

Claims

1. A neurokinin receptor 2 (NK2R) agonist according to formula (I):

5 (A)-(B) (I),

wherein;

(A) is a peptide comprising an amino acid sequence of the general formula $X_1X_2X_3X_4X_5X_6X_7$, wherein

10 X_1 is selected from the group consisting of: aspartic acid (D) and glutamic acid (E);
 X_2 is selected from the group consisting of: lysine (K), arginine (R), and histidine (H);
 X_3 is selected from the group consisting of: tyrosine (Y), phenylalanine (F), *meta*-tyrosine (*m*-Y), valine (V), tryptophan (W), methionine (M), leucine (L), isoleucine (I), and alanine (A);

15 X_4 is selected from the group consisting of: valine (V), threonine (T), serine (S), asparagine (N), glutamine (Q), glycine (G), and alanine (A);

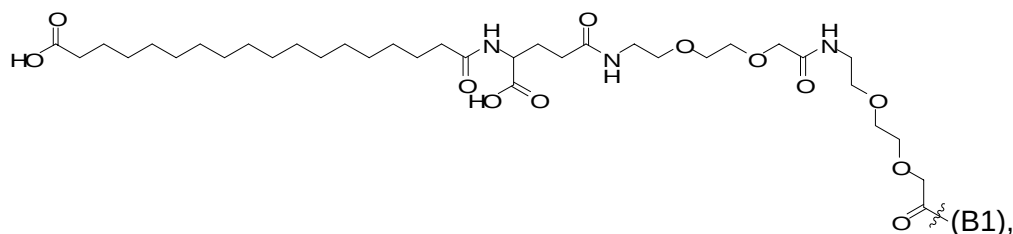
X_5 is selected from the group consisting of: glycine (G), 2-aminoisobutyric acid (Aib), serine (S), alanine (A), valine (V), leucine (L), beta-alanine (bA) and isoleucine (I);

20 X_6 is selected from the group consisting of: leucine (L), isoleucine (I), alanine (A) and N-methyl leucine (Me-Leu); and

X_7 is selected from the group consisting of: norleucine (Nle), methoxinine (Mox), methionine (M), 4-fluorophenylalanine (4fF), and 4-methoxyphenylalanine (4MeOF);

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(B) is a conjugated moiety of formula (B1)



and wherein (B) is covalently linked to a terminal amino acid.

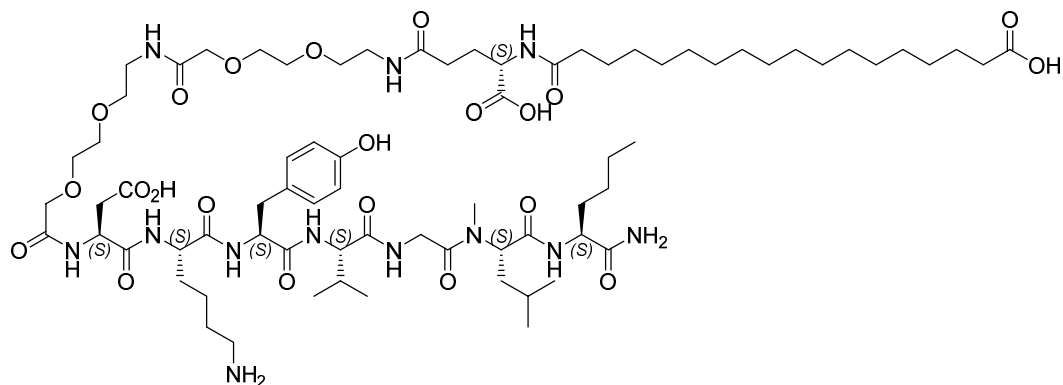
30 2. The NK2R agonist according to claim 1, wherein the peptide (A) is of the general formula $X_1X_2X_3X_4X_5X_6X_7$, wherein

- X_1 is selected from the group consisting of: aspartic acid (D) and glutamic acid (E);
 X_2 is selected from the group consisting of: lysine (K), and arginine (R);
 X_3 is selected from the group consisting of: tyrosine (Y), and phenylalanine (F), and
 5 *meta*-tyrosine (*m*-Y),
 X_4 is selected from the group consisting of: valine (V), and threonine (T);
 X_5 is selected from the group consisting of: glycine (G), 2-aminoisobutyric acid (Aib),
 beta-alanine (bA) and serine (S);
 X_6 is selected from the group consisting of: leucine (L), and N-methyl leucine (Me-
 10 Leu); and
 X_7 is selected from the group consisting of: norleucine (Nle), methoxinine (Mox),
 methionine (M), 4-fluorophenylalanine (4fF), and 4-methoxyphenylalanine (4MeOF).
- 15 3. The NK2R agonist according to any one of the preceding claims, wherein the
 conjugated moiety (B) is covalently attached to the N-terminus of (A), optionally via
 an amide bond.
 - 20 4. The NK2R agonist according to any one of the preceding claims, wherein the
 conjugated moiety (B) is covalently attached to the N-terminus of (A) via an amide
 bond with the N-terminal α -NH₂ group.
 - 25 5. The NK2R agonist according to any one of the preceding claims, wherein the peptide
 (A) is amidated on the C-terminus.
 6. The NK2R agonist according to any one of the preceding claims, wherein the peptide
 (A) consists of 7 amino acids of the general formula $X_1X_2X_3X_4X_5X_6X_7$.
 - 30 7. The NK2R agonist according to any one of the preceding claims, wherein
 (A) is: Asp;Lys;Phe;Val;Gly;Me-Leu;Nle;NH₂ (compound 305), and
 (B) is of formula (B1) covalently attached to the N-terminal aspartate of (A).
 - 35 8. The NK2R agonist according to any one of claims 1-**Error! Reference source not
 found.**, wherein
 (A) is: Asp;Lys;Tyr;Val;Gly;Me-Leu;Mx;NH₂ (compound 344), and
 (B) is of formula (B1) covalently attached to the N-terminal aspartate of (A).

