative according to any one of the preceding aspects 163-420, having the compound name [N-terminal(C18 diacid), 3P, 4P, 9V]mimylin.

422. The mimylin derivative according to any one of the preceding aspects 163-421, having the compound name [N-terminal(C18 diacid), 9V, 12K, 25K]mimylin.

5 423. The mimylin derivative according to any one of the preceding aspects 163-422, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G]mimylin.

424. The mimylin derivative according to any one of the preceding aspects 163-423, having the compound name [N-terminal(C20 diacid-gGlu-OEG), des1, 30S, 31G]mimylin.

10 425. The mimylin derivative according to any one of the preceding aspects 163-424, having the compound name [N-terminal(C20 diacid-gGlu-2xOEG), des1, 30S, 31G]mimylin.

426. The mimylin derivative according to any one of the preceding aspects 163-425, having the compound name [N-terminal(C20 diacid-gGlu-3xOEG), des1, 30S, 15 31G]mimylin.

427. The mimylin derivative according to any one of the preceding aspects 163-426, having the compound name [N-terminal(C20 diacid-gGlu-4xOEG), des1, 30S, 31G]mimylin.

428. The mimylin derivative according to any one of the preceding aspects 163-427, 20 having the compound name [N-terminal(C20 diacid-gGlu-5xOEG), des1, 30S, 31G]mimylin.

429. The mimylin derivative according to any one of the preceding aspects 163-428, having the compound name [N-terminal(C18 diacid-gGlu), des1, 30S, 31G]mimylin.

430. The mimylin derivative according to any one of the preceding aspects 163-429, 25 having the compound name [N-terminal(C16 diacid-gGlu), des1, 30S, 31G]mimylin.

431. The mimylin derivative according to any one of the preceding aspects 163-430, having the compound name [N-terminal(C18 diacid), des1, 30S, 31G]mimylin.

432. The mimylin derivative according to any one of the preceding aspects 163-431, having the compound name [N-terminal(C16 diacid), des1, 30S, 31G]mimylin.

30 433. The mimylin derivative according to any one of the preceding aspects 163-432, having the compound name [N-terminal(C14 diacid-gGlu), des1, 30S, 31G]mimylin.

434. The mimylin derivative according to any one of the preceding aspects 163-433, having the compound name [N-terminal(C14 diacid), des1, 30S, 31G]mimylin.

435. The mimylin derivative according to any one of the preceding aspects 163-434, 35 having the compound name [des1, 4K(C20 diacid-gGlu), 30S, 31G]mimylin.

436. The mimylin derivative according to any one of the preceding aspects 163-435, having the compound name [des1, 16K(C20 diacid-gGlu), 30S, 31G]mimylin.

437. The mimylin derivative according to any one of the preceding aspects 163-436, having the compound name [des1, 19K(C20 diacid-gGlu), 30S, 31G]mimylin.

5 438. The mimylin derivative according to any one of the preceding aspects 163-437, having the compound name [des1, 27K(C20 diacid-gGlu), 30S, 31G]mimylin.

439. The mimylin derivative according to any one of the preceding aspects 163-438, having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G]mimylin.

10 440. The mimylin derivative according to any one of the preceding aspects 163-439, having the compound name [N-terminal(C20 diacid-gGlu), 1A, 23Y, 30S, 31G]mimylin.

441. The mimylin derivative according to any one of the preceding aspects 163-440, having the compound name [N-terminal(C18 diacid-gGlu), des1, 23Y, 30S, 15 31G]mimylin.

442. The mimylin derivative according to any one of the preceding aspects 163-441, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33Y]mimylin.

443. The mimylin derivative according to any one of the preceding aspects 163-442, 20 having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33H]mimylin.

444. The mimylin derivative according to any one of the preceding aspects 163-443, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33F]mimylin.

25 445. The mimylin derivative according to any one of the preceding aspects 163-444, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33L]mimylin.

446. The mimylin derivative according to any one of the preceding aspects 163-445, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 30 33S]mimylin.

447. The mimylin derivative according to any one of the preceding aspects 163-446, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33G]mimylin.

448. The mimylin derivative according to any one of the preceding aspects 163-447, 35 having the compound name [N-terminal(C20 diacid-gGlu), des1, 30S, 31G, 33A]mimylin.

449. The mimylin derivative according to any one of the preceding aspects 163-448, having the compound name [N-terminal(C20 diacid-gGlu), des1, 15E, 30S, 31G]mimylin.

450. The mimylin derivative according to any one of the preceding aspects 163-449, 5 having the compound name [N-terminal(C20 diacid-gGlu), des1, 15e, 30S, 31G]mimylin.

451. The mimylin derivative according to any one of the preceding aspects 163-450, having the compound name [N-terminal(acetyl), des1, 4K(C20 diacid-gGlu), 30S, 31G]mimylin.

10 452. The mimylin derivative according to any one of the preceding aspects 163-451, having the compound name [N-terminal(acetyl), des1, 16K(C20 diacid-gGlu), 30S, 31G]mimylin.

453. The mimylin derivative according to any one of the preceding aspects 163-452, having the compound name [N-terminal(acetyl), des1, 19K(C20 diacid-gGlu), 30S, 15 31G]mimylin.

454. The mimylin derivative according to any one of the preceding aspects 163-553, having the compound name [N-terminal(acetyl), des1, 27K(C20 diacid-gGlu), 30S, 31G]mimylin.

455. The mimylin derivative according to any one of the preceding aspects 163-454, 20 having the compound name [N-terminal(C20 diacid-gGlu), des1, 12H, 30S, 31G]mimylin.

456. The mimylin derivative according to any one of the preceding aspects 163-455, having the compound name [N-terminal(C20 diacid-gGlu), des1, 25H, 30S, 31G]mimylin.

25 457. The mimylin derivative according to any one of the preceding aspects 163-456, having the compound name [N-terminal(C20 diacid-gGlu), des1, 30T, 31G, 32T]mimylin.

458. The mimylin derivative according to any one of the preceding aspects 163-457, having the compound name [N-terminal(C18 diacid-gGlu), des1, 30S, 31G, 30 32P]mimylin.

459. The mimylin derivative according to any one of the preceding aspects 163-458, having the compound name [N-terminal(C18 diacid-gGlu), des1, 9V, 30S, 31G]mimylin.

460. The mimylin derivative according to any one of the preceding aspects 163-459, 35 having the compound name [N-terminal(C18 diacid), 5I, 9I, 10I, 20I]mimylin.

461. The mimylin derivative according to any one of the preceding aspects 163-460, having the compound name [N-terminal(C18 diacid-gGlu), des1, 4Q, 30S, 31G]mimylin.

462. The mimylin derivative according to any one of the preceding aspects 163-461, 5 having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 23Y, 30S, 31G]mimylin.

463. The mimylin derivative according to any one of the preceding aspects 163-462, having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 33Y]mimylin.

10 464. The mimylin derivative according to any one of the preceding aspects 163-463, having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 32A]mimylin.

465. The mimylin derivative according to any one of the preceding aspects 163-464, having the compound name [N-terminal(C20 diacid-gGlu), des1, 21S, 23Y, 30S, 15 31G]mimylin.

466. The mimylin derivative according to any one of the preceding aspects 163-465, having the compound name [N-terminal(C20 diacid-gGlu), -1E, 1A, 23Y, 30S, 31G]mimylin.

467. The mimylin derivative according to any one of the preceding aspects 163-466, 20 having the compound name [N-terminal(C20 diacid-gGlu), des1, 12H, 25H, 30S, 31G]mimylin.

468. The mimylin derivative according to any one of the preceding aspects 163-467, having the compound name [N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30S, 31G]mimylin.

25 469. The mimylin derivative according to any one of the preceding aspects 163-468, having the compound name [N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 30S, 31G]mimylin.

470. The mimylin derivative according to any one of the preceding aspects 163-469, having the compound name [N-terminal(C18 diacid-gGlu), des1, 4Q, 16Q, 30S, 30 31G]mimylin.

471. The mimylin derivative according to any one of the preceding aspects 163-470, having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 33Y, C-terminal(-)]mimylin.

472. The mimylin derivative according to any one of the preceding aspects 163-471, 35 having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 34G, C-terminal(-)]mimylin.

473. The mimylin derivative according to any one of the preceding aspects 163-472, having the compound name [N-terminal(C20 diacid-gGlu), des1, 23Y, 30S, 31G, 34K, C-terminal(-)]mimylin.

474. The mimylin derivative according to any one of the preceding aspects 163-473, 5 having the compound name [N-terminal(C20 diacid-gGlu), des1, 9S, 23Y, 30S, 31G, 33Y]mimylin.

475. The mimylin derivative according to any one of the preceding aspects 163-474, having the compound name [N-terminal(C20 diacid-gGlu), des1, 9T, 21S, 23Y, 30S, 31G]mimylin.

10 476. The mimylin derivative according to any one of the preceding aspects 163-475, having the compound name [N-terminal(C20 diacid-gGlu), des1, 12H, 25H, 30T, 31G, 32T]mimylin.

477. The mimylin derivative according to any one of the preceding aspects 163-476, having the compound name [N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30S, 31G, 15 32T]mimylin.

478. The mimylin derivative according to any one of the preceding aspects 163-477, having the compound name [N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 30T, 31G, 32T]mimylin.

479. The mimylin derivative according to any one of the preceding aspects 163-478, 20 having the compound name [N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 10V, 30S, 31G]mimylin.

480. The mimylin derivative according to any one of the preceding aspects 163-479, having the compound name [N-terminal(C20 diacid-gGlu), des1, 21S, 23Y, 30S, 31G, 33Y]mimylin.

25 481. The mimylin derivative according to any one of the preceding aspects 163-480, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 23Y, 30S, 31G, 32T]mimylin.

482. The mimylin derivative according to any one of the preceding aspects 163-481, having the compound name [N-terminal(C20 diacid-gGlu), des1, 9T, 21S, 23Y, 30S, 30 31G, 33Y]mimylin.

483. The mimylin derivative according to any one of the preceding aspects 163-482, having the compound name [N-terminal(C20 diacid-gGlu), des1, 9S, 21S, 23Y, 30S, 31G, 33Y]mimylin.

484. The mimylin derivative according to any one of the preceding aspects 163-483, 35 having the compound name [N-terminal(C20 diacid-gGlu), des1, 12K, 23Y, 25K, 30S, 31G, 33Y]mimylin.

485. The mimylin derivative according to any one of the preceding aspects 163-484, having the compound name [N-terminal(C18 diacid-gGlu), des1, 5V, 9V, 10V, 20V, 30S, 31G]mimylin.

486. The mimylin derivative according to any one of the preceding aspects 163-485, 5 having the compound name [N-terminal(C20 diacid-gGlu), 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

487. The mimylin derivative according to any one of the preceding aspects 163-486, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 23Y, 30S, 31G, 32T, 33Y]mimylin.

10 488. The mimylin derivative according to any one of the preceding aspects 163-487, having the compound name [N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 14T, 21E, 30T, 31G, 32T]mimylin.

489. The mimylin derivative according to any one of the preceding aspects 163-488, having the compound name [N-terminal(C18 diacid-gGlu), des1, 6T, 9V, 14E, 21T, 15 30T, 31G, 32T]mimylin.

490. The mimylin derivative according to any one of the preceding aspects 163-489, having the compound name [des1, 4G, 15Q, 21Q, 23Y, 30S, 31K(C20 diacid-gGlu), 32T, 33Y]mimylin.

491. The mimylin derivative according to any one of the preceding aspects 163-490, 20 having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin.

492. The mimylin derivative according to any one of the preceding aspects 163-491, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

25 493. The mimylin derivative according to any one of the preceding aspects 163-492, having the compound name [N-terminal(C18 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

494. The mimylin derivative according to any one of the preceding aspects 163-493, having the compound name [N-terminal(C20 diacid), des1, 4G, 15Q, 21Q, 23Y, 30S, 30 31G, 32T, 33Y]mimylin.

495. The mimylin derivative according to any one of the preceding aspects 163-494, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 15T, 21E, 23Y, 30S, 31G, 32T, 33Y]mimylin.

496. The mimylin derivative according to any one of the preceding aspects 163-495, 35 having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 15E, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

497. The mimylin derivative according to any one of the preceding aspects 163-496, having the compound name [N-terminal(C20 diacid-gGlu), des1, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

498. The mimylin derivative according to any one of the preceding aspects 163-497, 5 having the compound name [N-terminal(C20 diacid-gGlu), 4Q, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y]mimylin.

499. The mimylin derivative according to any one of the preceding aspects 163-498, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4Q, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

10 500. The mimylin derivative according to any one of the preceding aspects 163-499, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 15Q, 21Q, 23Y, 25H, 30S, 31G, 32T, 33Y]mimylin.

501. The mimylin derivative according to any one of the preceding aspects 163-500, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 15 23Y, 30S, 31G, 32T, 33Y]mimylin.

502. The mimylin derivative according to any one of the preceding aspects 163-501, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

503. The mimylin derivative according to any one of the preceding aspects 163-502, 20 having the compound name [N-terminal(C20 diacid-gGlu-2xOEG), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

504. The mimylin derivative according to any one of the preceding aspects 163-503, having the compound name [N-terminal(C18 diacid-gGlu-2xOEG), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

25 505. The mimylin derivative according to any one of the preceding aspects 163-504, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31A, 32T, 33Y]mimylin.

506. The mimylin derivative according to any one of the preceding aspects 163-505, having the compound name [N-terminal(C20 diacid-gGlu), des1, 2L, 4G, 9V, 21S, 30 23Y, 30S, 31G, 32T, 33Y]mimylin.

507. The mimylin derivative according to any one of the preceding aspects 163-506, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9T, 15Q, 21Q, 23Y, 30S, 31G, 32T, 33Y]mimylin.

508. The mimylin derivative according to any one of the preceding aspects 163-507, 35 having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 23Y, 25P, 30S, 31Q, 32T, 33Y]mimylin.

509. The mimylin derivative according to any one of the preceding aspects 163-508, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 8L, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

510. The mimylin derivative according to any one of the preceding aspects 163-509, 5 having the compound name [N-terminal(C20 diacid-gGlu), des1, 2L, 4G, 9V, 15Q, 21Q, 23Y, 30S, 31Q, 32T, 33Y]mimylin.

511. The mimylin derivative according to any one of the preceding aspects 163-510, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9T, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin.

10 512. The mimylin derivative according to any one of the preceding aspects 163-511, having the compound name [N-terminal(C20 diacid-gGlu), 2L, 4G, 8L, 9V, 15Q, 21Q, 23Y, 27G, 30S, 31G, 32T, 33Y]mimylin.

513. The mimylin derivative according to any one of the preceding aspects 163-512, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 15Q, 21Q, 15 23aQ, 23bT, 23cY, 30S, 31Q, 32T, 33Y]mimylin.

514. The mimylin derivative according to any one of the preceding aspects 163-513, having the compound name [N-terminal(C20 diacid-gGlu), des1, 4G, 9V, 12K, 15Q, 21Q, 23Y, 25P, 30S, 31G, 32T, 33Y]mimylin.

515. The mimylin derivative according to any one of the preceding aspects 163-514, 20 having the compound name [N-terminal(C20 diacid-gGlu), des1, 4Q, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin.

516. The mimylin derivative according to any one of the preceding aspects 163-515, having the compound name [N-terminal(C20 diacid-gGlu), des1, 2L, 4Q, 8L, 9V, 15Q, 16R, 19R, 21Q, 23Y, 27Q, 30S, 31Q, 32T, 33Y]mimylin.

25 517. The mimylin derivative according to any one of the preceding aspects 163-515, having an IC₅₀ in a human amylin receptor binding assay (Assay V) of about 1200pM or less.

518. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC₅₀ in a human amylin receptor binding assay (Assay V) of about 1000pM 30 or less.

519. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC₅₀ in a human amylin receptor binding assay (Assay V) of about 900pM or less.

520. The mimylin derivative according to any one of the preceding aspects 163-515, 35 having an IC₅₀ in a human amylin receptor binding assay (Assay V) of about 800pM or less.

521. The mimylin derivative according to any one of the preceding aspects 163-515, having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 700pM or less.

522. The mimylin derivative according to any one of the preceding aspects 163-515
5 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 600pM or less.

523. The mimylin derivative according to any one of the preceding aspects 163-515
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 500pM or less.

10 524. The mimylin derivative according to any one of the preceding aspects 163-515
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 400pM or less.

525. The mimylin derivative according to any one of the preceding aspects v having
an IC_{50} in a human amylin receptor binding assay (Assay V) of about 300pM or less.

15 526. The mimylin derivative according to any one of the preceding aspects 163-515,
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 200pM or less.

527. The mimylin derivative according to any one of the preceding aspects 163-515
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 100pM
20 or less.

528. The mimylin derivative according to any one of the preceding aspects 163-515
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 90pM or less.

529. The mimylin derivative according to any one of the preceding aspects 163-515
25 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 80pM or less.

530. The mimylin derivative according to any one of the preceding aspects 163-515,
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 70pM or less.

30 531. The mimylin derivative according to any one of the preceding aspects 163-515
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 60pM or less.

532. The mimylin derivative according to any one of the preceding aspects 163-515,
having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 50pM or
35 less.

533. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 40pM or less.

534. The mimylin derivative according to any one of the preceding aspects 163-515, 5 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 30pM or less.

535. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 20pM or less.

10 536. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 19pM or less.

537. The mimylin derivative according to any one of the preceding aspects 163-515, having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 18pM or 15 less.

538. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 17pM or less.

539. The mimylin derivative according to any one of the preceding aspects 163-515, 20 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 16pM or less.

540. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 15pM or less.

25 541. The mimylin derivative according to any one of the preceding aspects 163-515, having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 14pM or less.

542. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 13pM or 30 less.

543. The mimylin derivative according to any one of the preceding aspects 163-515, having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 12pM or less.

544. The mimylin derivative according to any one of the preceding aspects 163-515, 35 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 10pM or less.

545. The mimylin derivative according to any one of the preceding aspects 163-515 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 5pM or less.

546. The mimylin derivative according to any one of the preceding aspects 163-515 5 having an IC_{50} in a human amylin receptor binding assay (Assay V) of about 1000pM or less.

547. The mimylin derivative according to any one of the preceding aspects 163-515 having wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 1000pM or less.

10 548. The mimylin derivative according to any one of the preceding aspects 163-515 EC_{50} in a human amylin receptor functional Assay IIb of about 900pM or less.

549. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 800pM or less.

15 550. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 700pM or less.

551. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb 20 of about 600pM or less.

552. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 500pM or less.

25 553. The mimylin derivative according to any one of the preceding aspects 151-542, wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 90pM or less.

554. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 80pM or less.

30 555. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb of about 70pM or less.

556. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC_{50} in a human amylin receptor functional Assay IIb 35 of about 60pM or less.

557. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 50pM or less.

558. The mimylin derivative according to any one of the preceding aspects 163-515 5 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 40pM or less.

559. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 30pM or less.

10 560. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 20pM or less.

561. The mimylin derivative according to any one of the preceding aspects 163-515 15 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 19pM or less.

562. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 18pM or less.

563. The mimylin derivative according to any one of the preceding aspects 163-515, 20 wherein said derivative has an EC₅₀ in a human amylin receptor functionl Assay IIbof about 17pM or less.

564. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 16pM or less.

25 565. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 15pM or less.

566. The mimylin derivative according to any one of the preceding aspects 163-515 30 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 14pM or less.

567. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 13pM or less.

568. The mimylin derivative according to any one of the preceding aspects 163-515 35 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 12pM or less.

569. The mimylin derivative according to any one of the preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 10pM or less.

570. The mimylin derivative according to any one of preceding aspects 163-515 wherein said derivative has an EC₅₀ in a human amylin receptor functional Assay IIb of about 5pM or less.

571. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative is selected from table 13.

10 572. The mimylin derivative according to any one of the preceding aspects 163-515, wherein said derivative is selected from table 14.

573. The mimylin derivative according to any one of the preceding aspects 163-515 which is physically stable.

574. The mimylin derivative according to any one of the preceding aspects 163-515 which is physically stable when tested in Assay III as disclosed herein.

15 575. The mimylin derivative according to any one of the preceding aspects 163-515 which is physically stable when tested in Assay IIIa as disclosed herein.

576. The mimylin derivative according to any one of the preceding aspects 163-515, which has as high lag-time and recovery as possible when tested in Assay III as disclosed herein.

20 577. The mimylin derivative according to any one of the preceding aspects 163-515, which has as high lag-time and recovery as possible when tested in Assay IIIa as disclosed herein.

578. The mimylin derivative according to any one of the preceding aspects 163-577, wherein said mimylin peptide or mimylin derivative reduces appetite.

25 579. The mimylin derivative according to any one of the preceding aspects 163-578 wherein said mimylin peptide or mimylin derivative increase appetite.

580. The mimylin derivative according to any one of the preceding aspects 163-580, wherein said mimylin peptide or mimylin derivative reduces food intake.

581. The mimylin derivative according to any one of the preceding aspects 163-581, 30 wherein said mimylin peptide or mimylin derivative increase food intake.

582. The mimylin derivative according to any one of the preceding aspects 163-582, wherein said mimylin peptide or mimylin derivative reduces body weight.

583. The mimylin derivative according to any one of the preceding aspects 163-583, wherein said mimylin peptide or mimylin derivative increase body weight.

584. The mimylin derivative according to any one of the preceding aspects 163-583, showing show food intake reduction in rats tested according to Assay I after administration of 3nmol/kg or 30nmol/kg.

585. The mimylin derivative according to any one of the preceding aspects 163-583, 5 showing food intake reduction in rats tested according to Assay I after administration of 3nmol/kg or 30nmol/kg.

586. The mimylin derivative according to any one of the preceding aspects 163-583, showing reduction in food intake in rats tested according to Assay I which can be seen within 0-24 hours after administration of 3nmol/kg or 30nmol/kg.

10 587. The mimylin derivative according to any one of the preceding aspects 163-583, showing reduction in food intake in rats tested according to Assay I which can be seen within 0-24 and/or 24-48 hours after administration of 3nmol/kg or 30nmol/kg.

588. The mimylin derivative according to any one of the preceding aspects 163-583, showing reduction in food intake by at least 10% in rats tested according to Assay I 15 which can be seen within 0-24 hours after administration of 3nmol/kg or 30nmol/kg.

589. The mimylin derivative according to any one of the preceding 163-583, showing reduction in food intake by at least 10% in rats tested according to Assay I which can be seen within 24-48 hours after administration of 3nmol/kg or 30nmol/kg.

590. The mimylin derivative according to ant of the preceding aspects 163-583 20 selected form the compounds listed in Table 8.

591. The mimylin derivative according to ant of the preceding aspects 163-583 selected form the compounds listed in Table 9.

592. The mimylin derivative according to ant of the preceding aspects 163-583 selected form the compounds listed in Table 10.

25 593. The mimylin derivative according to ant of the preceding aspects 163-583 selected form the compounds listed in Table 11.

594. The mimylin derivative according to ant of the preceding aspects 163-583 selected form the compounds listed in Table 12.

595. The mimylin peptide according to any pne pf the peceding aspects 1-162 or 30 mimylin derivative according to any one of the preceding aspects 163-583 which has low immunogenicity.

596. The mimylin peptide according to any pne pf the peceding aspects 1-162 or mimylin derivative according to any one of the preceding aspects 162-583 which has low immunogenicity determined by immunogenicity prediction as disclosed in Assay 35 XI.

597. The mimylin peptide according to any one of the preceding aspects 1-162 or mimylin derivative according to any one of the preceding aspects 162-583 being an agonist of the amylin and/or calcitonin receptor.

5 598. A pharmaceutical formulation comprising a mimylin peptide or mimylin derivative according to any one of the aspects 1-587.

599. An aqueous pharmaceutical formulation comprising a mimylin peptide 1-162 or mimylin derivative according to any one of the preceding aspects 162-583, wherein said formulation is suitable for injection and comprises pharmaceutical acceptable ingredients.

10 600. The pharmaceutical formulation according to aspect 599, wherein said pharmaceutical acceptable ingredients are selected from pH buffers, tonicity agents and antimicrobial agents

601. The pharmaceutical formulation according to aspect 599-600, wherein one or more of said pharmaceutical acceptable ingredients are selected from the list consisting of: glycerol, phosphate, propylene glycol, phenol, m-cresol, or a combination of phenol and m-cresol or equivalents of said ingredients listed.

602. The pharmaceutical formulation according to aspect 599-600, wherein

- a. said phosphate is present in a range of between about 4mM to about 12mM,
- 20 b. said propylene glycol about 1mg/mL to about 30mg/mL,
- c. m-cresol about 5mM to about 40mM,
- d. phenol about 5mM to about 90mM,
- e. said mimylin peptide concentration is selected in a concentration about 0.001mM to about 15mM, and
- 25 f. said glycerol about 1mg/mL to about 30mg/mL.

603. The pharmaceutical formulation according to aspect 599-600, wherein

- a. said phosphate is present in a range of between about 4mM to about 12mM, preferably about 6mM to about 10mM, more preferably about 7mM to about 9mM, even more preferred about 8mM,
- 30 b. said propylene glycol about 1mg/mL to about 30mg/mL, preferably about 5mg/mL to about 25mg/mL, more preferably about 10mg/mL to about 20mg/mL, even more preferred about 14mg/mL,
- c. m-cresol about 5mM to about 40mM, preferably about 10mM to about 35mM, more preferably about 20mM to about 35mM, even more preferred about 30mM,

- d. phenol about 5mM to about 90mM, preferably about 10mM to about 70mM, more preferably about 30mM to about 65mM, even more preferred about 58mM,
- e. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL
- f. said glycerol about 1mg/mL to about 30mg/mL, preferably about 5mg/mL to about 25mg/mL, more preferably about 10mg/mL to about 20mg/mL, even more preferred about 16mg/mL.

10 604. The pharmaceutical formulation accordig to any one of the aspects 599-600, wherein the concentration of antimicrobial agents, i.e. said concentration of either phenol, m-cresol, or a combination of phenol and m-cresol is selected to accommodate the Food and Drug Administration's (USA) or European Medicine Agency's (EU) requirements for antimicrobial preservation of the chosen 15 concentration of peptide.

605. The pharmaceutical formulation accordig to any one of the aspects 586-589, wherein the concentration of phenol is selected to accommodate the Food and Drug Administration's (USA) or European Medicine Agency's (EU) requirements for antimicrobial preservation of the chosen concentration of peptide.

20 606. The pharmaceutical formulation according to aspect 599-600, wherein

- a. said phosphate is about 8mM,
- b. said propylene glycol is about 14mg/mL,
- c. phenol is about 58mM,
- d. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, 25 more preferably about 0.1mg/mL to about 1mg/mL

607. The pharmaceutical formulation according to aspect 599-600, wherein

- a. said phosphate is about 8mM,
- b. said propylene glycol is about 14mg/mL,

30 35

- c. phenol is about 58mM, optionally said phenol can be exchanged with m-cresol or be combined with m-cresol according to any one of the preceding aspects 599-606,
- d. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL

608. The pharmaceutical formulation according to any one of the aspects 599-607, wherein the pH is between about 6.6 to about 8.6, preferably between about 7.0 to about 8.4, more preferably about 7.4 to about 8.2.

609. The pharmaceutical formulation according to any one of the aspects 599-608, 5 wherein the pH is about 7.4.

610. The pharmaceutical formulation according to aspects 599-609, wherein the pH is about 8.2.

611. The pharmaceutical formulation according to any one of the aspects 599-610, 10 wherein the formulation comprises a compound of Ex #40 or 46 and phosphate, preferably between about 8-10mM and

15 a. optionally phenol or m-cresol, between about 19-60mM, preferably about 19mM, about 30mM about 50mM or about 58mM, and

b. further optionally propylene glycol about 10-20mg/mL, preferably about 14mg/mL,

c. further optionally comprising glycerol about 10 to 100mg/mL, preferably about 10, about 16mg/mL,

d. further optionally comprising NaCl up to 50mM,

e. further optionally comprising HEPES in the range between 5-15mM, preferably 10mM,

20 f. at a pH 7.4 or 8.2.

612. The pharmaceutical formulation according to any one of the embodiments 599- 25 611 wherein the formulation comprises a compound of Ex. #40 or 46, wherein said formulation is selected from any one of the formulations selected from the group consisting of the formulations F1-F38, preferably Formulations F3, F4, F7, F8, F13, F14, F15, F16, F21, F22, F23, F24, F25, F26, F27, F28.

613. The pharmaceutical formulation according to any one of the aspects 599-612 wherein the formulation comprises a compound of Ex. # 2, wherein said formulation is selected from the list consisting of the formulations: F39-120.

614. The pharmaceutical formulation according to any one of the aspects 599-613, 30 wherein said formulation has any pH in the range pH 4 to pH 9.

615. The pharmaceutical according to any one of the aspects 599-614, wherein said formulation has a neutral pH.

616. The pharmaceutical according to any one of the aspects 599-615, wherein said formulation has a pH of about pH 6.5 to pH 8.

35 617. The pharmaceutical formulation according to any one of the aspects 599-616, wherein said formulation has a pH of about pH 6.5 to pH 7.

618. The pharmaceutical formulation according to any one of the aspects 599-617, wherein said formulation has a pH of about pH 7 to pH 7.5.

619. The pharmaceutical formulation according to any one of the aspects 599-618, further comprising another mimylin peptide or mimylin derivative.

5 620. A pharmaceutical formulation, co-formulation or co-treatment comprising a mimylin peptide according to any one of the aspects 1-162 or derivative according to any one of the aspects 162-583 and further comprising other peptides.

10 621. A pharmaceutical formulation, co-formulation or co-treatment comprising a mimylin peptide according to any one of the aspects 1-162 or derivative according to any one of the aspects 162- 583 and further comprising other peptides, wherein said further peptides are for the treatment of obesity.

15 622. A pharmaceutical formulation, co-formulation or co-treatment comprising a mimylin peptide according to any one of the aspects 1-162 or derivative according to any one of the aspects 162- 583 or formulations according to any one of the aspects 619-622 and further comprising other peptides for the treatment of obesity.

623. A pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 622 or 623, wherein said futher peptides for treatment of obesity are any GLP-1 peptide.

20 624. The pharmaceutical formulation according to aspect 623, wherein said GLP-1 peptide is a GLP-1 compound, GLP-1 analogue or GLP-1 derivative.

625. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 623 or 624, wherein said GLP-1 compound, GLP-1 analogue or GLP-1 derivative is semaglutide or liraglutide.

25 626. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects 620-625, wherein

a. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL

b. GLP-1 compound, GLP-1 analogue or GLP-1 derivative is semaglutide or liraglutide concentration is between about 0.5mg/mL and about 6mg/mL, preferably about 0.5mg/mL, about 1mg/mL, about 1.6mg/mL, about 2mg/mL, about 3mg/mL, about 4.1mg/mL or about 6mg/mL

30 627. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects 620-625, wherein the

a. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL

5 b. GLP-1 compound, GLP-1 analogue or GLP-1 derivative is semaglutide or liraglutide concentration is between about 0.5mg/mL and about 6mg/mL, preferably selected from the list consisting of: about 1mg/mL, about 3mg/mL, about 6mg/mL,

wherein said GLP-1 compound, GLP-1 analogue or GLP-1 derivative is selected to be liraglutide

10 628. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects 620-625, wherein the

a. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL

15 b. GLP-1 compound, GLP-1 analogue or GLP-1 derivative is semaglutide or liraglutide concentration is between about 0.5mg/mL and about 6mg/mL, preferably about 0.5mg/mL, about 2mg/mL, about 4.1mg/mL,

wherein said GLP-1 compound, GLP-1 analogue or GLP-1 derivative is selected to be semaglutide

20 629. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects 620-625, wherein

a. said phosphate is present in a range of between about 4mM to about 12mM, preferably about 6mM to about 10mM, more preferably about 7mM to about 9mM, even more preferred about 8mM,

25 b. said propylene glycol about 1mg/mL to about 30mg/mL, preferably about 5mg/mL to about 25mg/mL, more preferably about 10mg/mL to about 20mg/mL, even more preferred about 14mg/mL,

c. m-cresol about 5mM to about 40mM, preferably about 10mM to about 35mM, more preferably about 20mM to about 35mM, even more preferred about 30mM,

30 d. phenol about 5mM to about 90mM, preferably about 10mM to about 70mM, more preferably about 30mM to about 65mM, even more preferred about 58mM,

e. said mimylin peptide concentration is selected in a concentration about 0.001mg/mL to about 15mg/mL, preferably about 0.01 to about 10mg/mL, more preferably about 0.1mg/mL to about 1mg/mL

- f. GLP-1 compound, GLP-1 analogue or GLP-1 derivative is semaglutide or liraglutide in a concentration between about 0.5mg/mL and about 6mg/mL, preferably about 0.5mg/mL, about 2mg/mL, about 4.1mg/mL,
- 5 g. said glycerol about 1mg/mL to about 30mg/mL, preferably about 5mg/mL to about 25mg/mL, more preferably about 10mg/mL to about 20mg/mL, even more preferred about 16mg/mL.

630. The pharmaceutical formulation according to any one of the aspects 620-625, wherein the concentration of antimicrobial agents, i.e. said concentration of either phenol, m-cresol, or a combination of phenol and m-cresol is selected to accommodate the Food and Drug Administration's (USA) or European Medicine Agency's (EU) requirements for conservation of the chosen total antimicrobial preservation of peptides.

10 631. The pharmaceutical formulation according to any one of the aspects 615-618, wherein the concentration of phenol is selected to accommodate the Food and Drug Administration's (USA) or European Medicine Agency's (EU) requirements for antimicrobial preservation of the chosen total concentration of peptides.

15 632. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects 620-631, wherein the pH is between about 7.2 to about 8.6.

20 633. The pharmaceutical formulation, co-formulation or co-treatment according to aspect 620-632, wherein the pH is between about 7.2 to about 8.6, wherein said pH is selected to be about 7.4 when the GLP-1 derivative is semaglutide and to be about 8.2 when the GLP-1 derivative is selected to be liraglutide.

25 634. The pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 620-633, wherein said formulation, co-formulation or co-treatment is selected from the list consisting of: F121-150.

30 635. A pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 620-634 wherein said GLP-1 compound and said mimylin peptide will not affect each others pK profile (as described for a selection of compounds in Table 20), measured according to Assay (XV).

35 636. A pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 620-635 wherein said GLP-1 compound and said mimylin peptide will not affect each others pK profile, wherein said mimylin peptide is compound of Ex. #2 or Ex. #46 and said GLP-1 compound is liraglutide, measured according to Assay (XV).

637. A pharmaceutical formulation, co-formulation or co-treatment according to any one of the aspects 620-636 further comprising other peptides/polypeptides for the treatment of type 2 diabetes or other metabolic syndromes.

5 638. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use as a medicament.

639. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating subjects suffering from overweight or obesity.

10 640. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating subjects suffering from underweight.

15 641. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating subjects suffering reduced appetite.

20 642. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to aspect 639, wherein said formulation comprising a mimylin compound according to this invention induces body weight reduction in DIO rats by between about 4 to about 12%, most preferably about 10%, when measured as described by ASSAY (**XIV**).

25 643. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to aspect 639, wherein said formulation comprising a mimylin compound according to this invention induces body weight reduction in DIO rats by between about 4 to about 12%, most preferably about 10%, when measured as described by ASSAY (**XIV**), wherein said compound is Ex compound #2 in the concentrations given in Table 36.

30 644. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to aspect 639, wherein said co-formulation or co-treatment of mimylin peptide with a GLP-1 peptide induces body weight reduction in DIO rats by between about 5 to about 20%, preferably about 8 to about 12%, most preferably about 10%, when measured as described by ASSAY (**XIV**).

35 645. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to aspect 639, wherein said co-formulation or co-treatment of mimylin peptide with a GLP-1 peptide induces body weight reduction in DIO rats by between about 5 to about 20%, preferably about 8 to about 12%, most preferably

about 10%, when measured as described by ASSAY (XIV), wherein said compounds are example compound #2 and liraglutide in the concentrations given in Table 36.

646. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating 5 obesity, wherein a human subject suffering from obesity may have a BMI of ≥ 30 ; this subject may also be referred to as obese.

647. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating 10 obesity, wherein a human subject suffering from obesity may have a BMI of ≥ 35 or a BMI in the range of ≥ 30 to <40 .

648. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating obesity, wherein said obesity is severe obesity or morbid obesity, wherein the human subject may have a BMI of ≥ 40 .

649. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, for the use in treating 15 overweight subjects, wherein said subjects may have a BMI of ≥ 25 , such as a BMI of ≥ 27 .

650. The mimylin peptide, derivative, pharmaceutical formulations or co-formulations 20 according to any one of the preceding aspects.

651. The mimylin peptide, derivative, pharmaceutical formulations or co-formulations according to any one of the preceding aspects, for the use in treating osteoporosis.

652. The mimylin peptide, derivative or pharmaceutical formulations according to any 25 one of the preceding aspects, for the use in treating type I or II diabetes.

653. The mimylin peptide, derivative or pharmaceutical formulation, co-formulation or co-treatment according to any one of the preceding aspects, 1- 625 for the use in 30 treating neuropathic pain.

654. The use according the aspect 653, wherein said neuropathic pain is selected from the list of: spinal canal stenosis, migraine, diabetic neuropathy and complex regional pain syndrome.

DEFINITIONS

A receptor agonist may be defined as a peptide or analogue that binds to a receptor and elicits a response typical of the natural ligand. A full agonist may be defined as one that elicits a response of the same magnitude as the natural ligand (see e.g. 5 "Principles of Biochemistry ", AL Lehninger, DL Nelson, MM Cox, Second Edition, Worth Publishers, 1993, page 763).

Thus, for example, an "Amylin receptor agonist" may be defined as a compound which is capable of binding to the Amylin receptor and capable of activating it. And a "full" amylin receptor agonist may be defined as an Amylin receptor agonist which is 10 capable of eliciting a magnitude of Amylin receptor response that is similar to native amylin. An Amylin receptor agonist will often also be a calcitonin receptor agonist. Examples of Amylin receptor agonists are human amylin, pramlintide and calcitonin.

The term "**human amylin**" as used herein relates to the polypeptide human amylin having the sequence

15 KCNTATCATQRLANFLVHSSNNFGAILSSTNVGSNTY (SEQ ID NO: 2)

which structure can be shown as



The term "**pramlintide**" as used herein relates to the peptide having the sequence

20 KCNTATCATQRLANFLVHSSNNFGPILPPTNVGSNTY (SEQ ID NO: 3)

which structure can be shown as



Pramlintide has a disulfide bridge between the two Cys residues and a C-terminal amide group. 25

The term "**calcitonin**" means salmon calcitonin or human calcitonin.

The term "**salmon calcitonin**" or "**sCT**" means the native protein sequence of salmon calcitonin as disclosed in Niall et al (1969), *Biochemistry* vol 64, figure 2. Salmon calcitonin is a polypeptide which consists of 32 amino acids and the sequence

30

CSNLSTCVLGKLSQELHKLQTYPRTNTGSGTP (SEQ ID NO: 4)

which structure can be shown as



It has a disulfide bridge between the first and seventh amino acids at the amino-terminal end of the polypeptide chain and a prolinamide group at the carboxyl terminal amino acid being essential for its biological activity.

5 The term "**human calcitonin**" means the native protein sequence of human calcitonin as disclosed in Niall et al (1969), *Biochemistry* vol 64, figure 2. Human calcitonin is a polypeptide which consists of 32 amino acids and the sequence

CGNLSTCMLGTYTQDFNKFHTFPQTAIGVGAP (SEQ ID NO: 5)

which structure can be shown as



10

It has a disulfide bridge between the first and seventh amino acids at the amino-terminal end of the polypeptide chain, the disulfide bridge being essential for its biological activity, and a prolinamide group at the carboxyl terminal amino acid.

The term "**mimylin**" as used herein refers to the protein with the sequence

15 EASELSTAALGRLSAELHELALPRTETGPESP (SEQ ID NO: 1)

Mimylin is a novel amylin and calcitonin receptor agonist, with less than 60% sequence identity to salmon calcitonin and has no disulfide bridges.

20 The term "**analogue**" as used herein describes a peptide comprising one or more amino acid modifications, such as but not limited to substitution and/or one or more deletion and/or one or more addition of any one of the amino acid residues for any natural or unnatural amino acid, synthetic amino acids or peptidomimetics and/or the attachment of a side chain to any one of the natural or unnatural amino acids, synthetic amino acids or peptidomimetics at any available position. The addition or deletion of amino acid residues can take place at the N-terminal of the peptide and/or at the C-terminal of the peptide.

25 Thus the term "**mimylin analogue**" or "**analogue of mimylin**" as used herein refers to a peptide, wherein one or more amino acids have been modified relative to SEQ ID NO: 1. The term "**mimylin peptide**" as used herein refers to the group of compounds comprising mimylin or an analogue thereof. The term "mimylin peptide" will 30 thus also cover the term "backbone" and "polypeptides".

When used herein the term "**natural amino acid**" is an amino acid (with the usual three letter codes & one letter codes in parenthesis) selected from the group consisting of: Glycine (Gly & G), proline (Pro & P), alanine (Ala & A), valine (Val & V), leucine (Leu & L), isoleucine (Ile & I), methionine (Met & M), cysteine (Cys & C), 5 phenylalanine (Phe & F), tyrosine (Tyr & Y), tryptophan (Trp & W), histidine (His & H), lysine (Lys & K), arginine (Arg & R), glutamine (Gln & Q), asparagine (Asn & N), glutamic acid (Glu & E), aspartic acid (Asp & D), serine (Ser & S) and threonine (Thr & T). If anywhere in this invention reference is made to a mimylin peptide, analogue or derivative or peptides according to this invention comprising or not comprising G, P, A, V, 10 L, I, M, C, F, Y, H, K, R, Q, N, E, D, S or T, without specifying further, amino acids are meant. If not otherwise indicated amino acids indicated with a single letter code in CAPITAL letters indicate the L-isoform, if however the amino acid is indicated with a lower case letter, this amino acid is used/applied as it's D-form.

If, due to typing errors, there are deviations from the commonly used codes, the 15 commonly used codes apply. The amino acids present in the mimylin peptides of the present invention are, preferably, amino acids which can be coded for by a nucleic acid.

If the analogue contains either more than 33 amino acid residues or less than 33 amino acid residues then the skilled person can still align that sequence with the sequence of mimylin (SEQ ID NO: 1) to determine the placement number of the 20 corresponding, respective amino acid residue. A method for determination of "**sequence identity**" between two analogues the two peptides mimylin and [23Y, 30S, 31G]mimylin (i.e. EX. #24bb) are aligned. The sequence identity of the mimylin analogue relative to mimylin is given by the number of aligned identical residues minus the number of different residues divided by the total number of residues in mimylin (i.e. SEQ ID NO: 1) 25 Accordingly, in said example the sequence identity is (33-3)/33. A suitable alignment program can be tested with a suitable alignment program is "needle", which is a Needleman-Wunsch alignment. The alogorithm for this alignment program is described in Needleman, S.B. and Wunsch, C.D., (1970), Journal of Molecular Biology, 48: 443-453.

In the numbering sequence of SEQ ID NO: 1, and according to established 30 practice in the art, the amino acid residue at the N-terminal Glutamic acid (E) is assigned no. 1 and subsequent amino acid residues are numbered consecutively, ending at the C-terminal with proline (P) assigned no. 33. Therefore, generally, any reference herein to position number of an amino acid residue provides its location in a 33 amino acid sequence; said 33 amino acid sequence being an analogue of mimylin. For example, a 35 reference to an analogue modified at position 14 may refer to an analogue wherein the 14th amino residue out of the 33 amino acids in the analogue has been modified.

In other words, the amino acid sequence numbering of the analogue provides the position of each analogue with respect to a 33 amino acid sequence, wherein the numbering is consecutive and ascending in the direction from the N-terminal to the C-terminal.

5 Analogues may be described by reference to the number of the amino acid residue in mimylin (SEQ ID NO: 1) which is modified, i.e. by its position, and the nature of the modification. The following are non-limiting examples of appropriate analogue nomenclature.

For example:

10 [I9]-mimylin designates a mimylin analogue (mimylin) wherein the change from mimylin is the substitution of A position 9 with I, such as in example compound 10. One example can also be the designation des1 in relation to an analogue of mimylin, which refers to an analogue in which the N-terminal amino acid, Glutamic acid, has been deleted. An analogue of mimylin, where the N-terminal amino acid has been deleted may 15 also be designated des1 mimylin.

[des1, 4K, 30S, 31G]mimylin designates a mimylin analogue (mimylin), in which the E at position 1 has been deleted and E in position 4 had been substituted with K, P in position 30 with S and E in position 31 with G.