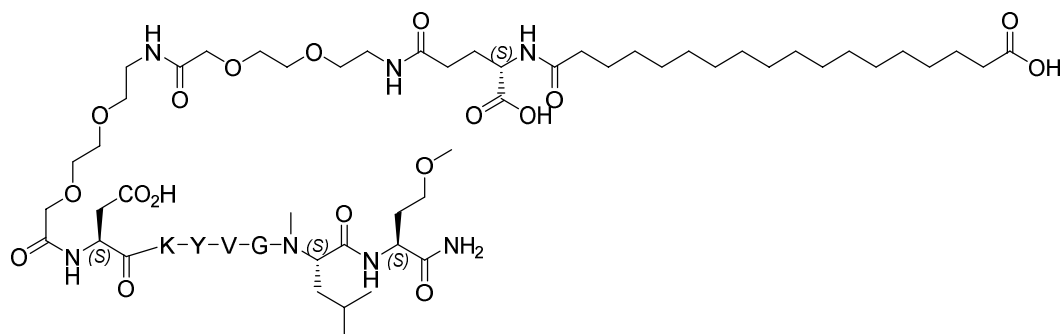
9. The NK2R agonist according to any one of claims 1-**Error! Reference source not found.**, wherein the NK2R agonist consists of the sequence of any one of SEQ ID NO: 1 to SEQ ID NO: 57.

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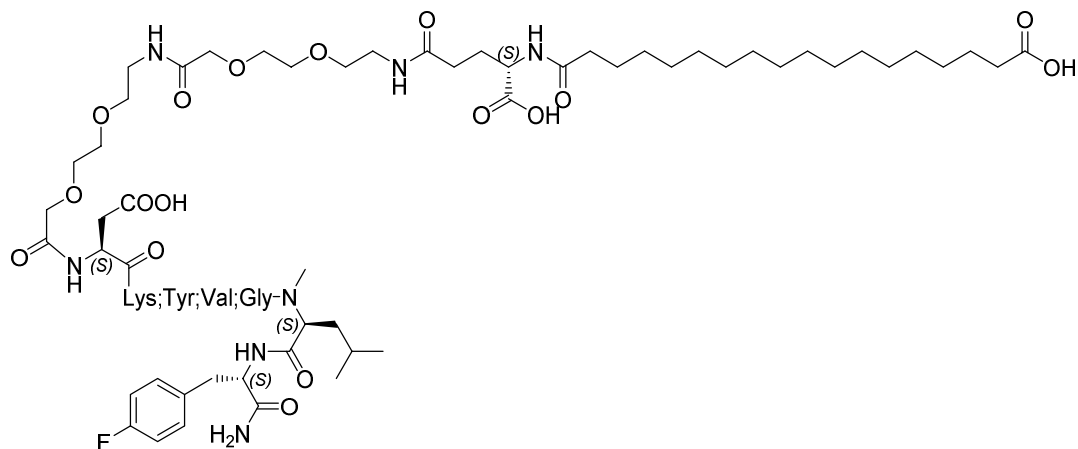
10. The NK2R agonist according to any one of claims 1-**Error! Reference source not found.**, wherein the NK2R agonist is:



(ID 305);