20 If an additional amino acid, such as Glutamic acid (E) is added to the N-terminal in the position before position 1, the amino acid change will be indicated as -1E, because no position 0 exist. In the aspects this may be described with the term that no amino acid is present in position -1, thus the term "**no amino acid**" as used herein is equivalent to the term "**absent**", which means that the position to which reference is made simply does not comprise any amino acid residue.

25 Thus the analogue of the derivative of compound 83 (EX. #83) is denominated as follows: [-1E, 1A, 23Y, 30S, 31G]mimylin and thus discloses a sequence in which E is added to the N-terminal amino acid, the N-terminal amino acid is modified from an E to A, P of position 30 in SEQ ID NO: 1 is substituted with S and E in position 31 of SEQ ID NO: 1 is substituted with G.

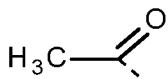
30 In mimylin peptides, such as EX. #130bb the indication of 23aQ, 23bT, 23cY means, that QTY has been inserted between amino acid position 23 and position 24 relative to the numbering of SEQ ID NO: 1 and the amino acid in position 23 is the original amino acid; L. The sequence of the mimylin peptide 1300bb is thus; ASGLSTAVLGR~~LSQ~~ELHELQ~~TL~~QTYPRTETGSQTY (SEQ ID NO: 130).

As is apparent from the above examples, amino acid residues may be identified by their full name, their one-letter code, and/or their three-letter code. These three ways are fully equivalent.

The expressions "**conforms to**", "**corresponds to**", "**a position equivalent to**" or "**corresponding position**" as used herein may be used to characterise the site of modification in an analogue of mimylin by reference to SEQ ID NO: 1. Equivalent, identical or corresponding positions are easily deduced, e.g. by simple handwriting and eyeballing; and/or a standard protein or mimylin peptide alignment program may be used, such as "needle" which is a Needleman-Wunsch alignment. The algorithm is described in Needleman, S.B. and Wunsch, C.D., (1970), Journal of Molecular Biology, 48: 443-453, and the align program by Myers and W. Miller in "Optimal Alignments in Linear Space" CABIOS (computer applications in the biosciences) (1988) 4:11-17. For the alignment, the default scoring matrix BLOSUM62 and the default identity matrix may be used, and the penalty for the first residue in a gap may be set at -10 and the penalties for additional residues in a gap at -0.5.

Naming the derivatives herein was performed as follows:

[Y(C)aa₁X(S)aa₂]P (Formula1), wherein P is the peptide (such as for example mimylin), aa₁ and aa₂ describe one, more or no amino acid modifications of said peptide, (S) discloses the side chain which is attached to the peptide and X describes the attachment site. X in formula 1 can thus indicate N-terminal, when the side chain (S) is attached in the N-terminal or a specific position such as K4, which then exemplified for a mimylin derivative would refer to a substitution of the amino acid E with K in position 4 corresponding to SEQ ID NO: 1, to which the side chain (S) is attached. Y(C) in formula 1 may be placed throughout the sequence, wherever relevant and indicates if additional modifications to the amino acid sequence of chemical nature are present; Y indicates the placement, so "c-terminal (-)" indicates that the chemical change is present in the c-terminal. The (-) of "c-terminal (-)" means "acid", thus "c-terminal(-)" means c-terminal acid. The if "N-terminal(acetyl)" is mentioned in the naming this means that and acetyl



is present at the N-terminal instead of the regular alpha amino group. If C is "c-terminal (-)" the c-terminal end of the peptide is a c-terminal acid instead of a c-terminal amide. If no indication of "c-terminal (-)" is made in the derivative name, the c-terminal of the derivatives according to the present invention are c-terminal amides.

The following are non-limiting examples of appropriate derivative nomenclature.

[N-terminal(C18diacid-gGlu)]mimylin designates a mimylin derivative, wherein mimylin in the N-terminal with a side chain comprising a C18diacid as the protracting moiety and gGlu as a linker.

[N-terminal(C18diacid-gGlu) 2P, 9V]mimylin designates a mimylin derivative, wherein a mimylin analogue comprising modification 2P and 9V, relative to the numbering of SEQ ID NO: 1 is derivatised in the N-terminal with a side chain comprising a C18diacid as the protracting moiety and gGlu as a linker.

The mimylin peptide may comprise one or more side chains on one or more of the amino acid residues. Such mimylin peptides may also be called mimylin derivatives or salmon calcitonin derivatives.

The term "**derivative**" as used herein means a chemically modified peptide, in which one or more side chains have been covalently attached to the peptide. The term "**side chain**" may also be referred to as a "**substituent**". A derivative comprising such side chains will thus be "**derivatised**" peptide or "**derivatised**" analogue.

The term "mimylin compound" as used herein refers to the analogues and derivatives according to this invention which comprise a backbone which make reference to the mimylin backbone. Such as, but not limited to the compounds of Table 1 and 4.

In a particular embodiment, the side chain is capable of forming non-covalent aggregates with albumin and may thus also be referred to as "**albumin binding moiety**", thereby promoting the circulation of the derivative with the blood stream, and also having the effect of protracting the time of action of the derivative, due to the fact that the aggregate of the mimylin-derivative and albumin is only slowly disintegrated to release the active pharmaceutical ingredient. Thus, the "**substituent**", or "**side chain**", as a whole is preferably referred to as an "**albumin binding moiety**".

The term "**albumin binding moiety**" as used herein refers to any chemical group capable of non-covalent binding to albumin, i.e. has albumin binding affinity. In some embodiments the albumin binding moiety comprises an acyl group.

In another particular embodiment the side chain comprises a portion which is particularly relevant for the albumin binding and thereby the protraction, which portion may accordingly be referred to as a "**protracting moiety**" or "**protractor**". The protracting moiety may be near, preferably at, the terminal (or distal, or free) end of the albumin binding moiety, relative to its point of attachment to the peptide.

In a still further particular embodiment the side chain comprises a portion between the protracting moiety and the point of attachment to the peptide, which portion may be referred to as a "**linker**", "**linker moiety**", "**spacer**", or the like. The linker

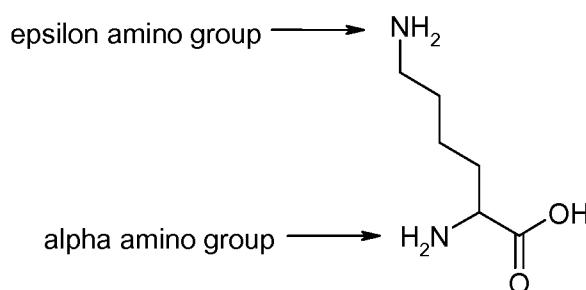
may be optional, and hence in that case the side chain may be identical to the protracting moiety.

The albumin binding moiety, the protracting moiety, or the linker may be covalently attached to a lysine residue of the mimylin peptide by acylation, i.e. via an 5 amide bond formed between a carboxylic acid group thereof (of the albumin binding moiety, the protracting moiety, or the linker) and an amino group of the lysine residue or amino acid residue in the N-terminal. Additional or alternative conjugation chemistry includes alkylation, ester formation, or amide formation, or coupling to a cysteine residue, such as by maleimide or haloacetamide (such as bromo-/chloro-/iodo-) coupling.

10 In a preferred embodiment, an active ester of the albumin binding moiety, preferably comprising a protracting moiety and a linker, is covalently linked to an amino group of a lysine residue, preferably the epsilon amino group thereof, under formation of an amide bond, as explained above.

15 Unless otherwise stated, when reference is made to an acylation of a lysine residue or N-terminal amino acid, it is understood to be to the epsilon-amino group of said lysine residue or alpha-amino group of the N-terminal amino acid.

20 The term "**epsilon amino group**" or " **ϵ -amino group**", used herein in relation to lysine, refers to the amino group at the 6 position, using the IUPAC standard numbering conventions. The term "**alpha amino group**" or " **α -amino group**" refers to the amino group at the 2 position, using the IUPAC standard numbering conventions. We refer to the following structure.



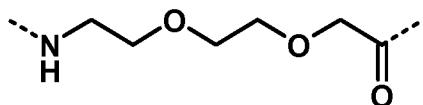
25 The term "**linker**" as used herein includes suitable side chains that can join a moiety, such as a chemical moiety, to the mimylin peptide, such as the mimylin peptide backbone. Thus, the linker and the chemical moiety become a side chain together. The moiety joined to the linker may be any suitable moiety. Examples include an albumin binding moiety.

30 A linker as used herein provides a bridge or link between an amino group on the mimylin peptide backbone and an acyl group on the moiety – such as an albumin binding

moiety. The linker may be bound to, or near to, the N terminal amino acid residue. Preferably the linker is bound to the amino acid in position 1 of the mimylin analogue.

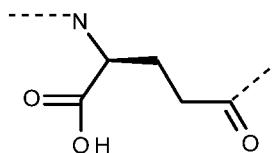
Another example of a linker is a combination of at least one amino acid and an amine.

5 The formula of another linker according to the present invention; OEG is shown below:

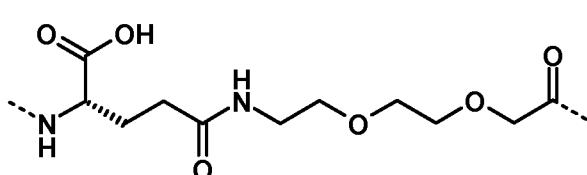


10 The linker can contribute to and/or enhance the binding effect of the moiety (for example the albumin binding moiety), e.g. a linker comprising γ Glu can enhance the albumin binding effect of the mimylin peptide.

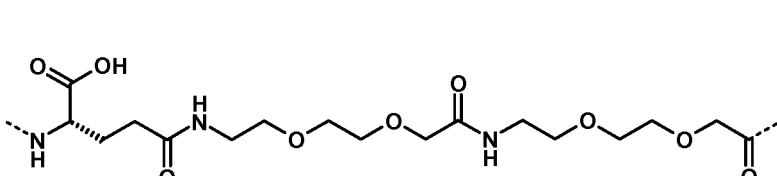
By using the term " **γ Glu**" or "**gGlu**" or "**gammaGlu**" or "**gamma-L-Glu**" is meant an amino acid with the following structure and used interchangeably herein (also shown in Figure 2):



15 By using the term " **γ Glu-OEG**" is meant a moiety with the following structure:



By using the term " **γ Glu-OEG-OEG**" is meant moiety with the following structure:



20 The term "**fatty acid**" refers to aliphatic monocarboxylic acids having from 4 to 28 carbon atoms, it is preferably un-branched, and it may be saturated or unsaturated.

25 In the present invention fatty acids comprising 10 to 16 amino acids are preferred.

The **term "fatty diacid"** refers to fatty acids as defined above but with an additional carboxylic acid group in the omega position. Thus, fatty diacids are

dicarboxylic acids. In the present invention fatty acids comprising 14 to 20 amino acids are preferred.

5 The term "**substituent**" or "**side chain**" as used herein means any suitable moiety bonded, in particular covalently bonded, to an amino acid residue, in particular to any available position on an amino acid residue. Typically, the suitable moiety is a chemical moiety.

10 "Albumin binding affinity" may be determined by several methods known within the art. In one method the compound to be tested is radiolabeled with e.g. ^{125}I or ^3H and incubated with immobilized albumin (Kurtzhals et.al., Biochem.J., 312, 725-731 (1995)). The binding of the compound relative to a standard is calculated. In another 15 method a related compound is radiolabeled and its binding to albumin immobilized on e.g. SPA beads is competed by a dilution series of the compound to be tested. The EC_{50} value for the competition is a measure of the affinity of the compound. In a third method, the receptor affinity or potency of a compound is tested at different concentrations of albumin, and the shift in relative affinity or potency of the compound as a function of albumin concentration reflects its affinity for albumin.

The term "**disulfide bridge**" can interchangeably be used for the term "**disulfide bond**".

20 The mimylin peptides of the present invention exhibit good potency. The term "**potency**" is used to describe the effect of a given compound in assays where a sigmoidal relationship between log concentration and the effect of a compound has been established. Furthermore, the response should be variable from 0 to 100%. EC (effective concentration) $_{50}$ can be used to describe the concentration of a given compound yielding a response of 50% in the assay, such as in the functional assay.

25 The mimylin peptides of the present invention exhibit good activity. The term "**activity**" refers to the ability to reduce appetite and/or increase satiety. The activity can be tested by the ability to reduce appetite as e.g. described in the Assay (I) herein.

30 The mimylin peptides of the present invention exhibit good physical stability. The term "**physical stability**" of a mimylin peptide according to the invention, or a formulation thereof refers to the tendency of the mimylin peptide not to form biologically inactive and/or insoluble aggregates as a result of exposure to thermo-mechanical stresses and/or interaction with interfaces and surfaces that are destabilizing, such as hydrophobic surfaces and interfaces. Physical stability of the aqueous mimylin peptide formulations may be evaluated by means of visual inspection, ThT fibrillation assay 35 (sometimes referred to as a ThT fibrillogenesis assay) and/or turbidity measurements as described elsewhere herein. Visual inspection of the formulations is performed in a sharp

focused light with a dark background. The turbidity of the formulation is characterised by a visual score ranking the degree of turbidity for instance on a scale from 0 to 3 (a formulation showing no turbidity corresponds to a visual score 0, and a formulation showing visual turbidity in daylight corresponds to visual score 3). A formulation is 5 classified physical unstable with respect to protein aggregation, when it shows visual turbidity in daylight. Alternatively, the turbidity of the formulation can be evaluated by simple turbidity measurements well-known to the skilled person.

The mimylin peptides of the present invention exhibit good chemical stability. The term "**chemical stability**" of a mimylin peptide according to the invention or of a 10 formulation thereof refers to no chemical covalent changes in the mimylin peptide structure hence avoiding the formation of chemical degradation products with potentially less potency and/or potentially increased immunogenic properties compared to the parent (native) mimylin peptide structure. Various chemical degradation products can be formed depending on the type and nature of the parent mimylin peptide and the 15 environment to which the mimylin peptide is exposed. Chemical degradation can most probably not be completely avoided and increasing amounts of chemical degradation products is often seen during storage and use of peptide formulations as well-known by the person skilled in the art. Most peptides are prone to deamidation, a process in which the side chain amide group in glutaminyl or asparaginyl residues is hydrolysed to form a 20 free carboxylic acid. Other degradations pathways involves formation of high molecular weight transformation products where two or more peptide molecules are covalently bound to each other through transamidation and/or disulfide interactions leading to formation of covalently bound dimer, oligomer and polymer degradation products (*Stability of Protein Pharmaceuticals*, Ahern. T.J. & Manning M.C., Plenum Press, New 25 York 1992). Oxidation (of for instance methionine residues) can be mentioned as another variant of chemical degradation. The chemical stability of the mimylin peptide formulation can be evaluated by measuring the amount of the chemical degradation products at various time-points after exposure to different environmental conditions (the formation of degradation products can often be accelerated by for instance increasing 30 temperature). The amount of each individual degradation product is often determined by separation of the degradation products depending on molecule size and/or charge using various chromatography techniques (e.g. SEC-HPLC and/or RP-HPLC).

While certain features of the invention have been illustrated and described herein, many modifications, substitutions, changes, and equivalents will now occur to 35 those of ordinary skill in the art. It is, therefore, to be understood that the appended

aspects are intended to cover all such modifications and changes as fall within the true spirit of the invention.

Non-limiting examples of GLP-1 compound include a natural GLP-1, a GLP-1 analogue or a GLP-1 derivative. In its broadest sense, the term "**natural GLP-1**" refers 5 to a naturally occurring molecule of the glucagon family of peptides or of the family of exendins. The glucagon family of peptides are encoded by the pre-proglucagon gene and encompasses three small peptides with a high degree of homology, i.e. glucagon (1-29), GLP-1 (1-37) and GLP-2 (1-33). The term "**natural GLP-1**" also refers to the human GLP-1(7-37), the sequence of which is disclosed as SEQ ID NO: 1 in WO 2006097537 10 and included herein by reference, and to the human GLP-1(7-36)NH2. Exendins are peptides expressed in lizards and like GLP-1, are insulinotropic. Examples of naturally occurring exendins are exendin-3 and exendin-4.

In a particular embodiment, the term "**natural GLP-1**" refers to glucagon (1-29), GLP-1 (1-37) and GLP-2 (1-33), the human GLP-1(7-37)), the human GLP-1(7-15 36)NH2, exendin-3 and exendin-4.

In a particular embodiment, the term "**GLP-1 compound**" does not include the human GLP-1(7-36)NH2. In a particular embodiment, the term "**GLP-1 compound**" does not include the human GLP-1(7-37).

In a particular embodiment, the term "**GLP-1 compound**" does not include 20 glucagon.

In a particular embodiment, the term "**GLP-1 compound**" does not include the human GLP-1(7-36)NH2 and glucagon or does not include human GLP-1(7-36)NH2, human GLP-1(7-37) and glucagon.

In a more particular embodiment, the term "**natural GLP-1**" only refers to the 25 human GLP-1(7-37).

In its broadest sense, the term "**GLP-1 analogue**" or "**analogue of GLP-1**" as used herein refers to an analogue of a natural GLP-1. It does not include a natural GLP-1 as such as defined herein. In particular, the term "**GLP-1 analogue**" does not include glucagon (1-29), GLP-1 (1-37) and GLP-2 (1-33), the human GLP-1(7-37)), the human 30 GLP-1(7-36)NH2, exendin-3 and exendin-4.

In a particular embodiment, the term "**GLP-1 analogue**" or "**analogue of GLP-1**" as used herein refers to an analogue of human GLP-1(7-37) or GLP-1(7-36)NH2.

Non-limiting examples of GLP-1 analogues comprise exenatide and taspooglutide.

In a particular embodiment, the "**GLP-1 analogues**" comprise analogues with a 35 maximum of 17 amino acid modifications (i.e. up to 17 amino acids have been modified in total, where the changes can be amino acid substitutions, additions and/or deletions)

compared to a natural GLP-1 of reference or, in particular, compared to human GLP-1-(7-36)NH2 or GLP-1(7-37).

All amino acids for which the optical isomer is not stated is to be understood to mean the L-isomer.

5 In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 17 amino acids which have been modified (substituted, deleted, added or any combination thereof) relative to a natural GLP-1 of reference or, in particular, relative to human GLP-1-(7-36)NH2 or GLP-1(7-37). In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a
10 maximum of 15 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 10 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 8 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a
15 maximum of 7 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 6 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 5 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 4 amino
20 acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 3 amino acids which have been modified. In embodiments of the invention a GLP-1 compound or GLP-1 analogue comprises a maximum of 2 amino acids which have been modified. In embodiments of the invention 1 amino acid has been modified relative to a natural GLP-1 of reference or, in particular,
25 relative to human GLP-1-(7-36)NH2 or GLP-1(7-37). In a particular embodiment, the amino acid modifications of this paragraph are relative to human GLP-1(7-37).

In a particular embodiment, the GLP-1 analogues comprise a substitution of the amino acid residue in position 34 from Lys to Arg, i.e. Arg³⁴, compared to GLP-1(7-37) or GLP-1-(7-36)NH2. In a particular embodiment, the GLP-1 analogues have a substitution 30 of the amino acid residue in position 8 from Ala to Aib (alpha-amino-iso-butyric acid), i.e. Aib⁸. In a particular embodiment, the GLP-1 analogues have the Arg³⁴ substitution, the Aib⁸ substitution, or both the Arg³⁴ and Aib⁸ substitutions, and possibly one more amino acid modification compared to GLP-1(7-37) or GLP-1-(7-36)NH2. In a particular embodiment, the amino acid modifications of this paragraph are relative to human GLP-35 1(7-37).

In its broadest sense, the term "**GLP-1 derivative**" or "**derivative of GLP-1**" as used herein refers to a derivative of a parent peptide selected from a natural GLP-1 or an analogue thereof. It does not include a natural GLP-1 as such as defined herein. In particular, the term "GLP-1 derivative" does not include glucagon (1-29), GLP-1 (1-37) 5 and GLP-2 (1-33), the human GLP-1(7-37)), the human GLP-1(7-36)NH₂, exendin-3 and exendin-4.

In a particular embodiment, the term "**GLP-1 derivative**" or "**derivative of GLP-1**" refers to a derivative of a parent peptide selected from human GLP-1(7-37) or GLP-1(7-36)NH₂ or an analogue thereof.

10 In a particular embodiment, the term "**GLP-1 derivative**" or "**derivative of GLP-1**" as used herein refers to a derivative of a parent peptide selected from a GLP-1 analogue, where said analogue comprises a maximum of 17 amino acid modifications compared to a natural GLP-1 of reference or, in particular, compared to human GLP-1-(7-36)NH₂ or GLP-1(7-37), or, in particular, compared to human GLP-1(7-37). In one 15 embodiment, the "**GLP-1 derivative**", in particular when defined in comparison to GLP-1(7-37), does not include GLP-1(7-36)NH₂.

Typical modifications are amides, carbohydrates, alkyl groups, acyl groups, esters, polyethylene glycol (PEG) groups, sialylation groups, glycosylation groups and the like of a parent peptide. In one embodiment, the parent peptide is a GLP-1 analogue as 20 defined above.

In particular embodiments, the side chain has at least 10 carbon atoms, or at least 15, 20, 25, 30, 35, or at least 40 carbon atoms. In further particular embodiments, the side chain may further include at least 5 hetero atoms, in particular O and N, for example at least 7, 9, 10, 12, 15, 17, or at least 20 hetero atoms, such as at least 1, 2, 25 or 3 N-atoms, and/or at least 3, 6, 9, 12, or 15 O-atoms.

In one embodiment, the term "**GLP-1 derivative**" refers to acylated GLP-1 parent peptide. In a particular embodiment, the term "**GLP-1 derivative**" refers to acylated GLP-1 parent peptide where the parent peptide is selected from a GLP-1 analogue comprising a maximum of 17 amino acid modifications compared to a natural 30 GLP-1 of reference or, in particular, compared to human GLP-1-(7-36)NH₂ or GLP-1(7-37).

The side chain may be covalently attached to a lysine residue of the GLP-1 parent peptide by acylation. Additional or alternative conjugation chemistry includes alkylation, ester formation, or amide formation, or coupling to a cysteine residue, such as 35 by maleimide or haloacetamide (such as bromo-/fluoro-/iodo-) coupling.

For the preparation, an active ester of the side chain is covalently linked to an amino group of a lysine residue, preferably the epsilon amino group thereof, under formation of an amide bond (this process being referred to as acylation).

Preferred side chains include, for example, fatty acids and fatty diacids. The term fatty acid refers to aliphatic monocarboxylic acids having from 4 to 28 carbon atoms. The fatty acid may be branched or unbranched. The fatty acid is preferably even numbered. The fatty acid may be saturated or unsaturated. The term fatty diacid refers to fatty acids as defined above but with an additional carboxylic acid group in the omega position. Thus, fatty diacids are dicarboxylic acids.

10 In a particular embodiment, the side chain(s) is a fatty acid having 10 to 20 carbon atoms, and preferably 14 to 20 or 16 to 18 carbon atoms, optionally with a spacer.

15 In a particular embodiment, the side chain(s) is a fatty acid of formula Chem.1: HOOC(CH₂)_mCO, wherein m is an integer from 8 to 18, optionally with a linker. In a particular embodiment, m is an integer from 12 to 18 or from 14 to 16.

In a particular embodiment, the side chain(s) is selected from the group consisting of HOOC(CH₂)₁₄CO-, HOOC(CH₂)₁₆CO-, HOOC(CH₂)₂₂CO-, CH₃(CH₂)₁₄CO-, CH₃(CH₂)₁₆CO- and CH₃(CH₂)₁₈CO-.

20 In one embodiment, the term "**GLP-1 derivative**" comprises or refers to monoacylated GLP-1 parent peptide, i.e. a GLP-1 parent peptide comprising only one acylation as defined above.

25 In a particular embodiment, the side chain is a fatty acid or a fatty diacid of which an acid group forms an amide bond with the epsilon amino group of a lysine residue in the GLP-1 compound, preferably via a spacer. In one embodiment, said lysine residue is Lys²⁶, especially when the parent peptide is human GLP-1(7-37), GLP-1(7-36)NH₂ or a GLP-1 analogue.

30 In a particular embodiment, the side chain is attached to the parent peptide by means of a linker. In a particular embodiment, the linker comprises a γ -glutamic acid (γ -Glu) and/or 1, 2 or 3 OEG molecules. In γ Glu the gamma carboxy group of the amino acid glutamic acid is used for connection to another linker element, or to the epsilon-amino group of lysine. An OEG molecule is also named a di-radical of 8-amino-3,6-dioxaoctanic acid, and/or it may be represented by the formula Chem. 2: -NH-(CH₂)₂-O-(CH₂)₂-O-CH₂-CO-.

35 The linker may include one or more γ Glu, and/or one or more OEG. More in particular, the γ Glu and OEG linker elements may, independently, be used p times where p is zero or an integer in the range of 1-3. Examples of preferred linkers are γ Glu-

2xOEG, and γ Glu-3xOEG where in all cases the alpha-amino group of Glu forms an amide bond with the carboxy group of the protracting moiety.

In a particular embodiment, the GLP-1 derivative is a derivative of a GLP-1 analogue which comprises the Arg³⁴ substitution or the Arg³⁴ and the Aib⁸ substitutions 5 compared to human GLP-1(7-37), GLP-1(7-36)NH₂ and which comprises a side chain attached to Lys²⁶. In a particular embodiment said side chain is a fatty acid as defined above, especially a fatty acid of formula Chem.1, with m being an integer from 8 to 18, optionally with a linker being γ Glu.

10 In one embodiment, the GLP-1 derivative is as defined in the patent applications WO 98/08871 and WO 06/097537, entirely included herein by reference. Non-limiting examples of monoacylated GLP-1 derivatives can be found in those applications.

Non-limiting examples of GLP-1 derivatives also include:

- N^{ε37}-[2-[2-[2-[2-[2-[(4S)-4-carboxy-4-[[4-[(19-
carboxynonadecanoylamino)methyl]cyclo
15 hexanecarbonyl]amino]butanoyl]amino]ethoxy]ethoxy]acetyl]amino]ethoxy]ethoxy]
y]acetyl]-[Imp⁷,Glu²²,Arg²⁶,Arg³⁴,Lys³⁷]-GLP-1-(7-37)-peptide;
- N^{ε26}-[2-[2-[2-[2-[2-[2-[(4S)-4-carboxy-4-(17-
carboxyheptadecanoylamino)butanoyl]amino]ethoxy]ethoxy]acetyl]
amino]ethoxy]ethoxy]acetyl]-[Aib⁸,Arg³⁴]-GLP-1-(7-37)-peptide, also called
20 semaglutide;
- N^{ε26}-[(4S)-4-carboxy-4-(hexadecanoylamino)butanoyl]-[Arg³⁴]-GLP-1-(7-37)-
peptide, also called liraglutide;
- N^{ε26}-[2-[2-[2-[2-[2-[2-[(4S)-4-carboxy-4-[10-(4-
carboxyphenoxy)decanoylamino]butanoyl]
25 amino]ethoxy]ethoxy]acetyl]amino]ethoxy]ethoxy]acetyl],N³⁷-[2-[2-[2-[2-[2-
[2-[(4S)-4-carboxy-4-[10-(4-
carboxyphenoxy)decanoylamino]butanoyl]amino]ethoxy]ethoxy]acetyl]
amino]ethoxy]ethoxy]acetyl]-[Aib⁸,Arg³⁴,Lys³⁷]-GLP-1-(7-37)-peptide;
- N^{ε26}-[2-[2-[2-[2-[2-[2-[(4S)-4-carboxy-4-[12-(3-
carboxyphenoxy)dodecanoylamino]butanoyl]
30 amino]ethoxy]ethoxy]acetyl]amino]ethoxy]ethoxy]acetyl],N³⁷-[2-[2-[2-[2-[2-
[2-[(4S)-4-carboxy-4-[12-(3-
carboxyphenoxy)dodecanoylamino]butanoyl]amino]ethoxy]ethoxy]acetyl]
amino]ethoxy]ethoxy]acetyl]-[Aib⁸,Arg³⁴,Lys³⁷]-GLP-1-(7-37)-peptide;
- lixisenatide;
- albiglutide;

- dulaglutide.

In a particular embodiment, the GLP-1 derivative is liraglutide or semaglutide.

The chemically modified derivatives of natural GLP-1 can be prepared for example as described in patent US 6,451,762 or in Knudsen et. al. (2000) J Med Chem 43, 1664-

5 1669.

When using terms such as "**about**" and "**approximately**" in relation to numerical values the skilled person should immediately recognise that any effect or result, which may be associated with the given values can be obtained within a certain tolerance from the particular values. The term "**about**" as used herein thus means in 10 reasonable vicinity of the stated numerical value, such as plus or minus 10%.

EXAMPLES

MATERIALS AND METHODS

ABBREVIATIONS

15 Some of the abbreviations used in the Examples are as follows:

Acm: acetamidomethyl

BHK: Baby hamster kidney

CHO: Chinese hamster ovary

20 **HATU:** (O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate)

HBTU: 2-(1H-Benzotriazol-1-yl)-1,1,3,3 tetramethyluronium hexafluorophosphate

Fmoc: 9 H-fluoren-9-ylmethoxycarbonyl

Boc: tert butyloxycarbonyl

Mtt: 4-methyltrityl

DCM: dichloromethane

TIPS: triisopropylsilane

TFA: trifluoroacetic acid

30 **NMP:** 1-Methyl-pyrrolidin-2-one

HOAt: 1-Hydroxy-7-azabenzotriazole

DIC: Diisopropylcarbodiimide

Trt: triphenylmethyl

35 **BHK tk'ts 13 cells:** This line is a thymidine kinase deficient mutant of a ts 13, a temperature-sensitive mutant of BHK 21.

General Methods of Preparation

The production of peptides like mimylin is well known in the art.

40 The mimylin peptide/mimylin analogue of the invention may for instance be produced by classical peptide synthesis, e.g., solid phase peptide synthesis using t-Boc or Fmoc chemistry or other well established techniques, see, e.g., Greene and Wuts,

"Protective Groups in Organic Synthesis", John Wiley & Sons, 1999, Florencio Zaragoza Dörwald, "Organic Synthesis on solid Phase", Wiley-VCH Verlag GmbH, 2000, and "Fmoc Solid Phase Peptide Synthesis", Edited by W.C. Chan and P.D. White, Oxford University Press, 2000.

5 Also, or alternatively, they may be produced by recombinant methods, viz. by culturing a host cell containing a DNA sequence encoding the analogue and capable of expressing the peptide in a suitable nutrient medium under conditions permitting the expression of the peptide. Non-limiting examples of host cells suitable for expression of these peptides are: *Escherichia coli*, *Saccharomyces cerevisiae*, as well as mammalian
10 BHK or CHO cell lines.

Those peptides, analogues or derivatives of the invention which include non-natural amino acids and/or a covalently attached N-terminal mono- or dipeptide mimetic may e.g. be produced as described in the experimental part. Or see e.g., Hodgson et al: "The synthesis of peptides and proteins containing non-natural amino acids", Chemical
15 Society Reviews, vol. 33, no. 7 (2004), p. 422-430; and WO 2009/083549 A1 entitled "Semi-recombinant preparation of GLP-1 analogues".

Preparations of peptides and derivatives

The mimylin peptide sequences were prepared according to the below-mentioned
20 mimylin peptide synthesis and the compounds as presented in the Tables (e.g. Table 1 or Table 2) were prepared according to the below-mentioned synthesis.

One method of mimylin peptide synthesis was by Fmoc chemistry on a microwave-based Liberty peptide synthesizer (CEM Corp., North Carolina). The resin was Tentagel S RAM with a loading of about 0.25 mmol/g or PAL-ChemMatrix with a loading
25 of about 0.43 mmol/g or PAL AM matrix with a loading of 0.5-0.75 mmol/g. The coupling chemistry was DIC/HOAt or DIC/Oxyma in NMP or DMF using amino acid solutions of 0.3 M and a molar excess of 6-8 fold. Coupling conditions was 5 minutes at up to 70°C. Deprotection was with 10% piperidine in NMP at up to 70°C. The protected amino acids used were standard Fmoc-amino acids (supplied from e.g. Anaspec or Novabiochem or
30 Protein Technologies).

Another method of mimylin peptide synthesis was by Fmoc chemistry on a Prelude peptide synthesizer (Protein Technologies, Arizona). The resin was Tentagel S RAM with a loading of about 0.25 mmol/g or PAL-ChemMatrix with a loading of about 0.43 mmol/g or PAL AM with a loading of 0.5-0.75 mmol/g. The coupling chemistry was
35 DIC/HOAt or DIC/Oxyma in NMP or DMF using amino acid solutions of 0.3 M and a molar excess of 6-8 fold. Coupling conditions was single or double couplings for 1 or 2 hours at room temperature. Deprotection was with 20% piperidine in NMP. The protected amino

acids used were standard Fmoc-amino acids (supplied from e.g. Anaspec or Novabiochem or Protein Technologies).

N-terminal attachment of fatty acids, linkers etc. were usually performed by including the relevant building blocks in the standard peptide synthesis.

5 When a chemical modification of a lysine side chain was desired, the lysine was incorporated as Lys(Mtt) and the N-terminal amino acid was either incorporated into the sequence as a Boc-amino acid or, if the N-terminal amino acid was incorporated as an Fmoc-amino acid, the Fmoc group was removed and the N-terminal was protected by treatment with 6 equivalents of Boc-carbonate and 6 equivalents of DIPEA in NMP for 30
10 minutes. The resin was washed with NMP and DCM and the Mtt group was removed by suspending the resin in neat hexafluoroisopropanol or HFIP/DCM 3:1 for 20 minutes followed by washing with DCM and NMP. The chemical modification of the lysine was performed by adding one or more of the building blocks listed below by the same methods as used for the mimylin peptide synthesis, i.e. by one or more automated steps
15 on the Liberty or by one or more manual coupling steps at room temperature. After synthesis the resin was washed with DCM and dried, and the mimylin peptide was cleaved from the resin by a 2 hour treatment with TFA/TIPS/water (92.5/5/2.5 or 95/2.5/2.5) followed by precipitation with 4 volumes of diethylether, further washing with diethylether and drying.

20 Purification: The crude mimylin peptide was purified by semipreparative HPLC on a 20 mm x 250 mm column packed with either 5um or 7um C-18 silica. Mimylin peptide solutions were pumped onto the HPLC column and precipitated mimylin peptides were dissolved in 5 ml 50% acetic acid H₂O and diluted to 20 ml with H₂O and injected on the column which then was eluted with a gradient of 40-60 % CH₃CN in 0.1% TFA 10 ml/min
25 during 50 min at 40°C. The mimylin peptide containing fractions were collected. The purified mimylin peptide was lyophilized after dilution of the eluate with water.

30 For analysis of HPLC-fractions and final product RP-HPLC analysis was performed using UV detection at 214 nm and e.g. a Vydac 218TP54 4.6mm x 250mm 5um C-18 silica column (The Separations Group, Hesperia, USA) and eluted at e.g. 1 ml/min at 42°C. Most often one of four different elution conditions was used:

A1: Equilibration of the column with a buffer consisting of 0.1M (NH₄)₂SO₄, which was adjusted to pH 2.5 with concentrated H₂SO₄ and elution by a gradient of 0% to 60% CH₃CN in the same buffer during 50 min.

B1: Equilibration of the column with 0.1% TFA / H₂O and elution by a gradient of 0% CH₃CN / 0.1% TFA / H₂O to 60% CH₃CN / 0.1% TFA / H₂O during 50 min.

B6: Equilibration of the column with 0.1% TFA / H₂O and elution by a gradient of 0% CH₃CN / 0.1% TFA / H₂O to 90% CH₃CN / 0.1% TFA / H₂O during 50 min.

Alternatively the RP-HPLC analysis was performed using UV detection at 214 nm and a Symmetry300, 3.6mm x 150mm, 3.5um C-18 silica column (Waters) which was eluted at 5 1 ml/min at 42°C.

B4: Equilibration of the column with 0.05% TFA / H₂O and elution by a gradient of 5% CH₃CN / 0.05% TFA / H₂O to 95% CH₃CN / 0.05% TFA / H₂O during 15 min.

The identity of the mimylin peptide was confirmed by MALDI-MS on a Bruker Microflex.

10 **Example synthesis:**

Synthesis of mimylin, SEQ ID NO: 1 (Example #1) an example of a mimylin peptide

400 mg PAL AM resin (0.61mmol/g) was swollen in DCM/NMP and synthesis was performed on a Prelude peptide synthesizer using 1 hour couplings in DMF as described 15 above. After cleavage with TFA cleavage cocktail, the peptide was precipitated with ether and dried yielding 800 mg crude mimylin with a purity of about 50%. HPLC purification (as described above) gave about 200 mg mimylin with a purity of >90%

20 **Synthesis of Compound [N-terminal(C18 diacid)]mimylin (Example #2) an example of a mimylin derivative**

600 mg PAL ChemMatrix resin (0.43mmol/g) was swollen in DCM/NMP and synthesis was performed on a Liberty peptide synthesizer using 5 min couplings in NMP at 70°C as described above. As the last step of the synthesis C18-diacid-mono-t-butylester was coupled under the same conditions. After cleavage, the peptide was precipitated with 25 ether and dried yielding 700 mg crude [N-terminal(C18 diacid)]mimylin with a purity of about 55%. HPLC purification gave about 150 mg [N-terminal(C18 diacid)]mimylin with a purity of >90%

30 **Alternative synthesis of Compound [N-terminal(C18 diacid)]mimylin (Example #2)**

Mimylin is synthesized and purified as described above, dissolved in water or a suitable mixture of water and an organic solvent such as e.g. NMP, DMF, DMSO, or acetonitrile. A solution of activated C18-diacid, e.g. C18-diacid-succinimidyl ester is added and the resulting solution of Example 2 is purified.

35

Observations

All references, including publications, patent applications, and patents, cited herein are hereby incorporated by reference in their entirety and to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein (to the maximum extent permitted by law).

5 All headings and sub-headings are used herein for convenience only and should not be construed as limiting the invention in any way.

The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the 10 specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

The citation and incorporation of patent documents herein is done for convenience only and does not reflect any view of the validity, patentability, and/or enforceability of such patent documents.

15 This invention includes all modifications and equivalents of the subject matter recited in the aspects appended hereto as permitted by applicable law.

In the following examples reference is made to the following Assays:

20 **Table 7- list of assays**

ASSAY #	Assay Title
I	Experimental protocol for efficacy testing on appetite using an ad libitum fed rat model
IIa	<i>Functional assay</i> - Human calcitonin and amylin receptor assay with albumin
IIb	<i>Functional assay</i> - Human calcitonin and amylin receptor assay without albumin
IIc	<i>Functional assay</i> - Rat calcitonin and rat amylin receptor assays
III	ThT fibrillation – Determination of physical stability of protein formulations
IIIa	ThT fibrillation – Determination of physical stability of protein formulations
IV	Determination of solubility
V	Determination of binding to the human amylin receptor (membrane)
V a	Determination of binding to the human amylin receptor (whole cell)
VI	Determination of the binding to the rat amylin receptor

ASSAY #	Assay Title
VII	Determination of binding to the human calcitonin receptor (membrane)
VIIa	Determination of binding to the human Calcitonin Receptor (whole cell)
VIII	Determination of binding to the rat calcitonin receptor
IX	pK – Determination of T _{1/2} in mini-pig
X	pK – Determination of T _{1/2} in rat
XI	Determining potential MHC Class II binding sites
XII	<u>SEC-HPLC</u>
XIII	<u>Quiescent storage stability of formulations</u>
XIV	Experimental protocol for testing effect on body weight using DIO rat model
XV	Determination subcutaneous mimylin derivative PK in LYD-pigs when co-formulated with liraglutide
XVI	Determination of T _{1/2} and subcutaneous bioavailability in LYD-pigs
XVII	Determination of T _{1/2} and subcutaneous bioavailability in Beagle dogs

ASSAY (I) - Experimental protocol for efficacy testing on appetite using an *ad libitum* fed rat model

Sprague Dawley (SD) rats from Taconic Europe, Denmark are used for the experiments.

5 The rats have a body weight 200-250 g at the start of experiment. The rats arrive at least 10-14 days before start of experiment to allow acclimatisation to experimental settings. During this period the animals are handled at least 2 times. After arrival rats are housed individually for one week in a reversed light/dark phase (meaning that lights are off during daytime and on during nighttime) for two weeks. Since rats are normally active and eat their major part of their daily food intake during the dark period, rats are dosed in the morning right before lights are turned off. This set-up results in the lowest data variation and highest test sensitivity. The experiment is conducted in the rats' home cages and rats have free access to food and water throughout the acclimatization period and the experiment period. Each dose of derivative is tested in a group of 5-8 rats. A 10 vehicle group of 6-8 rats is included in each set of testing. Rats are dosed once according to body weight with a 0.01-3 mg/kg solution administered intraperitoneally (ip), orally (po) or subcutaneously (sc). The time of dosing is recorded for each group.

15

After dosing, the rats are returned to their home cages, where they then have access to food and water. The food consumption is recorded individually continuously by 20 on-line registration or manually every hour for 7 hours, and then after 24 h and sometimes 48 h. At the end of the experimental session, the animals are euthanised. The

individual data are recorded in Microsoft excel sheets. Outliers are excluded after applying the Grubbs statistical evaluation test for outliers, and the result is presented graphically using the GraphPad Prism program.

5 **ASSAY(II)a - Human calcitonin and amylin receptor assay**

1. Luciferase assay outline

Activation of calcitonin and amylin (co-expression of calcitonin receptor and receptor activity modifying proteins (RAMP)) receptors lead to increased intracellular concentrations of cAMP. Consequently, transcription is activated by promoters containing 10 multiple copies of the cAMP response element (CRE). It is thus possible to measure amylin activity by the use of a CRE luciferase reporter gene introduced into BHK cells also expressing calcitonin or amylin receptors.

2. Construction of calcitonin (a) - and amylin 3(a)- receptor/CRE-luc cell line.

15 A BHK570 cell line was stably transfected with the human calcitonin receptor and a CRE-responsive luciferase reporter gene. The cell line was further transfected with RAMP-3, using standard methods. This turns the calcitonin receptor into an amylin 3(a) receptor. Methotrexate, Neomycin, and Hygromycin are selection markers for luciferase, the calcitonin receptor, and RAMP-3, respectively.

20

3. Luciferase assays

To perform activity assays, BHK calcitonin (a) receptor- or amylin 3(a)-receptor/CRE-luc cells were seeded in white 96 well culture plates at a density of about 20.000 cells/well. The cells were in 100 μ l growth medium (DMEM with 10% FBS, 1% Pen/Strep, 1 mM Na-pyruvate, 250 nM Methotrexate, 500 μ g/ml Neomycin, and 400 μ g/ml Hygromycin). After 25 incubation overnight at 37°C and 5% CO₂, the growth medium was replaced by 50 μ l/well assay medium (DMEM (without phenol red), Glutamax™, 10% FBS, and 10 mM Hepes, pH 7,4). Further, 50 μ l/well of standard or sample in assay buffer were added.

After 3 hours incubation at 37°C and 5% CO₂, the assay medium with standard 30 or sample were removed and replaced by 100 μ l/well PBS. Further, 100 μ l/well LucLite™ was added. The plates were sealed and incubated at room temperature for 30 minutes. Finally, luminescence was tested on a TopCounter (Packard) in SPC (single photon counting) mode.

35 **ASSAY(II)b - Human calcitonin and amylin receptor assay without albumin**

1. Luciferase assay outline

Activation of calcitonin and amylin (co-expression of calcitonin receptor and receptor activity modifying proteins (RAMP)) receptors lead to increased intracellular concentrations of cAMP. Consequently, transcription is activated by promoters containing multiple copies of the cAMP response element (CRE). It is thus possible to measure 5 amylin activity by the use of a CRE luciferase reporter gene introduced into BHK cells also expressing calcitonin or amylin receptors.

2. Construction of calcitonin (a) - and amylin 3(a)- receptor/CRE-luc cell line.

A BHK570 cell line was stably transfected with the human calcitonin receptor and a CRE-10 responsive luciferase reporter gene (Hollex-1 cell line, obtained from ZymoGenetics described in US patent 5622839). The cell line was further transfected with RAMP-3, using standard methods. This turns the calcitonin receptor into an amylin 3(a) receptor. Methotrexate, Neomycin, and Hygromycin are selection markers for luciferase, the calcitonin receptor, and RAMP-3, respectively. To prepare the batches of frozen cells used 15 in the luciferase assay described in the section below, the cells were cultured in growth medium (DMEM with 10 % FBS, 1 % Pen/Strep and 1 mM Napyruvate). Methotrexate (250 nM) and Neomycin (500 µg/ml) were used as selection markers for the expression of the luciferase reporter and the calcitonin receptor, respectively. Cells at approximately 80-90 % confluence were washed with PBS and loosened from the plates with Versene. 20 After centrifugation (2 min, 1300 rpm, in a Centrion Scientific centriuge C2 series with a BRK 5510 rotor head), the cell pellet was dissolved in 10 % DMSO, 30 % FBS and 60 % growth medium and frozen (-80°C) until utilization.