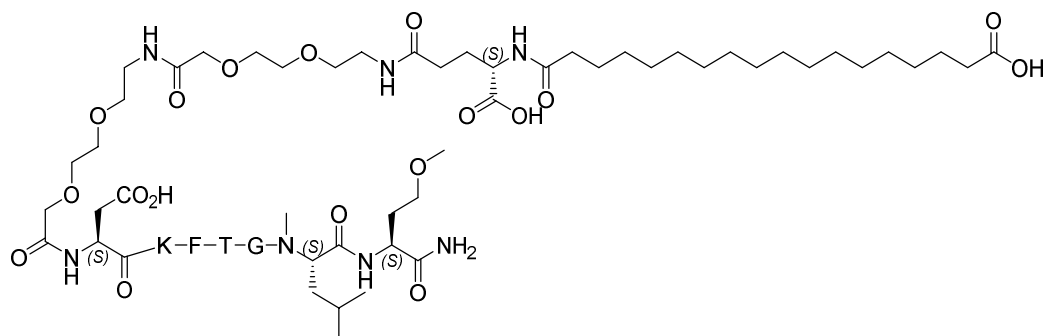


(ID 344); or

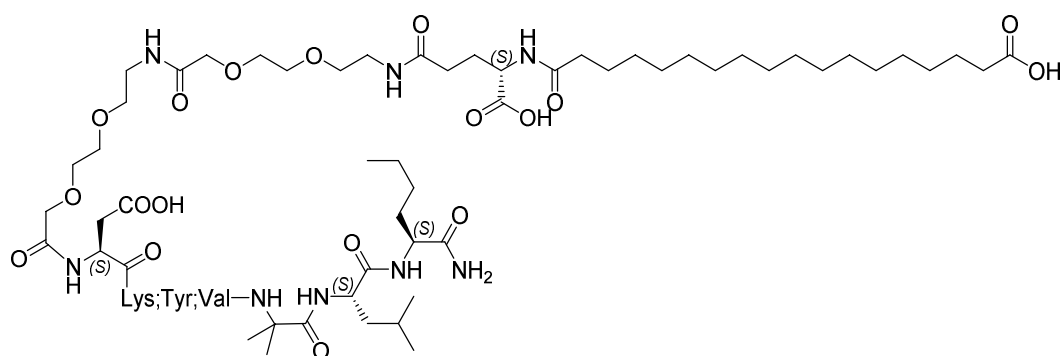


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ID 369);

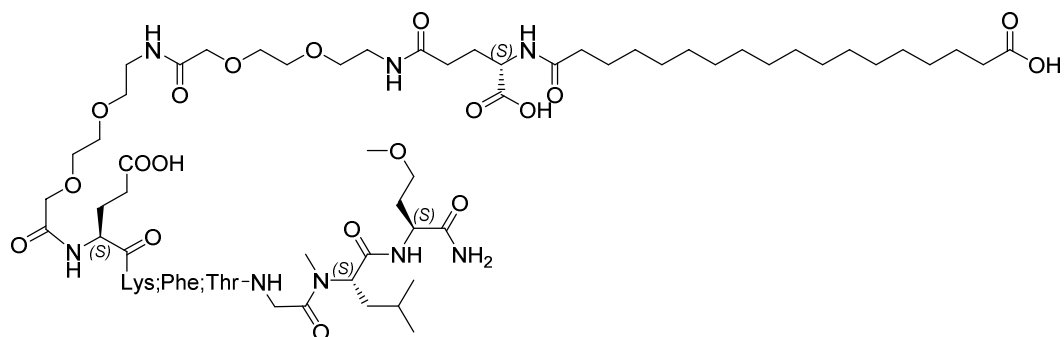


(ID 383);



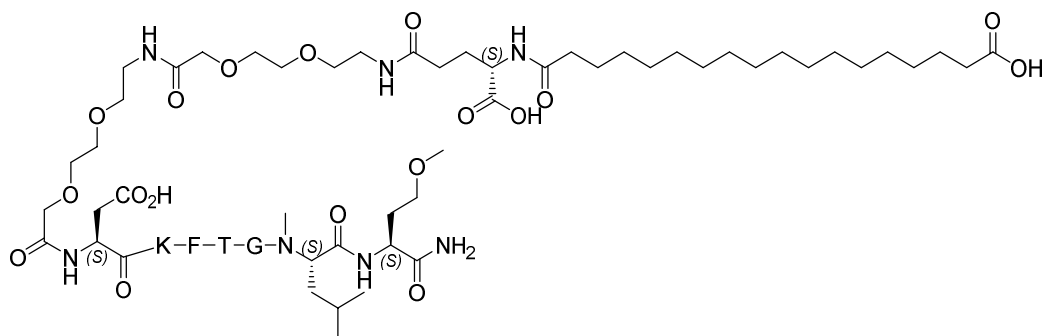
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395) or;



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11. A NK2R agonist which is



(compound 383).

- 5 12. A pharmaceutical composition comprising the neurokinin receptor 2 (NK2R) agonist as defined in any one of the preceding claims, and one or more pharmaceutically acceptable adjuvants, excipients, carriers, buffers and/or diluents.
- 10 13. A neurokinin receptor 2 (NK2R) agonist as defined in any one of claims 1 to 11 for use as a medicament.
- 15 14. The neurokinin receptor 2 (NK2R) agonist for use as defined in claim 13 in treating a NK2R mediated disorder, wherein the NK2R mediated disorder is selected from the group consisting of: obesity, dysfunctional voiding, diabetes, such as type-II diabetes, and diabetes-related disorders, such as impaired insulin tolerance and impaired glucose tolerance.
- 20 15. Use of a neurokinin receptor 2 (NK2R) agonist as defined in any one claims 1 to 11 in the manufacture of a medicament for the treatment of a metabolic disorder, such as a diabetes-related, such as impaired insulin tolerance and impaired glucose tolerance.