3. Luciferase assays

25 The day before the experiment, BHK calcitonin (a) receptor- or amylin 3(a)- receptor/CRE-luc cells were thawed, washed twice, and seeded in 40 µl growth medium on white 384 well culture plates (4.000 cells/well). On the assay day, the cells were washed 3 times in assay media (Dulbecco media W/o phenol red, 500 ml (Gibco, 11880-028); 0,1 % ovalbumin; 10 mM Hepes pH 7,4; 1x Glutamin; 1% Pen/Strep). Then, 30 30 µl/well of sample diluted in assay buffer was added. After 3 hours of incubation at 37°C and 5% CO₂, the the reaction was terminated by adding 30 µl/well SteadyLite plus TM. The plates were shaken at 300 rpm for 5 min at RT. Then, the plates were sealed and incubated at room temperature for 30 minutes. Finally, luminescence was tested on a TopCounter (Packard) in SPC (single photon counting) mode. 35 EC50 values were calculated in GraphPad Prism using a nonlinear regression with hillslope=1.

Additional comment regarding use of data retrieved via this method

This assay provides confirmation of biologic activity and confirms that all mimylin peptides or derivatives as described herein are amylin and calcitonin receptor agonists.

5 Due to the presence of HSA it should be noted that mimylin derivatives with different protracting moieties should not be compared relative regarding their EC₅₀ value, because different side chains bind to HSA with different affinities and thus influence the EC₅₀ and thus shift the EC₅₀ towards higher values when the protracting moiety binds more efficiently to HSA. For the same reasons, measurements made in Assay IIa should not be
10 compared in Assay IIb.

ASSAY (II)c - Rat calcitonin and rat amylin receptor assays**cAMP assay outline**

Activation of calcitonin and amylin (co-expression of calcitonin receptor and receptor
15 activity modifying proteins (RAMP)) receptors lead to increased intracellular concentrations of cAMP. In order to quantify the cAMP levels in transiently transfected cells the Adenylyl Cyclase Activation FlashPlate® Assay from Perkin Elmer was used. The basic principle of the FlashPlate® Assay is a competition between radioactive and non-radioactive cAMP generated by the cells for a fixed number of binding sites.

20

Construction of rat calcitonin(a) - and rat amylin 3(a)-receptor cells.

BHK tk' ts 13 cells were transiently transfected with either rat calcitonin (a) receptor or amylin 3 (a) receptor (rat calcitonin(a) receptor+ rat RAMP3) using FuGENE® 6 (Roche), according to the manufacturers recommendations.

25

cAMP assay

24 hours after transient transfection the cells (rat calcitonin(a) - or rat amylin 3(a) - receptor cells) were added (100.000 cells/well) to the 96 well FlashPlates® with samples or standard in FlashPlate stimulation buffer with IBMX and incubated for 30 min.
30 Detection mix was created according to manufacturer's protocol and scintillation tested after 3h of incubation on TopCounter™ (Packard).

ASSAY (III) - ThT fibrillation – Determination of physical stability of protein formulations

35 Low physical stability of a mimylin peptide may lead to amyloid fibril formation, which is observed as well-ordered, thread-like macromolecular structures in the sample

eventually resulting in gel formation. This has traditionally been tested by visual inspection of the sample. However, that kind of measurement is very subjective and depending on the observer. Therefore, the application of a small molecule indicator probe is much more advantageous. Thioflavin T (ThT) is such a probe and has a distinct 5 fluorescence signature when binding to fibrils [Naiki et al. (1989) *Anal. Biochem.* **177**, 244-249; LeVine (1999) *Methods. Enzymol.* **09**, 274-284].

The time course for fibril formation can be described by a sigmoidal curve with the following expression [Nielsen et al. (2001) *Biochemistry* **40**, 6036-6046]:

10

$$F = f_i + m_i t + \frac{f_f + m_f t}{1 + e^{-[(t-t_0)/\tau]}} \quad \text{Eq. (1)}$$

Here, F is the ThT fluorescence at the time t. The constant t_0 is the time needed to reach 15 50% of maximum fluorescence. The two important parameters describing fibril formation are the lag-time calculated by $t_0 - 2\tau$ and the apparent rate constant $k_{app} = 1/\tau$.

Formation of a partially folded intermediate of the mimylin peptide is suggested as a general initiating mechanism for fibrillation. Few of those intermediates nucleate to form a template onto which further intermediates may assemble and the fibrillation proceeds. The lag-time corresponds to the interval in which the critical mass of nucleus is 20 built up and the apparent rate constant is the rate with which the fibril itself is formed.

Sample preparation

Samples were prepared freshly before each assay. Each sample composition is described in each example. The pH of the sample was adjusted to the desired value using 25 appropriate amounts of concentrated NaOH and HClO₄ or HCl. Thioflavin T was added to the samples from a stock solution in H₂O to a final concentration of 1 μM. Sample aliquots of 200 μl were placed in a 96 well microtiter plate (Packard OptiPlate™-96, white polystyrene). Usually, four or eight replica of each sample (corresponding to one test condition) were placed in one column of wells. The plate was sealed with Scotch Pad 30 (Qiagen).

Incubation and fluorescence measurement

Incubation at given temperature, shaking and measurement of the ThT fluorescence emission were done in a Fluoroskan Ascent FL fluorescence plate reader or Varioskan 35 plate reader (Thermo Labsystems). The temperature was adjusted to 37°C. The orbital

shaking was adjusted to 960 rpm with an amplitude of 1 mm in all the presented data. Fluorescence measurement was done using excitation through a 444 nm filter and measurement of emission through a 485 nm filter.

5 Each run was initiated by incubating the plate at the assay temperature for 10 min. The plate was tested every 20 minutes for a desired period of time. Between each measurement, the plate was shaken and heated as described.

Data handling

10 The measurement points were saved in Microsoft Excel format for further processing and curve drawing and fitting was performed using GraphPad Prism. The background emission from ThT in the absence of fibrils was negligible. The data points are typically a mean of four or eight samples and shown with standard deviation error bars. Only data obtained in the same experiment (i.e. samples on the same plate) are presented in the same graph ensuring a relative measure of fibrillation between experiments.

15 The data set may be fitted to Eq. (1). However, since full sigmoidal curves in this case are not always achieved during the measurement time, the degree of fibrillation is expressed as ThT fluorescence tabulated as the mean of the samples and shown with the standard deviation at various time points.

20 Measurement of initial and final concentrations

The mimylin peptide concentration in each of the tested formulations was tested both before application in the ThT fibrillation assay ("Initial") and after completion of the ThT fibrillation ("After ThT assay"). Concentrations were determined by reverse HPLC methods using a pramlintide standard as a reference. Before measurement after 25 completion 150 µl was collected from each of the replica and transferred to an Eppendorf tube. These were centrifuged at 30000 G for 40 mins. The supernatants were filtered through a 0.22 µm filter before application on the HPLC system.

30 ASSAY (IIIa) - ThT fibrillation – Determination of physical stability of protein formulations

Sample preparation, incubation and fluorescence measurements were done according to the principles described under ASSAY (III).

Data handling

35 Fluorescence measurements for each microtiter plate well were plotted against time and the lag-time (time until an increase in ThT fluorescence was observed) was estimated

based on the intercept between the linear initial lag-phase and the first part of the subsequent exponential growth phase.

Measurement of peptide recovery of mimylin-formulations

5 Done according to the principles described above in Assay III; however, ASSAY (XII) was used for quantification of peptide concentration before and after incubation.

Measurement of peptide recovery of mimylin/GLP-1 co-formulations

RP-UPLC was conducted using an Acquity UPLC BEH C18 1.7 μ m (2.1 x 30 mm) column 10 (Eluent A: 0.1 v/v % TFA in water; Eluent B: 0.1 v/v % TFA in acetonitrile) with gradient elution (0 min: 95% A; 2 min: 20% A; 2.3 min: 20% A; 2.4 min: 95% A) in a flow rate of 0.9 ml/min and a column temperature of 30°C. UV-detection at 215 nm was used to assess the total peptide recovery (on an individual basis if separated) whereas detection at 280 nm was used to determine the recovery of the GLP-1 component (no UV-280 nm 15 absorption from the mimylin component).

ASSAY (IV) – Determination of solubility

The mimylin peptide was dissolved in water at ~500 nmol/ml and mixed 1:1 with a series of buffers (100 mM glycylglycine pH 3.0, 100 mM glycylglycine pH 4.0, 100 mM 20 glycylglycine pH 5.0, 100 mM bistrispropane pH 6.0, 100 mM bistrispropane pH 6.5, 100 mM bistrispropane pH 7.0, 100 mM bistrispropane pH 7.5, 100 mM bistrispropane pH 8.0). After 18 hours at room temperature the samples were centrifuged and the mimylin peptide concentration determined by UPLC.

ASSAY (V) – Determination of binding to the human amylin receptor

The binding assay was performed using scintillation proximity assay (SPA) beads (RPNQ0001) from PerkinElmer and cell membranes from the Amylin 3(a)/CRE-luc cells (as described in Assay (II)) were used. Membranes were prepared in the following way; the cells were rinsed with PBS and incubated with Versene for approximately 5 min 30 before harvesting. The cells were flushed with PBS and the cell-suspension was centrifuged for 5 min at 1000 rpm. Cells were homogenized (ultrathurax) in a buffer containing 20mM Na-HEPES and 10mM EDTA (pH 7.4) and centrifuged at 20.000rpm for 15min. The resulting pellet was resuspended, homogenized and centrifuged (20.000rpm, 15min) in a buffer containing 20mM Na-HEPES and 0.1mM EDTA (pH 7.4, buffer 2). The 35 resulting pellet was resuspended in buffer 2 and protein concentration was tested (BCA protein Assay, Pierce). The homogenate was kept cold during the whole procedure. The

membranes were kept at -80°C until use. The assay was performed in a 384 well Optiplate (PerkinElmer) in a total volume of 40ul. Membranes were mixed with SPA beads. Final concentration of membranes 35 ng/µL final and SPA beads was 0.05mg/well. Test-compounds were dissolved in DMSO and further diluted in assay buffer (50 mM Hepes, pH 7.4, 1 mM CaCl₂, 5 mM MgCl₂, 0.1% OA and 0.02% Tween20). Radioligand ¹²⁵I-rat amylin (NEX448 PerkinElmer) was dissolved in assay buffer and added to the Optiplate at a final concentration of 50pM/well (approx. 20.000cpm/10ul). The final mixture was incubated with shaking at 400 rpm for 120 min at 25°C prior to centrifugation (1500rpm, 10min). Samples were analyzed on TopCounter™ (Packard). The IC₅₀ was calculated using (one site binding competition analysis) GraphPad Prism5 as a measure of receptor affinity.

ASSAY (Va) – Determination of binding to the human Amylin receptor (whole cell binding)

15 The binding assay was performed using a BHK tk'ts 13 cell line was stably transfected with the human calcitonin receptor, the human RAMP3 and a CRE-responsive luciferase reporter gene.

The day before the assay the cells were Seeded into Poly-D-Lysin coated 384W Opaque White, BD BioCoat plates (10000 cells/well) and Incubated overnight at 37 °C, 5 % CO₂, 20 95% humidity. Then, the cells were washed in HBSS (4°C), and incubated overnight at 4°C in a binding buffer containing test compounds, 50 pM [125I]-rat amylin, Dulbecco media w/o phenol red, 500 ml, 0,1 % ovalbumin (5 ml 10 % ovalbumin), 10 mM Hepes (5 ml 1M) 1x Glutamin (5 ml 100x) 1% P/S (5 ml 100%) Complete (1 tablet/50 ml) 0,1% Pluronic F68®. The morning after, the plates were washed three times in HBSS (4°C), and lyzed in Lysis buffer (0,1 M NaOH (VWR #1.09136.1000), 1% SDS. Then MicroScint40 was addes and the plated were shaken at 500 rpm for a short period. Then the plate was incubated at room temperature in the dark for 1 hour and Read on a TopCounter. The IC₅₀ was calculated using (one site binding competition analysis) GraphPad Prism5 as a measure of receptor affinity.

30

ASSAY (VI) – Determination of the binding to the rat amylin receptor (membrane)

The assay was performed as described above (Assay (V) – Determination of binding to the human amylin receptor) with the exception that we used membranes prepared from 35 BHK tk'ts 13 cells that were transiently transfected with the rat calcitonin receptor rat RAMP 3 at an equimolar ratio (1:2). The BHK tk'ts 13 cells were transiently transfected

with rat calcitonin receptor using FuGENE® 6 (Roche), according to the manufacturer's recommendations. Cells were grown in DMEM with 10% FBS and 1% Pen/Strep. Approximately 48 hours after transfection, the cells were harvested and membranes were prepared.

5

ASSAY (VII) – Determination of binding to the human calcitonin receptor (membrane)

The binding assay was performed using scintillation proximity assay (SPA) beads (RPNQ0001) from PerkinElmer® and cell membranes prepared from a BHK tk'ts 13 cell line was stably transfected with the human calcitonin receptor and a CRE-responsive luciferase reporter gene. Membranes were prepared in the following way; the cells were rinsed with PBS and incubated with Versene for approximately 5 min before harvesting. The cells were flushed with PBS and the cell-suspension was centrifuged for 5 min at 1000 rpm. Cells were homogenized in a buffer containing 20mM Na-HEPES and 10mM EDTA (pH 7.4) and centrifuged at 20.000rpm for 15min. The resulting pellet was resuspended, homogenized and centrifuged (20.000rpm, 15min) in a buffer containing 20mM Na-HEPES and 0.1mM EDTA (pH 7.4, buffer 2). The resulting pellet was resuspended in buffer 2 and protein concentration was tested (BCA protein Assay, Pierce). The homogenate was kept cold during the whole procedure. The membranes were kept at -80°C until use. Assay was performed in a 384 well Optiplate (PerkinElmer®) in a total volume of 40ul. Membranes were mixed with SPA beads. Final concentration of membranes 35 ng/µL final and Final concentration of SPA beads was 0.05mg/well. Test-compounds were dissolved in DMSO and further diluted in assay buffer (50 mM Hepes, pH 7.4, 1 mM CaCl₂, 5 mM MgCl₂, 0.1% OA and 0.02% Tween20). Radioligand ¹²⁵I-Calcitonin was dissolved in assay buffer and added to the Optiplate at a final concentration of 75pM/well (approx. 30.000cpm/10ul). The final mixture was incubated for 120 min with shaking at 400 rpm at 25°C prior to centrifugation (1500rpm, 10min). Samples were analyzed on TopCounter™ (Packard). The IC₅₀ was calculated using (one site binding competition analysis) GraphPad Prism5 as a measure of receptor affinity.

ASSAY (VIIa) – Determination of binding to the human Calcitonin Receptor (whole cell binding)

The binding assay was performed using a BHK tk'ts 13 cell line was stably transfected with the human calcitonin receptor, and a CRE-responsive luciferase reporter gene.

The day before the assay the cells were Seeded into Poly-D-Lysin coated 384W Opaque White, BD BioCoat plates (10000 cells/well) and Incubated overnight at 37 °C, 5 % CO₂, 95% humidity. Then, the cells were washed in HBSS (4°C), and incubated overnight at 4°C in a binding buffer containing test compounds, 50 pM [125I]-human calcitonin, 5 media w/o phenol red, 500 ml 0,1 % ovalbumin (5 ml 10 % ovalbumin) 10 mM Hepes (5 ml 1M) 1x Glutamin (5 ml 100x) 1% P/S (5 ml 100%) Complete (1 tablet/50 ml) 0,1 % Pluronic F68®. The morning after, the plates were washed three times in HBSS (4°C), and lysed in Lysis buffer (0,1 M NaOH), 1% SDS. Scintillation cocktail (MicroScint40®) was added and the plates were shaken at 500 rpm for a short period. The plate was 10 incubated at room temperature in the dark for 1 hour and Read on a TopCounter™ (Packard). The IC₅₀ was calculated using (one site binding competition analysis) GraphPad Prism5 as a measure of receptor affinity.

ASSAY (VIII) – Determination of binding to the rat calcitonin receptor

15 The assay was performed as described above (Assay (VII) – Determination of binding to the human calcitonin receptor) with the exception that we used membranes prepared from BHK tk' ts 13 cells that were transiently transfected with the rat calcitonin receptor. The BHK tk' ts 13 cells were transiently transfected with rat calcitonin receptor using FuGENE® 6 (Roche), according to the manufacturer's recommendations. Cells were 20 grown in DMEM with 10% FBS and 1% Pen/Strep. Approximately 48 hours after transfection, the cells were harvested and membranes were prepared.

ASSAY (IX) - pK – Determination of T_{1/2} in mini-pig

25 Pharmacokinetic (PK) studies in Göttingen mini-pigs were conducted in order to determine the T_{1/2} of the mimylin compound according to the Examples as indicated after i.v. administration.

T_{1/2} values of the amylin analogues of the invention is determined by pharmacokinetic studies in female Göttingen mini-pigs from Ellegaard Göttingen Minipigs ApS and the principles of laboratory animal care are followed.

30 An acclimatisation period of approximately 6-10 days was allowed before the animals entered the study. At start of the acclimatisation period the mini-pigs were about 5 to 12 months old and in the weight range of 15-35 kg. The mini-pigs had two central venous catheters inserted which were used for blood sampling.

35 The studies were conducted in an animal room which was illuminated to give a cycle of approximately 12 hours light and 12 hours darkness. The animals were housed individually.

The animals had free access to domestic quality drinking water during the study, and no food restrictions applied for PK studies. The animals were weighed on arrival and on the days of dosing.

In the present studies the test substances were administered intravenously in 5 approximately 5 nmol/kg dose. The animals received a single intravenous injection in one central venous catheter and blood sampling was performed from the other catheter, where possible. Each test substance was given to typically three but in some cases two or four animals.

10 A full plasma concentration-time profile, employing 12-16 sampling points, was obtained from each animal. In example blood samples were collected according to the following schedule:

After intravenous administration:

15 Pre-dose (0), 0.5, 1, 2, 4, 6, 8, 12, 24, 48, 72, 96, 120, 168 and 240 hours after injection. In some cases also additional blood samples up to 288 hours post injection were taken.

At each sampling time, 0.5 to 2 ml of blood was drawn from each animal. The blood samples were taken via the central venous catheter.

20 The 0.8 mL blood samples were collected into EDTA test tubes (8mM EDTA). Blood samples were kept on ice for max 20 min. before centrifugation. Plasma was separated using centrifugation (i.e. at 4 °C, 10 min., 2000G) and was immediately transferred to Micronic tubes on dry ice. Approximately 200 µl plasma was transferred to each Micronic tube. The plasma was stored at -20°C until assayed. The plasma samples were assayed for the content of compound using LCMS.

25 The plasma concentration-time profiles were analysed by a non-compartmental pharmacokinetic analysis (NCA) using Phoenix WinNonlin 6.3 (Pharsight Inc., Mountain View, CA, USA). NCA was performed using the individual plasma concentration-time profiles from each animal. $T_{1/2}$ is the terminal half-life = $\ln 2/\lambda_z$ and was determined from λ_z , the first order rate constant associated with the terminal (log-linear) portion of the curve, estimated by linear regression of time vs. log concentration.

30

MS-method for amylin and mimylin quantification

40 µl plasma is diluted with 120 µl 66.67% EtOH + 1% HCOOH and mixed. Centrifuged for 20 min. at 13000 rpm, 4°C. The supernatant is analyzed by an LC-MS method on a Sciex API 3000 and quantitated with a standard made up in plasma

35

ASSAY (X) - pK – Determination of T_{1/2} in rat

Pharmacokinetic (PK) studies rats were conducted in order to determine the T_{1/2} of mimylin peptide after i.v. and s.c. administration.

T_{1/2} values of the mimylin derivates of the invention is determined by pharmacokinetic 5 studies in Sprague Dawley male rats, from Taconic Europe and the principles of laboratory animal care are followed.

An acclimatisation period of approximately 7 days was allowed before the animals entered the study. At start of the acclimatisation period the rats were in the weight range of 250-400g.

10 The studies were conducted in an animal room which was illuminated to give a cycle of approximately 12 hours light and 12 hours darkness. The animals were group housed and had food and water ad lib. The animals were weighed on the days of dosing.

15 In the present studies the test substances were administered subcutaneously or intravenously in approximately 20 nmol/kg dose. The animals received a single subcutaneous injection to the neck for subcutaneous administration or directly into the tail vein for intravenous administration. Each test substance was given to typically three but in some cases two or four animals.

20 A full plasma concentration-time profile, employing 8-10 sampling points, was obtained from each animal. In example blood samples were collected according to the following schedule:

After subcutaneous or intravenous administration:

Predose (0), 0.5, 1, 1.5, 2, 4, 6, 12, 24, 48 and 72 hours after injection.

25 At each sampling time, 0.08 to 0.10 ml of blood was drawn from each animal. The blood samples were taken in the sublingual vein via venous puncture and the use of a capillary tube.

30 The blood samples were stabilised with EDTA. Blood samples were kept on ice for max 20 min. before centrifugation. Plasma was separated using centrifugation (i.e. at 4°C, 10 min., 1500G) and was immediately transferred to Micronic tubes or PCR plates. Approximately 40 µl plasma was transferred and was stored at -20°C until assayed. The plasma samples were assayed for the content of mimylin compound by LCMS

35 The plasma concentration-time profiles were analysed by a non-compartmental pharmacokinetic analysis (NCA) using Phoenix WinNonlin 6.3 (Pharsight Inc., Mountain View, CA, USA). NCA was performed using the individual plasma concentration-time profiles from each animal. T_{1/2} is the terminal half-life = $\ln 2/\lambda_z$ and was determined from λ_z , the first order rate constant associated with the terminal (log-linear) portion of the curve, estimated by linear regression of time vs. log concentration.

ASSAY (XI)- Determining potential MHC Class II binding sites

The in-silico study investigated whether the novel peptides sequences that result from protein engineering to generate mimylin analogues could result in peptide sequences 5 capable of binding to major histocompatibility complex class II (MHC-II), also known as HLA-II in humans. Such binding is pre-requisite for the presence of T-cell epitopes. The peptide/HLA-II binding prediction software used in this study was based on two algorithms, NetMHCIIpan 2.1 (Nielsen et al. 2010), performing HLA-DR predictions, and NetMHCII 2.2 (Nielsen et al. 2009) performing HLA-DP/DQ predictions.

10 It should be noted that there are certain caveats that need to be considered when analysing sequences for MHC class II binding peptides alone, in particular that this method will not account for antigen processing, T cell receptor recognition of the MHC class II/peptide complex or T cell tolerance to any non-germline peptide. Indeed, for these reasons, any analysis of sequences using predictive MHC class II binding tools will 15 result in an over-prediction of the number of actual T cell epitopes.

Any of the HLA-II binding peptides identified in this analysis have the potential to be an active CD4+ T cell epitope although, from the literature it is known that only a minority of such peptides will be actual T cell epitopes when tested in human T cell assays

20 Nevertheless, any individual promiscuous non-germline HLA-II binding peptide has a risk of being an active CD4+ T cell epitope
Therefore it is recommended that additional assessment is performed using ex vivo T-cell assays to assess their immunogenicity. The results of this ex vivo analysis can be compared to benchmark data on existing protein therapeutics to generate a more 25 accurate pre-clinical assessment of the potential for immunogenicity.

Both wilde-type Salmon calcitonin and the mimylin peptide according to SEQ ID NO: 1 showed no binding prediction for MHC Class II peptides.

ASSAY (XII) - SEC-HPLC

30 SEC-HPLC was conducted using a Waters Insulin HMWP column with isocratic elution (0.5M NaCl, 10 mM NaH₂PO₄ and 5 mM H₃PO₄, 50% (v/v) isopropanol) with a flow rate of 0.5 ml/min, a column temperature at 50°C with UV-detection at 215 nm. Typical column load was one-digit nmol/injection. The total peptide peak area was used as a measure of "total peptide concentration" and absolute total peptide concentration was 35 estimated using UV molar extinctions coefficients calculated based on the primary structure of the individual peptides. The total peptide peak area eluting prior to the monomeric main peak was termed HMWP (High-Molecular-Weight-Protein) and given on

a percentage scale relative to the total peptide peak area. The total peptide peak area eluting posterior to the monomeric main peak was termed post-monomer and given on a percentage scale relative to the total peptide peak area.

5 **ASSAY (XIII) - Quiescent storage stability of formulations**

Before, during and after incubation at specified temperatures one/more of the following examinations are done on a regular basis to assess the quiescent storage stability.

SEC-HPLC

10 The "total peptide concentration", HMWP (High-Molecular-Weight-Protein) and post-monomer were determined according to ASSAY (1).

RP-UPLC

15 The peptide purity was measured by UPLC using a CSH 1.7 µm, 150x2.1mm column (60°C) with UV detection at 215 nm. Eluent A (0.09 di-ammoniumphosphate pH 3.6, 10% MeCN v/v%) and eluent B (80% MeCN v/v%) in a total flow rate of 0.3 ml/min were used (initial:45% B; 2 min:45% B; 27 min:65% B; 28 min:95% B; 31 min:95% B; 32 min:45% B; 35 min:45% B). Purity was given in % based on the relative area ratio between main peak and total peptide related peak area.

ASSAY (XIV) - Experimental protocol for testing effect on body weight using

20 **DIO rat model (Subchronic effects of the GLP-1 analogue liraglutide, an amylin analogue (EX. #2) and combination of liraglutide and EX. #2 in DIO rats)**

Animals and diet

25 All animal protocols were approved by an Institutional Animal Care and Use Committee and Ethical Review Committee of Novo Nordisk. Diet-induced obese (DIO) male Sprague Dawley rats maintained on a high fat diet (45% kcal fat, RD12451, Research Diets, New Brunswick, NJ, USA) were obtained from Vital River (Beijing, China) and were housed in a temperature (23 ± 2 °C) and light-controlled (12h:12h light/dark cycle, lights on at 1800h) environment with ad libitum access to food and water. Upon arrival, the rats 30 were allowed to acclimate and body weights were monitored on a bi-weekly basis during this period.

Formulation buffers

35 Liraglutide was formulated in 8 mM phosphate, 184 mM propylene glycol, 58 mM phenol, pH=8.15. EX. #2 was formulated in 10 mM phosphate, 250 mM glycerol, 0.025%

polysorbate 20, pH=7.4; Vehicle-treated animals were dosed with the latter formulation buffer.

Group allocation, dosing and body weight measurements

5 Prior to initiation of the study, animals were single-housed and acclimated to handling and injection procedures for 7 days. The DIO rats were distributed into groups (n=10/group) such that statistical variations in the mean and standard deviations of fat mass and body weight were minimized between groups. Animals were dosed once daily, subcutaneously at 16:00 with either vehicle (days 0-28; Group A), liraglutide (0.1 mg/kg
10 days 0-28, Group B), compound of EX. #2 (3.7 µg/kg days 0-28, Group C), or a combination of liraglutide and compound of EX. #2 (0.1mg/kg liraglutide days 0-28, and 3.7 ug/kg compound of EX.#2 days 15-28; Group D). Body weights were measured immediately prior to dosing each day.

15 **Termination**

Animals were sacrificed on day 28. Animals were anesthetized with O₂/N₂O/isoflurane, and blood was taken by cardiac puncture into EDTA tubes, kept on ice and centrifuged within 30 minutes of collection. All EDTA plasma samples were stored at -80°C thereafter, until analyzed. Liver and brain samples were also collected and stored
20 at -80°C for later analysis

ASSAY (XV) – Determination subcutaneous mimylin derivative PK in LYD-pigs when co-formulated with liraglutide

To determine if co-formulation with liraglutide would change the PK properties of either
25 the mimylin derivatives or liraglutide co-formulation studies were performed in Landrace Yorkshire Duroc crossbreed (LYD) pigs and compared with co-dosing studies.

The studies were performed in female LYD pigs of SPF origin delivered from Lars Jonson, Hillerødvej 70, Lyngé.

30 At start of the acclimatisation period, the body weight of the pigs was in the range of 55 – 70 kg and the pigs were of app. 5 month of age.

Before the animals arrived, the animal rooms and pens were cleaned and disinfected with Virkon S. During the study, the animal rooms were cleaned and washed regularly.

35 The pigs were group housed during the acclimatisation period. The pigs were fitted with a central venous catheter while under anaesthesia and after the single housed after catheterization in pens ≥ 3.1 m² with straw as bedding. The temperature in the rooms

was set at 20-23°C and the relative humidity to 30-70%. The rooms were illuminated to give a cycle of 12 hours light and 12 hours darkness. Light was on from 07.00 to 19.00 h.

The subcutaneous formulations used for co-dosing contained either 1.6 mM liraglutide or 5 1.6 mM mimylin derivative in 8 mM phosphate, 58 mM phenol, 14 mg/ml propylenglycol, pH 8.2. The co-formulation contained 1.6 mM liraglutide and 1.6 mM mimylin derivative in 8 mM phosphate, 58 mM phenol, 14 mg/ml propylenglycol, pH 8.2. The formulations was prepared similarly and filled in cartridges in all cases.

The animals were dosed subcutaneously as follows.

10 The s.c. dosing was performed in 4 mm depth, in a site of injection which was secured on beforehand by ultrasound to avoid muscular tissue or heavy vascularization. Dosing was made using NovoPen®4 and needle Novofine 28 G and a needle stopper to ensure 4 mm depth of injection. The needle was kept in the subcutis for 10 seconds after the injection to secure deposition of compound. For co-dosing animals received two separate 15 injections on different sides of the neck of liraglutide and Compound 2. The co-formulation was administered as one injection. Study was performed as a cross over study with adequate wash out between dosings. Animals were in all studies dosed with 2 nmol/kg liraglutide and 2 nmol/kg mimylin derivate.

20 **Blood sampling**

Blood was sampled at predefined time points for up till 15 days post dosing to adequately cover the full plasma concentration-time profile of the mimylin derivative. Blood samples were drawn from a central venous catheter to jugularis made through the catheter which was afterwards flushed with 10 ml 0.9% NaCl.

25 For each blood sampling time point approximately 0.8 mL of whole blood was collected in a 1.5 mL EDTA coated tube, and the tube was gently turned to allowing mixing of the sample with the anticoagulant. Blood samples (for example 0.8 mL) were collected in EDTA buffer (8mM) and then centrifuged at 4°C and 2000G for 10 minutes. Plasma was pipetted into Micronic tubes on dry ice, and kept at -20°C until analysis.

30

Analysis

The plasma concentration of the respective mimylin derivative was analysed using LC-MS and liraglutide by LOCI. Individual plasma concentration-time profiles were analysed by a non-compartmental model in Phoenix WinNonlin version 6.3 (Pharsight Inc., Mountain 35 View, CA, USA).

The area under the plasma concentration versus time curve (AUC, [time x concentration]) was calculated (by the Pharsight programme) after subcutaneous administration, typically until 240-288 hours post dosing, or until last measured concentration. The AUC was calculated and given as AUC_{inf-pred} and dose normalized.

5 However, in cases where the extrapolated area in the profile exceeded 20% then AUC_{last} was used to calculate AUC and dose-normalized.

Results of co-formulation studies in LYD-pigs are summarized below

ASSAY (XVI)– Determination of T_{1/2} and subcutaneous bioavailability in LYD-

10 pigs

Pharmacokinetic (PK) studies in Landrace Yorkshire Duroc crossbreed (LYD) pigs were conducted in order to determine a) the protraction of the mimylin derivative after i.v. administration, and b) the bioavailability of the mimylin derivative after s.c. administration

15 The LYD pig were delivered, treated and acclimatised as described in ASSAY **XV** above.

In the i.v. and s.c. studies, the mimylin derivative was dissolved in 50 mM phosphate, 70 mM sodium chloride and 0.05% polysorbate 80, pH=8.0 to a concentration of approximately 100 nmol/mL. Animals were dosed with 2 nmol/kg s.c. and 5 nmol/kg i.v.

20 The animals were dosed subcutaneously or intravenously as follows.

The s.c. dosing was performed in 4 mm depth, in a site of injection which was secured on beforehand by ultrasound to avoid muscular tissue or heavy vascularization. Dosing was made using NovoPen®4 and needle Novofine 28 G and a needle stopper to ensure 4 mm depth of injection. The needle was kept in the subcutis for 10 seconds after the injection

25 to secure deposition of compound.

Intravenous administration was performed either by an ear vein or through a venflon.

Blood sampling

Blood was sampled at predefined time points for up till 10-12 days post dosing to 30 adequately cover the full plasma concentration-time profile of the mimylin derivative. The remainder followed the protocol as described in ASSAY (XV) blood sampling above,

Analysis

The plasma concentration of the respective mimylin derivative was analysed using LC-35 MS. Individual plasma concentration-time profiles were analysed by a non-

compartmental model in Phoenix WinNonlin version 6.3 (Pharsight Inc., Mountain View, CA, USA).

The resulting terminal half-life was determined based on intravenous administration. $T_{1/2}$ is the terminal half-life = $\ln 2/\lambda_z$ and was determined from λ_z , the first order rate constant associated with the terminal (log-linear) portion of the curve, estimated by linear regression of time vs. log concentration.

5 The absolute bioavailability (F) was calculated as follows:

The area under the plasma concentration versus time curve (AUC, [time x concentration]) was calculated (by the Pharsight programme) after both subcutaneous administration and intravenous administration, typically until 240-288 hours post dosing, or until last measured concentration. The AUC was calculated by extrapolating to infinity and dose normalized. The absolute bioavailability (F%) was then calculated based on the dose-corrected AUC values, namely as AUC/D_{sc} divided by $AUC/D_{iv} \times 100$, where D_{sc} is the subcutaneous dose per kg, and D_{iv} the dose per kg given intravenously.

ASSAY (XVII)- Determination of $T_{1/2}$ and subcutaneous bioavailability in Beagle dogs

Pharmacokinetic (PK) studies in Beagle dogs were conducted in order to determine a) the protraction of the mimylin derivative after i.v. administration, and b) the bioavailability of the mimylin derivative after s.c. administration.

20 By protraction is meant the prolongation of the time in the body and thereby the time of action of the mimylin derivatives. This was done in PK studies, where the terminal half-life of the derivative in question was determined following i.v. administration. By terminal half-life is generally meant the period of time it takes to halve a certain plasma concentration, measured after the initial distribution phase.

The mimylin compound was subjected to PK studies as described below.

For the studies with the mimylin derivative Compound 2 the Beagle dogs were 1 to 5 years of age and weighing approximately 10-12 kg at the start of the studies. The dogs were group housed in pens (12 hours light: 12 hours dark), and fed individually and restrictedly once daily with Royal Canin Medium Adult dog (Royal Canin Products, Brogaarden A/S, Denmark). Exercise and group social was permitted daily, whenever possible. The dogs were used for repeated pharmacokinetic studies with a suitable wash-out period between dosings. An appropriate acclimatisation period was given prior to initiation of the first pharmacokinetic study. All handling, dosing and blood sampling of

the animals was performed by trained and skilled staff. Before the studies the dogs were fasted overnight and from 0 to 4 h after dosing. Besides, the dogs were restricted to water 1 hour before dosing until 4 hours after dosing, but otherwise had ad libitum access to water during the whole period.

5

Intravenous and subcutaneous administration

In the i.v. and s.c. studies, the mimylin derivative, dissolved 10 mM phosphate; 250 mM glycerol; 0.025% polysorbate 20, pH=7.4, to a concentration of approximately 10 nmol/ml (i.v.) and 50 nmol/ml (s.c.), were administered to the dogs by intravenous or 10 subcutaneous injections (the volume corresponding to 1-5 nmol/kg, for example 0.1-0.2ml/kg) in the cephalic or in subcutaneously in the dorsal part of the neck.

Blood sampling

Blood was sampled at predefined time points for up till 10-12 days post dosing to 15 adequately cover the full plasma concentration-time profile of the mimylin derivative.

For each blood sampling time point approximately 0.8 mL of whole blood was collected in a 1.5 mL EDTA coated tube (8mM), and the tube was gently turned to allowing mixing of the sample with the anticoagulant, and then centrifuged at 4°C and 1942G for 4 minutes. Plasma was pipetted into Micronic tubes on dry ice, and kept at -20°C until analysis.

20 Blood samples were taken as appropriate, for example a) from the jugular vein using a standard 21G needle and a syringe, or b) from a venflon in the cephalic vein in the front leg for the first 2 hours and then with syringe from the jugular vein for the rest of the time points (the first few drops were allowed to drain from the venflon to avoid heparin saline from the venflon in the sample).

25

Analysis

The plasma concentration of the respective mimylin derivative was analysed using LC-MS. Individual plasma concentration-time profiles were analysed by a non-compartmental model in Phoenix WinNonlin version 6.3 (Pharsight Inc., Mountain View, 5 CA, USA).

The resulting terminal half-life was determined based on intravenous administration. $T_{1/2}$ is the terminal half-life = $\ln 2/\lambda_z$ and was determined from λ_z , the first order rate constant associated with the terminal (log-linear) portion of the curve, estimated by linear regression of time vs. log concentration.

10 The absolute bioavailability (F) was calculated as follows:

The area under the plasma concentration versus time curve (AUC, [time x concentration]) was calculated (by the Pharsight programme) after both subcutaneous administration and intravenous administration, typically until 240-288 hours post dosing, or until last measured concentration. The AUC was calculated by extrapolating to infinity 15 and dose normalized. The absolute bioavailability (F%) was then calculated based on the dose-corrected AUC values, namely as AUC/D_{sc} divided by $AUC/D_{iv} \times 100$, where D_{sc} is the subcutaneous dose per kg, and D_{iv} the dose per kg given intravenously.

RESULTS

20 **Table 8** - 3nmol/kg mimylin compound and effects on food intake reduction in the time spans 0-24 hours after administration and 24-48 hours after administration (Assay I)

EX. #	PD rat 3nmol/kg reduction (%) 0-24h	PD rat 3nmol/kg Reduction (%) 24-48h
2	79	60,66667
3	63	9
4	13,5	-4
5	3	-3
6	2	-12
9	58,5	39
13	70	18
21	71	46
22	55,5	63,5
28	84	77
29	52	0
31	62	12
33	73	39
40	49	79
46	82	78
47	66	10
48	52	11
49	28	-2
56	45	67

EX. #	PD rat 3nmol/kg reduction (%) 0-24h	PD rat 3nmol/kg Reduction (%) 24-48h
58	74	63
72	17	11
73	55	62
80	49	56
84	7	3
85	44	24
98	52	57
99	46	68
103	23	10
104	26	28
107	4	-5
108	27	26
109	40	42
110	44	8
113	21	6
117	20	14
118	26	15
119	25	29
120	22	19
121	0	0
125	9	5
126	34	24
127	36	21
129	32	0
130	25	10
131	8	9

Table 9 - 3nmol/kg mimylin compound and effects on food intake reduction of above 0 in the period 0h-24h after administration (Assay I)

EX. #						
2	21	46	73	104	118	130
3	22	47	80	107	119	131
4	28	48	84	108	120	-
5	29	49	85	109	125	-
6	31	56	98	110	126	-
9	33	58	99	113	127	-
13	40	72	103	117	129	-

5 **Table 10** - 3nmol/kg mimylin compound and effects on food intake reduction of 10 or more in the period 0h-24h after administration (Assay I)

EX. #						
2	22	46	72	103	117	128
3	28	47	73	104	118	129
4	29	48	80	108	119	130
9	31	49	85	109	120	
13	33	56	98	110	126	

EX. #						
21	40	58	99	113	127	

Table 11 - 3nmol/kg mimylin compound and effects on food intake reduction of above 0 in the period 24h-48h after administration (Assay I)

EX. #						
2	28	48	84	108	119	131
3	31	56	85	109	120	-
9	33	58	98	110	125	-
13	40	72	99	113	126	-
21	46	73	103	117	127	-
22	47	80	104	118	130	-

5

Table 12 - 3nmol/kg mimylin compound and effects on food intake reduction of 10 or more in the period 24h-48h after administration (Assay I)

EX. #					
2	31	56	98	117	130
9	33	58	99	118	-
13	40	72	103	119	-
21	46	73	104	120	-
22	47	80	108	126	-
28	48	85	109	127	-

Table 13 - EC50 (pM) of mimylin compounds in functional human calcitonin and amylin receptor assay without HSA (Assay IIb)

EX. #	Tested without HSA		EX. #	Tested without HSA	
	hAmylin-R funct. EC50 (pM)	hCTR funct. EC50 (pM)		hAmylin-R funct. EC50 (pM)	hCTR funct. EC50 (pM)
1	3	1	73	27	18
2	8	5	74	50	45
3	8	4	75	80	19
4	6	2	76	10	14
5	27	7	77	10	6
6	23	8	78	9	11
7	10	13	79	38	42
8	7	7	80	32	29
9	12	9	81	37	41
10	16	5	82	33	27
11	7	5	83	17	15
12	6	5	84	26	12
13	4	3	85	33	28
14	28	13	86	32	13
15	9	7	87	9	13
16	15	9	88	461	127
17	8	6	89	187	64

18	20	17	90	239	88
19	8	3	91	37	41
20	11	7	92	22	23
21	9	6	93	64	24
22	11	9	94	42	30
23	9	4	95	65	32
24	20	14	96	11	8
25	10	7	97	50	34
26	7	6	98	47	28
27	8	4	99	20	23
28	8	7	100	17	16
29	10	7	101	51	37
30	14	7	102	12	6
31	14	6	103	43	23
32	31	12	104	67	70
33	8	7	105	235	45
34	12	14	106	386	66
35	13	8	107	68	36
36	23	54	108	ND	ND
37	10	5	109	37	25
38	12	6	110	ND	ND
39	16	8	111	22	24
40	13	14	112	54	18
41	27	18	113	36	21
42	17	12	114	76	60
43	18	11	115	66	56
44	24	13	116	62	63
45	15	10	117	41	27
46	16	17	118	57	65
47	18	15	119	72	49
48	18	17	120	89	52
49	10	10	121	50	22
50	6	4	122	53	52
51	7	5	123	24	28
52	39	34	124	40	34
53	22	31	125	70	57
54	28	19	126	52	40
55	41	29	127	31	31
56	22	23	128	23	19
57	20	22	129	25	25
58	10	10	130	54	45
59	46	37	131	18	15
60	53	48	132	16	15

61	50	40	133	10	12
62	55	31	134	481	45
63	63	38	72bb	14	3
64	142	66	95bb	46	9
65	67	40	127bb	11	6
66	41	25	22bb	5	2
67	20	14	86bb	7	2
68	36	27	106bb	629	103
69	21	28	135	23628	840
70	32	19	124bb	5	4
71			118bb, 120bb, 121bb	8	4
72	17	12			

Table 14- EC50 (pM) of mimylin compounds in functional human calcitonin and amylin receptor assay withSA (Assay IIa)

EX. #	Tested with HSA		hCTR funct. EC50 (pM)
	hAmylin-R funct.	EC50 (pM)	
21	39		19
22	61		26
23	26		9
34	143		74
35	39		19
40	51		29
41	73		30
42	67		35
43	68		25
44	62		25
45	66		27
46	26		11
47	4		2
48	9		8
49	4		3
50	4		4
51	6		4
52	74		30
53	57		48
54	49		28
55	140		42
56	67		24
57	82		51
58	24		15

EX. #	Tested with HSA		
	hAmylin-R funct. (pM)	EC50	hCTR funct. EC50 (pM)
59	62		49
60	125		72
61	94		73
62	168		78
63	328		154
64	435		239
65	265		102
66	85		40
67	94		23
68	72		37
69	100		44
70	47		22
71	164		59
72	230		48
73	185		22
74	134		56
75	413		95
76	17		11
79	71		45
80	93		71
81	100		37
82	58		30
83	181		113
84	440		123
85	19		9
86	356		87
88	976		418
89	210		50
90	209		53
91	81		42
92	150		105
93	729		109
94	30		75
95	52		13
96	38		11
97	64		48
98	66		35
99	92		40
100	143		108
101	93		73
102	106		28
103	128		92
104	122		53
105	179		22

EX. #	Tested with HSA	
	hAmylin-R funct. (pM)	EC50
106	157	31
107	335	113
108	150	68
109	158	108
110	70	53
111	52	49
112	291	67
113	159	57
114	142	97
115	546	366
116	67	36
117	212	99
118	105	54
119	86	61
120	123	68
121	80	38
122	77	37
123	64	34
124	122	92
125	152	72
126	223	142
127	140	73
128	173	77
129	565	852
130	185	99
131	154	62
132	37	50
133	44	50

Table 15 - Stability of selected mimylin compounds (Assay III)

Ex. #	ThT pH 7.5 lag time (h)	ThT pH 7.5 recovery (%)
40	>45	100
41	>45	100
42	>45	100
43	>45	100
44	>45	100
45	>45	100
46	>45	100
47	>45	100
50	>45	98
52	>45	100
53	>45	100
54	>45	100
55	>45	94

Ex. #	ThT pH 7.5 lag time (h)	ThT pH 7.5 recovery (%)
56	>45	100
58	>45	100
59	>45	100
60	>45	100
61	>45	100
62	>45	100
63	>45	100
64	>45	100
65	>45	100
80	>45	100
98	>45	100
101	0	100
104	>45	100
107	0,3	0
108	>45	100
109	>45	100
110	>45	100
116	1	16
118	0	23
119	1,5	39,5
120	>45	100
121	>45	100
125	>45	100
126	8,4	90
127	>45	100
130	8	2

Table 16 - Solubility of mimylin compounds (Assay IV)

Solubility (μM)									
Ex. #	pH 3.0	pH 4.0	pH 5.0	pH 6.0	pH 6.5	pH 7.0	pH 7.5	pH 8.0	
63	≥ 200								
64	≥ 200								
65	≥ 200								
66	≥ 200								
67	≥ 200								
68	≥ 200								
69	≥ 200								
70	≥ 200								
71	≥ 200								
72	≥ 200								
73	≥ 200								
74	≥ 200								
75	≥ 200								
76	≥ 200								
77	≥ 200	7	11	≥ 200					
78	≥ 200								
79	≥ 200								
80	≥ 200	≥ 200	10	≥ 200					
81	≥ 200								
82	≥ 200	≥ 200	1	≥ 200					
83	≥ 200								
84	≥ 200								
85	≥ 200								
86	≥ 200	≥ 200	≥ 200	38	≥ 200				
87	≥ 200								
88	≥ 200	1	6	≥ 200					
89	ND								
90	ND								
91	≥ 200	7	29	≥ 200					
92	≥ 200	≥ 200	169	≥ 200					
93	≥ 200								
94	≥ 200								
95	≥ 200								
96	≥ 200	177	45	≥ 200					
97	≥ 200	≥ 200	40	≥ 200					
98	≥ 200								
99	≥ 200	≥ 200	19	≥ 200					
100	≥ 200	0	1	63	180	≥ 200	≥ 200	≥ 200	≥ 200
101	≥ 200								
102	6	0	≥ 200						
103	≥ 200	≥ 200	156	≥ 200					
104	≥ 200	≥ 200	119	≥ 200					
105	≥ 200								
106	≥ 200								
107	≥ 200	≥ 200	≥ 200	148	129	74	≥ 200	≥ 200	≥ 200

Solubility (μ M)								
Ex. #	pH 3.0	pH 4.0	pH 5.0	pH 6.0	pH 6.5	pH 7.0	pH 7.5	pH 8.0
108	≥ 200	≥ 200	65	≥ 200				
109	≥ 200	≥ 200	7	≥ 200				
110	≥ 200	≥ 200	149	≥ 200				
111	≥ 200	1	2	0	1	0	0	0
112	≥ 200	132	22	≥ 200				
113	≥ 200	195	57	≥ 200				
114	≥ 200	65	7	≥ 200				
115	ND							
116	≥ 200	≥ 200	32	≥ 200				
117	≥ 200	≥ 200	38	≥ 200				
118	≥ 200	2	8	17	5	26	90	173
119	≥ 200	170	56	≥ 200				
120	≥ 200	≥ 200	96	≥ 200				
121	≥ 200	≥ 200	110	≥ 200				
122	≥ 200	≥ 200	32	≥ 200				
123	≥ 200	≥ 200	2	≥ 200				
124	≥ 200	≥ 200	61	≥ 200				
125	≥ 200	28	≥ 200					
126	≥ 200	0	0	161	≥ 200	≥ 200	≥ 200	≥ 200
127	≥ 200	31	0	≥ 200				
128	≥ 200	25	≥ 200					
129	≥ 200	≥ 200	1	1	1	1	52	185
130	≥ 200	174	9	≥ 200				
131	≥ 200	10	≥ 200					

Table 17 – Amylin and calcitonin receptor IC50 (pM) for mimylin compounds (Assay V & VII)

Ex. #	hAmylin-R binding IC50 (pM)	hCT-R binding IC50 (pM)	rAmylin-R binding IC50 (pM)	rCT-R binding IC50 (pM)
41	141	85	146	44
42	159	50	ND	ND
43	164	50	ND	ND
45	389	112	ND	ND
46	516	84	ND	ND
47	37	24	22	13
48	77	34	63	13
49	15	11	64	11
50	54	23	122	17
51	773	140	ND	123
52	724	136	ND	114
53	114	215	1302	65
54	442	85	455	44
55	202	84	242	27
56	394	70	3986	202
57	124	108	25	44

Ex. #	hAmylin-R binding IC50 (pM)	hCT-R binding IC50 (pM)	rAmylin-R binding IC50 (pM)	rCT-R binding IC50 (pM)
59	243	113	29	23
60	57	34	46	20
67	29	22	17	17
68	50	10	46	10
69	74	46	115	42
70	206	77	684	71
71	251	70	374	31
72	565	97	1529	85
81	141	102	26	39
99	159	154	45	69
100	171	100	46	62
105	309	222	162	72
109	131	51	78	12
110	122	57	13	13
114	297	85	146	21
117	166	150	26	31
119	152	67	53	16
120	166	91	29	27
121	371	120	357	32
126	225	193	91	31
128	216	53	98	28
131	720	651	385	246
132	390	131	1159	69

Table 18 – T1/2 of mimylin compounds in mini pigs (Assay IX)

Ex. #	PK mini pig iv T1/2 (h)
Salmon calcitonin	0
1	0
2	85
3	17
4	2
6	1
9	90
13	86
21	118
22	108
40	171
46	118
56	88
110	32
116	87

5 **Table 19** – T1/2 of mimylin compounds in rats (Assay X)

EX. #	PK rat iv T1/2 (hours)	PK rat sc T1/2 (hours)
Salmon Calcitonin	ND	1

Ex. #	PK rat iv T _{1/2} (hours)	PK rat sc T _{1/2} (hours)
2	12	13
3	3	3
4	3	3
5	6	13

Table 20 – Subcutaneous mimylin derivative PK in LYD-pigs co-formulated or co-dosed with liraglutide (Assay XV)

Pharmacokinetic parameter	Co-formulation		Co-dosing	
	Liraglutide	Ex #2	Liraglutide	Ex # 2
T _{1/2} (hours)	20	67	19	67
C _{max} /D (kg/L)	3.9	5.8	3.4	6.9
AUC/D (hr*kg/L)	129	732	114	712
Compound	Liraglutide	Ex #46	Liraglutide	Ex #46
T _{1/2} (hours)	25	133	21	129
C _{max} /D (kg/L)	3.7	5.7	3.4	5.2
AUC/D (hr*kg/L)	136	656	111	624

5 **Table 21** – T_{1/2} and subcutaneous bioavailability in LYD-pigs (Assay XVI)

Ex. #	LYD-pigs iv PK, t _{1/2} (hours)*	Subcutaneous bioavailability (%)
2	64	99

* terminal half-life (t_{1/2}) is harmonic mean, n=3

Table 22 – In vivo pharmacokinetic evaluation in Beagle dogs after intravenous and subcutaneous administration (Assay XVII)

Ex. #	Beagle dogs iv PK, t _{1/2} (hours)*	Subcutaneous bioavailability (%)
2	95	98

10 * terminal half-life (t_{1/2}) is harmonic mean, n=2

Example A- Preparation of formulations

Aqueous formulations are prepared by mixing aqueous stock solutions containing well-defined concentrations of excipients (antimicrobial agent, tonicity agent, pH buffer) with an aqueous stock solution containing a well-defined concentration of mimylin peptide and/or a GLP-1 compound. Alternatively, the mimylin peptide is dissolved directly in an aqueous solution containing well-defined concentrations of excipients and a GLP-1 compound. Following pH-adjustment, each formulation is sterile filtered (0.22μm filter) to sterile glass containers.

Example B- Stability of formulations comprising compounds of EX. #40 and EX. #46

Formulations containing 0.8 mM compound of EX. #40 or 0.8 mM compound of EX. #46 were prepared according to Example A. All formulations contained 8 mM phosphate and 5 were pH-adjusted to pH 8.2. An additional set of formulations also containing 58 mM phenol and 14 mg/ml propylene glycol were prepared. Each formulation was tested according to ASSAY (IIIa).

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Table 23- Stability of formulations comprising compounds of EX. #40 and EX. #46

Formulation	EX.#40 (mM)	EX.#46 (mM)	Phosphate (mM)	Phenol (mM)	Propylene glycol (mg/ml)	ThT Lag-time (h)	Peptide Rec. (%)
F1	0.8	-	8	-	-	>45	102
F2	0.8	-	8	58	14	>45	101
F3	-	0.8	8			>45	102
F4	-	0.8	8	58	14	>45	102

Each formulation was tested according to ASSAY (XIII), and the results are presented 15 below.

Table 24- Stability of formulations comprising compounds of EX. #40 and EX. #46

Formulation	EX.#40 (mM)	EX.#46 (mM)	Phosphate (mM)	Phenol (mM)	Propylene glycol (mg/ml)	Pep. Conc.* (%)	HMWP [‡] (%)	Post monomer ^{\$} (%)	Purity Loss [¶]
F5	0.8	-	8	-	-	101	0.75	8.2	5.9
F6	0.8	-	8	58	14	101	1.2	4.2	4.3
F7	-	0.8	8	-	-	98	0.40	4.8	8.9

F8	-	0.8	8	58	14	102	0.81	1.4	4.0
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* Peptide concentration after 8 weeks at 37°C relative to start value

£ HMWP after 8 weeks at 37°C

\$ Post monomer after 8 weeks at 37°C minus start value

¤ Purity loss in %/month at 37°C

5

Example C- Solubility of formulations comprising compounds of EX. #40 and EX. #46

Formulations containing 0.5 mM compound of EX. #40 or 0.5 mM compound of EX. #46 were prepared according to Example A. All formulations contained 10 mM phosphate and 10 mM NaCl and/or 50 mM phenol were prepared. Total peptide concentration was measured after 4-5 days storage at 5°C or at room temperature.

Table 25- Solubility of formulations comprising compounds of EX. #40 and EX. #46

Formulation	EX.#40 (mM)	EX.#46 (mM)	Phosphate (mM)	NaCl (mM)	Phenol (mM)	pH	Pep. Conc. 5°C (mM)	Pep. Conc. 25°C (mM)
F9	0.5		10			7.4	0.47	0.47
F10	0.5		10	50		7.4	0.48	0.48
F11	0.5		10		50	7.4	0.48	0.48
F12	0.5		10	50	50	7.4	0.48	0.48
F13		0.5	10			7.4	0.48	0.48
F14		0.5	10	50		7.4	0.50	0.49
F15		0.5	10		50	7.4	0.50	0.50
F16		0.5	10	50	50	7.4	0.50	0.50
F17	0.5		10			8.2	0.4.	0.48
F18	0.5		10	50		8.2	0.48	0.48
F19	0.5		10		50	8.2	0.48	0.49
F20	0.5		10	50	50	8.2	0.49	0.49
F21		0.5	10			8.2	0.49	0.50
F22		0.5	10	50		8.2	0.50	0.50
F23		0.5	10		50	8.2	0.50	0.50

Formulation	EX.#40 (mM)	EX.#46 (mM)	Phosphate (mM)	NaCl (mM)	Phenol (mM)	pH	Pep. Conc. 5°C (mM)	Pep. Conc. 25°C (mM)
F24		0.5	10	50	50	8.2	0.50	0.50

Example D- Stability of formulations compounds of EX. #46

Four formulations containing 0.3 mM or 0.03 mM compound of EX. #46 were prepared according to Example A. All formulations contained 16 mg/ml glycerol and pH was 5 adjusted to pH 7.4. On top of that, two of the formulations contained 19 mM phenol, 19 mM m-cresol, 5 mM phosphate, 20 mM NaCl and the other two formulations contained 28 mM m-cresol. All formulations were tested according to ASSAY (IIIA).

Table 26- Stability of formulations compounds of EX. #46

Formulation	EX.#46 (mM)	Glycerol (mg/ml)	Phenol (mM)	m-Cresol (mM)	Phosphate (mM)	NaCl (mM)	pH	ThT Lag-time (h)	Peptide Rec. (%)
F25	0.3	16	19	19	5	20	7.4	>45	98
F26	0.03	16	19	19	5	20	7.4	>45	105
F27	0.3	16	-	28	-	-	7.4	>45	104
F28	0.03	16	-	28	-	-	7.4	>45	84

10

Example E- Stability of formulations comprising compound of EX. #40

Formulations containing 0.2 mM compound of EX. #40 were prepared according to Example A. All formulations contained 8 mM phosphate pH was adjusted to pH 8.2. On top of that, four of the formulations contained increasing concentration of propylene glycol (10-20-50-100 mg/ml) whereas four other formulations contained increasing concentration of glycerol (10-20-50-100 mg/ml). All formulations were tested according to ASSAY (XII) before and after 4 weeks storage at 5°C and 37°C.

Table 27- Stability of analogue EX. #40

Formulation	EX.#40 (mM)	Phosphate (mM)	Propylene glycol (mg/ml)	Glycerol (mg/ml)	pH	Total Pep. START(% of start)	Total Pep. 4w5°C (% of start)	HMWP. START(% of start)	HMWP 4w5°C(% of start)	HMWP 4w37°C(% of start)	Post mon. START(%)	Post mon. 4w5°C(%)	Post mon. 4w37°C(%)		
F29	0.2	8	-	-	8.2	100	113	104	0.9	0.8	0.5	1.1	3.4	4.2	
F30	0.2	8	10	-	8.2	100	103	102	0.8	0.8	0.5	1.1	1.5	3.4	
F31	0.2	8	20	-	8.2	100	102	103	0.8	0.8	0.5	1.0	1.6	3.1	
F33	0.2	8	50	-	8.2	100	101	101	0.8	0.9	0.4	1.0	1.6	3.2	
F34	0.2	8	10	0	-	8.2	100	101	101	0.8	0.8	0.4	1.1	1.4	2.8
F35	0.2	8	-	10	8.2	100	101	102	0.8	0.8	0.9	1.0	1.5	3.0	
F36	0.2	8	-	20	8.2	100	101	103	0.8	0.8	2.2	1.0	1.4	3.3	
F37	0.2	8	-	50	8.2	100	101	100	0.8	0.8	0.9	1.1	1.8	13	
F38	0.2	8	-	10	8.2	100	100	101	0.8	0.8	0.6	1.0	2.1	16	

Example F- Stability of formulations comprising compound of EX. #2

Formulations containing compound of EX. #2 were prepared according to Example A and tested according to ASSAY (IIIa).

5

Table 28- Stability of formulation comprising compound of EX. #2

	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	HEPES (mM)	m-Cresol (mM)	NaCl (mM)	pH	T _{HT} Lag-time (h)	Peptide Rec. (%)
F39	0.4	14	58	8	-	-	-	8.2	>45	103
F40	0.4	14	58	8	-	-	-	7.8	>45	102
F41	0.4	14	58	8	-	-	-	7.4	>45	103

	Ex.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	HEPES (mM)	m-Cresol (mM)	NaCl (mM)	pH	T_{ThT} Lag-time (h)	Peptide Rec. (%)
F42	0.4	14	58	8	-	-	-	7.0	>45	106
F43	0.4	14	58	8	-	-	-	6.6	>45	103
F44	0.3	14	58	8	-	-	-	6.6	>45	99
F45	0.3	14	58	8	-	-	-	7.0	>45	101
F46	0.3	14	58	8	-	-	-	7.4	>45	101
F47	0.3	14	58	8	-	-	-	7.8	>45	105
F48	0.3	14	58	8	-	-	-	8.2	>45	100
F49	0.3	14	58	8	-	-	-	8.6	>45	100
F50	0.003	14	58	8	-	-	-	7.4	>45	72
F51	0.013	14	58	8	-	-	-	7.4	>45	99
F52	0.027	14	58	8	-	-	-	7.4	>45	101
F53	0.134	14	58	8	-	-	-	7.4	>45	102
F54	0.268	14	58	8	-	-	-	7.4	>45	104
F55	1.34	14	58	8	-	-	-	7.4	>45	103
F56	2.68	14	58	8	-	-	-	7.4	>45	103
F57	0.4	14	58	8	-	-	-	8.2	>45	101
F58	0.4	14	58	-	10	-	-	8.2	>45	101
F59	0.4	14	-	-	10	30	-	8.2	>45	101
F60	0.4	14	58	8	-	-	-	8.2	>45	102
F61	0.4	14	58	8	-	-	5	8.2	>45	101
F62	0.4	14	58	8	-	-	10	8.2	>45	102
F63	0.4	14	58	8	-	-	30	8.2	>45	102
F64	0.4	14	58	8	-	-	50	8.2	>45	103
F65	0.4	14	58	8	-	-	100	8.2	>45	101
F66	0.4	14	58	8	-	-	150	8.2	>45	100
F67	0.4	14	58	8	-	-	-	8.2	>45	98
F68	0.4	14	58	-	-	-	-	8.2	>45	101
F69	0.4	14	58	-	8	-	-	8.2	>45	100
F70	0.4	14	-	8	-	-	-	8.2	>45	101

	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	HEPES (mM)	m-Cresol (mM)	NaCl (mM)	pH	ThT Lag-time (h)	Peptide Rec. (%)
F71	0.4	14	-	-	8	-	-	8.2	>45	101
F72	0.4	-	58	8	-	-	-	8.2	>45	103
F73	0.4	-	-	-	8	-	-	8.2	>45	100

Example G- Stability of fromulations cporising compound of EX. #2

Formulations containing variable concentrations of compound of EX. #2 were prepared according to Example A. All formulations contained 14 mg/ml propylene glycol, 58 mM phenol and 8 mM phosphate. pH was adjusted to specific levels between pH 6.6 and pH 8.6. All formulations were tested according to ASSAY (XIII).

Table 29- Stability of formulations comprising compound of EX. #2

Formulation	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	HMWP^f (%)	Post monomer^g (%)	Purity Loss^h
F74	0.268	14	58	8	7.4	98	0.27	3.2	1.0
F75	1.34	14	58	8	7.4	98	0.25	3.4	0.77
F76	2.68	14	58	8	7.4	97	0.24	3.6	0.75
F77	0.268	14	58	8	8.2	98	0.15	4.0	2.8
F78	1.34	14	58	8	8.2	94	0.26	4.7	2.2
F79	2.68	14	58	8	8.2	94	0.26	4.6	2.0
F80	0.3	14	58	8	6.6	-	0.102	-	0.22
F81	0.3	14	58	8	7.0	-	0.075	-	0.39
F82	0.3	14	58	8	7.4	-	0.064	-	0.58
F83	0.3	14	58	8	7.8	-	0.053	-	0.88
F84	0.3	14	58	8	8.2	-	0.047	-	2.26
F85	0.3	14	58	8	8.6	-	0.021	-	4.39

* Peptide concentration after 11 weeks at 37°C relative to start value

£ %HMWP after 11 weeks at 37°C (Formulation F74-F79) or HMWP formation rate (%/month) at 37°C (Formulation F80-F85)

\$ Post monomer after 11 weeks at 37°C minus start value

¤ Purity loss in %/month at 37°C

5

Example H- Stability of formulations comprising compound of EX. #2

Formulations containing 0.05 to 2 mM compound of EX. #2 were prepared according to Example A. All formulations contained 14 mg/ml propylene glycol, 58 mM phenol and 8 mM phosphate, pH 8.2. All formulations were tested according to ASSAY (XIII).

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Table 30- Stability of formulations comprising compound of EX. #2

Formulation	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	HMWP [£] (%)	Post monomer ^{\$} (%)	Purity Loss [¤]
F86	2	14	58	8	8.2	100	0.22	0.24	1.8
F87	1	14	58	8	8.2	100	0.20	2.1	2.1
F88	0.5	14	58	8	8.2	100	0.27	2.2	2.6
F89	0.2	14	58	8	8.2	99	0.17	1.2	2.4
F90	0.0 5	14	58	8	8.2	97	0.06	nd	3.0

* Peptide concentration after 8 weeks at 37°C relative to start value

£ HMWP after 8 weeks at 37°C

\$ Post monomer after 8 weeks at 37°C minus start value (nd=not possible to detect)

¤ Purity loss in %/month at 37°C

5

Example I- Stability of formulations comprising compound of Ex. #2

Formulations containing 0.01 to 0.5 mM compound of EX. #2 were prepared according to Example A. All formulations contained 14 mg/ml propylene glycol, 58 mM phenol and 8 mM phosphate, pH 8.2. All formulations were tested according to ASSAY (XIII).

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Table 31- Stability of formulations comprising compound of EX. #2

Formulation	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	Purity Loss [¤]
F91	0.01	14	58	8	8.2	84	2.8
F92	0.02	14	58	8	8.2	94	2.7
F93	0.05	14	58	8	8.2	98	2.7
F94	0.1	14	58	8	8.2	98	2.7
F95	0.2	14	58	8	8.2	99	2.9
F96	0.5	14	58	8	8.2	99	2.5

* Peptide concentration after 8 weeks at 37°C relative to start value

¤ Purity loss in %/month at 37°C

Example J- Stability of formulation comprising compound of EX. #2

Formulations containing 2.7 μ M to 2.7 mM compound of EX. #2 were prepared according to Example A. All formulations contained 14 mg/ml propylene glycol, 58 mM phenol and 5 8 mM phosphate, pH 7.4. All formulations were tested according to ASSAY (XIII).

Table 32- Stability of formulations comprising compound of EX. #2

Formulation	EX.# 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	HMWP ^f (%)	Purity Loss ^x
F97	0.00268	14	58	8	7.4	77	0.09	6.1
F98	0.0134	14	58	8	7.4	89	0.05	2.1
F99	0.0268	14	58	8	7.4	92	0.04	1.2
F100	0.134	14	58	8	7.4	94	0.24	1.1
F101	0.268	14	58	8	7.4	94	0.28	0.9
F102	1.34	14	58	8	7.4	99	0.41	1.0
F103	2.68	14	58	8	7.4	99	0.42	0.7

* Peptide concentration after 11 weeks at 37°C relative to start value

£ HMWP after 11 weeks at 37°C

10 x Purity loss in %/month at 37°C

Example K- Stability of a formulations comprising compound of EX. #2

Formulations containing a compound of EX. #2 were prepared according to Example A and tested according to ASSAY (XIII).

Table 33- Stability of formulations comprising compound of EX. #2

Formulation	Ex. # 2 (mM)	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	HEPES (mM)	m-Cresol (mM)	NaCl (mM)	pH	Pept. Conc.* (%)	HMWP ^f (%)	Post monomer ^g (%)
F104	0.4	14	58	8	-	-	-	8.2	107	0.30	3.4
F105	0.4	14	58	-	10	-	-	8.2	105	0.25	3.2
F106	0.4	14	-	-	10	30	-	8.2	105	0.23	3.0
F107	0.4	14	58	8	-	-	-	8.2	99	0.31	0.77
F108	0.4	14	58	8	-	-	5	8.2	99	0.38	0.99
F109	0.4	14	58	8	-	-	10	8.2	99	0.36	0.85
F110	0.4	14	58	8	-	-	30	8.2	97	0.41	0.71
F111	0.4	14	58	8	-	-	50	8.2	98	0.53	0.43
F112	0.4	14	58	8	-	-	100	8.2	99	0.67	0.94
F113	0.4	14	58	8	-	-	150	8.2	99	0.69	0.66
F114	0.4	14	58	8	-	-	-	8.2	104	0.27	0.51
F115	0.4	14	58	-	-	-	-	8.2	99	0.14	0.72
F116	0.4	14	58	-	8	-	-	8.2	101	0.20	0.66
F117	0.4	14	-	8	-	-	-	8.2	101	0.18	1.02
F118	0.4	14	-	-	8	-	-	8.2	101	0.17	0.68
F119	0.4	-	58	8	-	-	-	8.2	101	0.37	0.70
F120	0.4	-	-	-	8	-	-	8.2	102	0.20	0.73

* Peptide concentration after one month at 37°C relative to start value

^f HMWP after one month at 37°C^g Post monomer after one month at 37°C minus start value

Example L- Stability of co-formulations comprising compound of EX. #2 In combination with liraglutide

Co-formulations containing a compound of EX. #2 and liraglutide were prepared according to Example A together with mono-formulations containing the same amount of the two peptide components. All formulations (mono- and co-) were tested according to ASSAY (IIIa) and ASSAY (XIII).

Table 34- Stability of co-formulations comprising compound of EX. #2 in combination with liraglutide

Formulation	EX.# 2 (mg/ml) ^a	Liraglutide (mg/ml) ^a	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	HMWP ^f (%)	ThT Lag-time (h)	EX.# 2 recovery (%) [#]	Liraglutide recovery (%) ^x
F121	0.6	-	14	58	8	8.2	97	0.02	>45	107	-
F122	1	-	14	58	8	8.2	98	0.03	>45	96	-
F123	2	-	14	58	8	8.2	98	0.03	>45	106	-
F124	-	1	14	58	8	8.2	99	2.54	>45	-	104
F125	-	3	14	58	8	8.2	101	1.17	>45	-	105
F126	-	6	14	58	8	8.2	100	0.62	>45	-	100
F127	0.6	1	14	58	8	8.2	98	1.78	>45	105	97
F128	0.6	3	14	58	8	8.2	99	1.06	>45	98	106
F129	0.6	6	14	58	8	8.2	99	0.67	>45	107	103
F130	1	1	14	58	8	8.2	98	1.55	>45	110	98
F131	1	3	14	58	8	8.2	99	0.85	>45	99	95
F132	1	6	14	58	8	8.2	100	0.75	>45	102	104
F133	2	1	14	58	8	8.2	99	1.14	>45	97	95
F134	2	3	14	58	8	8.2	99	0.79	>45	99	98
F135	2	6	14	58	8	8.2	100	0.66	>45	110	98

a 1 mg/ml EX.# 2 ~ 0.27 mM; 1 mg/ml liraglutide ~ 0.27 mM

5 * Peptide concentration after twelve weeks at 37°C relative to start value

£ HMWP formation rate at 37°C (%/month)

UV-215 nm detection; not baseline separated from liraglutide

¤ UV-280 nm detection

10 **Example M- Stability of co formulations comprising compound of EX. #2 in combination with semaglutide**

Co-formulations containing compound of EX. #2 and semaglutide were prepared according to Example A together with mono-formulations containing the same amount of

the two peptide components. All formulations (mono- and co-) were tested according to ASSAY (IIIa) and ASSAY (XIII).

5 **Table 35-** Stability of co formulations comprising compound of EX. #2 in combination with semaglutide

Formulation	EX.# 2 (mg/ml) ^a	Semaglutide (mg/ml) ^a	Propylene glycol (mg/ml)	Phenol (mM)	Phosphate (mM)	pH	Pep. Conc.* (%)	HMWP ^f (%)	T _{thT} Lag-time (h)	Total peptide recovery (%) ^g	Semaglutide recovery (%) ^g
F136	0.6	-	14	58	8	7.4	95	0.00	>45	101	-
F137	6	-	14	58	8	7.4	96	0.08	>45	102	-
F138	12	-	14	58	8	7.4	90	0.09	>45	103	-
F139	-	0.5	14	58	8	7.4	98	1.36	>45	96	107
F140	-	2	14	58	8	7.4	97	0.68	>45	117	97
F141	-	4.1	14	58	8	7.4	99	0.47	>45	100	106
F142	0.6	0.5	14	58	8	7.4	97	0.74	>45	100	101
F143	0.6	2	14	58	8	7.4	95	0.37	>45	102	102
F144	0.6	4.1	14	58	8	7.4	96	0.34	>45	95	97
F145	6	0.5	14	58	8	7.4	95	0.14	>45	104	96
F146	6	2	14	58	8	7.4	96	0.20	>45	103	91
F147	6	4.1	14	58	8	7.4	97	0.26	>45	98	98
F148	12	0.5	14	58	8	7.4	96	0.13	>45	100	96
F159	12	2	14	58	8	7.4	96	0.17	>45	107	92
F150	12	4.1	14	58	8	7.4	95	0.19	>45	98	99

a 1 mg/ml EX.# 2 ~ 0.27 mM; 1 mg/ml semaglutide ~ 0.24 mM

* Peptide concentration after twelve weeks at 37°C relative to start value

£ HMWP formation rate at 37°C (%/month)

\$ Total peptide recovery reflects the recovery of EX.# 2 and semaglutide in total (EX.# 2 co-elutes with semaglutide)

¤ UV-280 nm detection of semaglutide

Example N- Compound EX. #2 when co-formulated with liraglutide: Effect on body weight using DIO rat model ASSAY(XIV)

Monotherapy with liraglutide and compound of EX. #2 induced a 5.9% and 10.9% reduction in body weight at the given doses, respectively. Addition of compound EX. #2 on day 15 to the treatment regimen with liraglutide caused an additional 9.7% reduction in body weight by day 28 relative to monotherapy with liraglutide. See Fig. 1 and Table 36.

Table 36- Effects on body weight reduction with liraglutide and compound of Ex. #2 at the given doses ASSAY (XIV)

Group	Absolute BW (g)			Relative BW (% of initial BW)	
	Day 0	Day 15	Day 28	Day 15	Day 28
Vehicle	834.7 ± 40 ^a	824.4 ± 39.6 ^a	833.2 ± 41 ^a	98.8 ± 0.8 ^a	99.8 ± 1.1 ^a
Liraglutide, 0.1 mg/kg	824.6 ± 44.7 ^a	774.2 ± 42.9 ^a	773.9 ± 41.2 ^a	93.9 ± 0.5 ^b	93.9 ± 0.7 ^b
EX. #2, 3.7 µg/kg	815.5 ± 33.3 ^a	740.3 ± 34.3 ^a	726.5 ± 33.9 ^a	90.6 ± 0.6 ^c	88.9 ± 0.7 ^c
Liraglutide, 0.1 mg/kg + EX. #2, 3.7 µg/kg	819.3 ± 27.7 ^a	765.1 ± 27.1 ^a	681.5 ± 26 ^b	93.4 ± 0.5 ^b	83.2 ± 1.3 ^d

^{a-d} *p*<0.05, one-way ANOVA and Tukey's multiple comparison test for each day; groups not connected by the same letter (in each column) are significantly different from each other. Results expressed as mean ± SEM, *n*=10.

Table 37- Amylin and calcitonin receptor IC50 (pM) for mimylin compounds (Assay Va & VIIa)

Ex. #	hAmylin-R binding IC50 (pM)	hCT-R binding IC50 (pM)	Ex. #	hAmylin-R binding IC50 (pM)	hCT-R binding IC50 (pM)	Ex. #	hAmylin-R binding IC50 (pM)	hCT-R binding IC50 (pM)
1	511	431	34	1592	2266	97	186	307
2	902	798	43	432	352	100	3167	2824
3	498	413	56	2609	2935	101	588	628
4	1189	1050	57	1231	2536	102	1649	1242

Ex. #	hAmylin- R binding	hCT-R binding	Ex. #	hAmylin- R binding	hCT-R binding	Ex. #	hAmylin-R binding	hCT-R bindin g
	IC50 (pM)	IC50 (pM)		IC50 (pM)	IC50 (pM)		IC50 (pM)	IC50 (pM)
5	8377	6506	60	1067	1527	105	22900	17318
6	8972	5684	61	1360	1760	106	19721	9146
7	435	834	62	3053	2332	107	5445	1267
8	429	368	63	4066	2597	111	222	747
9	796	736	64	4360	3632	112	431	547
10	417	523	65	1888	1246	114	278	326
11	1475	1369	72	697	438	115	338	796
12	511	419	73	608	442	117	142	450
13	329	279	74	606	1085	121	801	300
15	275	473	75	21984	20475	122	244	318
16	1312	981	76	764	855	123	11784	5624
17	832	577	77	998	1100	124	79	312
18	1265	1172	78	587	605	126	1481	1833
19	1144	515	79	111	385	128	116	200
21	187	315	81	2015	4929	129	2560	3624
22	240	188	83	1916	1567	132	3701	1549
23	830	541	85	653	821	133	10698	9664
24	824	749	86	812	943	134	297898	42425
25	400	413	87	428	590	135	294388	630425
26	891	570	88	92023	24195	106 bb	71390	62870
27	374	219	89	7260	3600	127 bb	1183	959
28	375	351	90	21010	6843	22b b	469	481
29	352	309	92	2609	2935	72b b	5100	4529
30	323	478	93	1507	1028	86b b	982	520
31	383	506	94	652	651	95b b	20158	15330
32	9000	3348	95	2147	1696	-	-	-
33	745	752	96	1170	767	-	-	-

CLAIMS

1. A mimylin peptide comprising a sequence which is at least 66% identical to EASELSTAALGRLSAELHELATLPRTEGPESP (SEQ ID NO: 1) and does not comprise any N.
- 5 2. The mimylin peptide according to claim 1, wherein said mimylin peptide comprises up to 11, preferably 10, 9, 8 or 7, most preferably 6, 5, 3, 2 or 1 of the following amino acids or modifications relative to SEQ ID NO: 1:
 - a. E or no amino acid in position -1,
 - b. E, A or no amino acid in position 1,
 - 10 c. A, L or P in position 2,
 - d. S or P in position 3,
 - e. E, P, K, Q or G in position 4,
 - f. L, V, I or H in position 5,
 - 15 g. S, T or H in position 6,
 - h. T in position 7,
 - i. L or A in position 8,
 - j. A, V, I, S or T in position 9,
 - k. L, A, I, H or V in position 10,
 - 20 l. G in position 11,
 - m. R, H or K in position 12,
 - n. L in position 13,
 - o. S, T or E in position 14,
 - p. A, Q, E, e or T in position 15,
 - 25 q. E, R, K or Q in position 16,
 - r. L or I in position 17,
 - s. H or A in position 18,
 - t. E, R or K in position 19,
 - u. L, I or V in position 20,
 - 30 v. A, Q, S, E or T in position 21,
 - w. T in position 22,
 - x. L or Y in position 23,
 - y. P in position 24,
 - z. R, P, H or K in position 25,
 - aa. T in position 26,
 - 35 bb. E, Q, G or K in position 27,
 - cc. T or P in position 28,
 - dd. G in position 29,
 - ee. P, S or T in position 30,
 - ff. E, Q, G, A, P or K in position 31,
 - 40 gg. T, S, H, P or A in position 32,
 - hh. P, Y, H, F, L, S, G or A in position 33,
 - ii. G or K in position 34 or no amino acid.
3. The mimylin peptide according to claim 1, wherein said mimylin peptide comprises up to 11, preferably 10, 9, 8 or 7, most preferably 6, 5, 3, 2 or 1 of the following amino acids or modifications relative to SEQ ID NO: 1:
 - a. E or no amino acid in position -1,
 - b. E, A or no amino acid in position 1, preferably E,
 - 45 c. A, L or P in position 2,
 - d. S or P in position 3,
 - e. E, P, K, Q or G in position 4,
 - f. L, V, I or H in position 5,
 - 50 g. S, T or H in position 6, preferably S,
 - h. T in position 7,
 - i. L or A in position 8, preferably A,

- j. A, V, I, S or T in position 9, preferably A or V or I,
- k. L, A, I, H or V in position 10, preferably L or I,
- l. G in position 11,
- m. R, H or K in position 12,
- 5 n. L in position 13,
- o. S, T or E in position 14,
- p. A, Q, E, e or T in position 15, preferably A,
- 10 q. E, R, K or Q in position 16, preferably E,
- r. L or I in position 17,
- s. H or A in position 18,
- t. E, R or K in position 19, preferably E,
- 15 u. L, I or V in position 20, preferably L,
- v. A, Q, S, E or T in position 21, preferably A,
- w. T in position 22,
- x. L or Y in position 23,
- y. P in position 24,
- 20 z. R, P, H or K in position 25, preferably R,
- aa. T in position 26,
- bb. E, Q, G or K in position 27, preferably E,
- cc. T or P in position 28,
- 25 dd. G in position 29,
- ee. P, S or T in position 30,
- ff. E, Q, G, A, P or K in position 31, preferably E or G,
- gg. T, S, H, P or A in position 32, preferably S or T,
- 25 ii. P, Y, H, F, L, S, G or A in position 33, preferably P or Y,
- ii. G or K in position 34 or no amino acid.

- 4. The mimylin peptide according to any one of the preceding claims, wherein position 30 is S and position 31 is G, wherein the amino acid numbering corresponds to SEQ ID NO: 1.
- 30 5. The mimylin peptide according to any of the preceding claims, wherein position 9 is V and/or position 1 is E, wherein the amino acid numbering corresponds to SEQ ID NO: 1.
- 6. The mimylin peptide according to any of the preceding claims, wherein position 33 is P, wherein the amino acid numbering corresponds to SEQ ID NO: 1.
- 35 7. The mimylin peptide according to any one of the preceding claims, wherein said peptide has a c-terminal amide.
- 8. The mimylin peptide according to any one of the preceding claims, wherein said mimylin peptide is derivatised in the N-terminal amino acid or any K within said mimylin peptide sequence.
- 40 9. The mimylin peptide according to any one of the preceding claims, wherein said mimylin peptide does not comprise a disulfide bridge between the amino acids in positions 2 and 8, wherein the amino acid numbering corresponds to SEQ ID NO: 1.
- 10. A mimylin derivative, wherein a mimylin peptide according to any one of the preceding claims is derivatised with a side chain comprising a protracting moiety and a linker, wherein said linker preferably is selected from the list of gGlu, gGlu-OEG, gGlu-OEG-OEG, gGlu-OEG-OEG-OEG, gGlu-OEG-OEG-OEG-OEG, gGlu-OEG-OEG-OEG-OEG-OEG.
- 45 11. The mimylin derivative according to claim 10, wherein said protracting moiety is a fatty acid or diacid which preferably comprises between 14 and 20 carbon atoms.
- 12. The mimylin derivative according to any one of the claims 10-11, which is an agonist of the amylin and calcitonin receptor.
- 50 13. The mimylin peptide according to any one of the claims 1-7 or the mimylin derivative according to any one of the claims 10-12, for use of a medicament.

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14. The mimylin peptide according to any one of the claims 1-7 or mimylin derivative according to any one of the claims 10-12, for the treatment of subjects suffering from overweight, obesity and/or diabetes type I or II and/or osteoporosis and/or neuropathic pain.

5 15. The mimylin peptide according to any one of the claims 1-7 and the mimylin derivative according to any one of the claims 10-12, for use in reduction of food intake.

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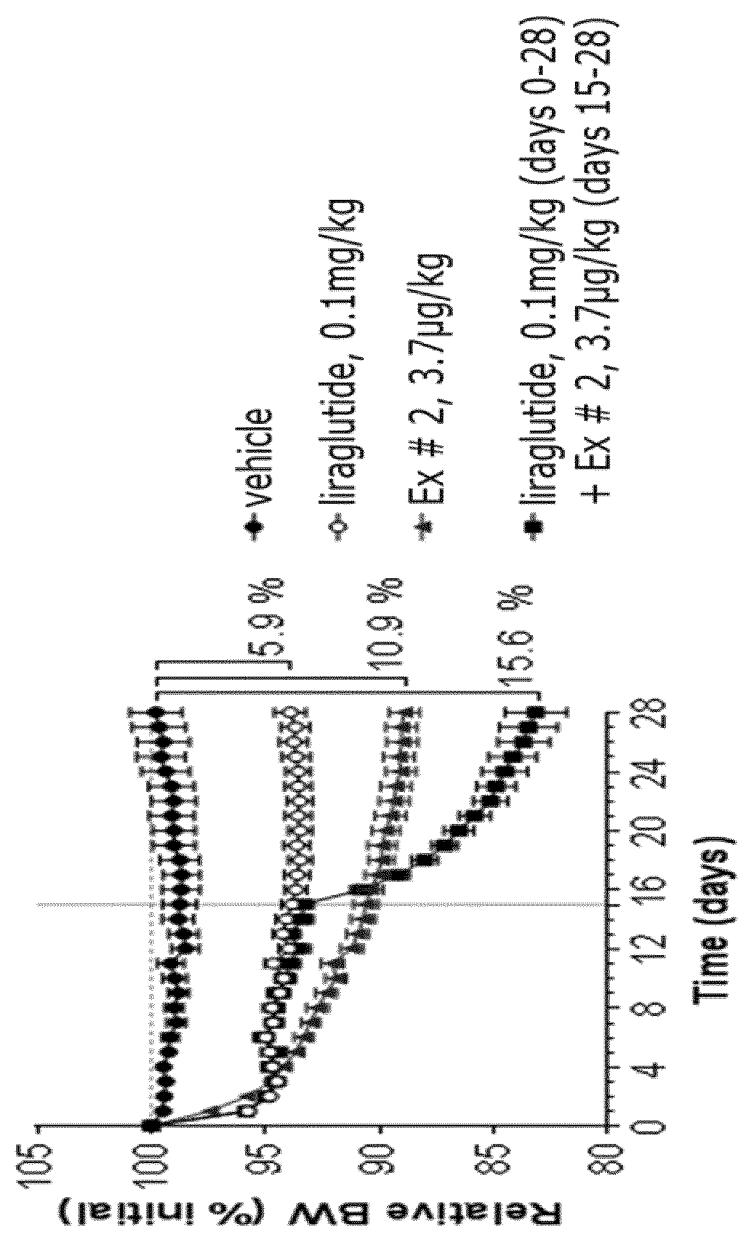


Fig. 1/1

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/069996

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/575
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, EMBASE, FSTA, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 622 386 A (ORLOWSKI RONALD C [US] ET AL) 11 November 1986 (1986-11-11) the whole document -----	1-15
X	EP 0 297 159 A1 (ARMOUR PHARMA [US]) 4 January 1989 (1989-01-04) the whole document -----	1-15
A	WO 2009/156473 A1 (NOVO NORDISK AS [DK]; SCHAEFFER LAUGE [DK]; KRUSE THOMAS [DK]) 30 December 2009 (2009-12-30) the whole document -----	1-15
A	WO 2012/050925 A2 (AMYLIN PHARMACEUTICALS INC [US]; ERICKSON MARY [US]) 19 April 2012 (2012-04-19) the whole document ----- - / --	1-15

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 3 November 2015	Date of mailing of the international search report 03/12/2015
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Luo, Xinmei

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/069996

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JOSEPH J. GINGELL ET AL: "Activity of Pramlintide, Rat and Human Amylin but not A[beta] 1-42 at Human Amylin Receptors", ENDOCRINOLOGY, vol. 155, no. 1, 29 October 2013 (2013-10-29), pages 21-26, XP055172996, ISSN: 0013-7227, DOI: 10.1210/en.2013-1658 the whole document -----	1-15

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2015/069996

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. forming part of the international application as filed:
 - in the form of an Annex C/ST.25 text file.
 - on paper or in the form of an image file.
 - b. furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. furnished subsequent to the international filing date for the purposes of international search only:
 - in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).
 - on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2015/069996

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: 1-15 (partially) because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-15(partially)

Present claims 1-15 relate to an extremely large number of possible compounds. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds claimed, see Tables 1, 5, 8, 13-19, especially Tables 20-37.

The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 1-15 (PCT Guidelines 9.19 and 9.23).

The search of claims 1-15 was restricted to those claimed compounds which appear to be supported and a generalisation of their structural formulae, namely compounds of Ex. number 2, 40 and 46 and their derivatives comprising a protracting moiety and a linker.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2015/069996

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 4622386	A	11-11-1986	NONE	
EP 0297159	A1	04-01-1989	NONE	
WO 2009156473	A1	30-12-2009	CN 102076353 A EP 2293811 A1 JP 2011525895 A US 2011152183 A1 WO 2009156473 A1	25-05-2011 16-03-2011 29-09-2011 23-06-2011 30-12-2009
WO 2012050925	A2	19-04-2012	CA 2813038 A1 CA 2813087 A1 CN 103403019 A CN 103547590 A EA 201390474 A1 EA 201390497 A1 EP 2621515 A2 EP 2621519 A2 JP 2013543497 A JP 2014502252 A US 2013203661 A1 US 2013274182 A1 WO 2012050925 A2 WO 2012050930 A2	19-04-2012 19-04-2012 20-11-2013 29-01-2014 30-07-2013 30-09-2013 07-08-2013 07-08-2013 05-12-2013 30-01-2014 08-08-2013 17-10-2013 19-04-2012 19-04-2012