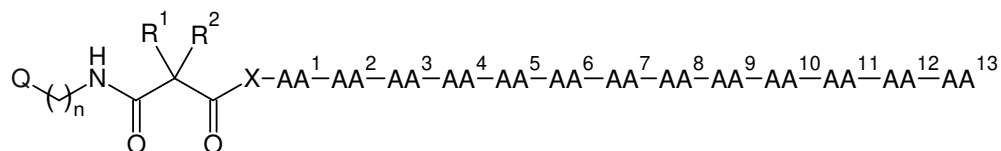


Claims

1. A compound comprising the sequence of formula (1):



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(1);

wherein;

Q is selected from phenyl or a monocyclic heteroaryl ring each of which may be optionally substituted with one or more R^q groups; or Q is a polyether chain of formula $-(\text{OCH}_2\text{CH}_2)_m\text{OCH}_3$, wherein m is 1 to 5;

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R^q is selected from halogen, hydroxyl, amino or C_{1-6} alkyl having an alkyl chain optionally containing one or more heteroatoms selected from O, N, or S;

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n is 1 to 3;

R^1 and R^2 are independently selected from hydrogen or a C_{1-6} alkyl group, or together with the carbon to which they are attached join to form a C_{3-8} cycloalkyl or a heterocyclyl group;

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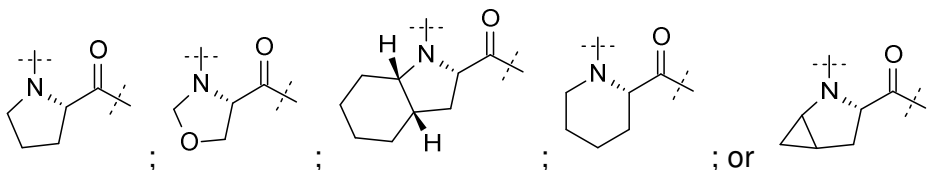
X is -DArg- or a bond;

AA^1 is $-\text{NHCR}^{3a}\text{R}^{3b}\text{CO}-$ or $-\text{N}(\text{Me})\text{CR}^{3a}\text{R}^{3b}\text{CO}-$; wherein R^{3a} is hydrogen or C_{1-3} alkyl; and R^{3b} is $-\text{CH}_2(\text{CH}_2)_p\text{CONH}_2$ or $-(\text{CH}_2)_p\text{benzyl}$, where p is 0 or 1;

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AA^2 is -Arg-, -DArg- or a homoarginine residue;

AA^3 is a residue selected from:



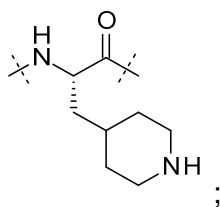
AA⁴ is -Arg- or -DArg-;

AA⁵ is -NHCH(CH₂R⁴)CO- or -N(Me)CH(CH₂R⁴)CO-; wherein R⁴ is C₁₋₆ alkyl,
5 C₁₋₆ cycloalkyl or C₁₋₆ branched alkyl;

AA⁶ is -Aib-, -DAla- or -Ser-;

AA⁷ is -NHCR^{5a}R^{5b}CO- or -N(Me)CR^{5a}R^{5b}CO-; wherein R^{5a} is hydrogen or C₁₋₃
10 alkyl and R^{5b} is C₁₋₃ alkyl, CH₂-aryl or CH₂-heteroaryl optionally substituted with
one or more halo groups or C₁₋₃ alkyl groups;

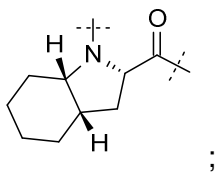
AA⁸ is the residue:



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AA⁹ is -Gly-, -Ala-, -DAla- or an N-methyl glycine residue;

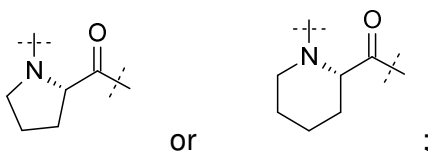
AA¹⁰ is the residue:



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AA¹¹ is -NHCHR⁶CO-; wherein R⁶ is C₁₋₆ alkyl, benzyl, -CH₂-naphthyl or -CH₂-
biphenyl optionally substituted with one or more halo groups;

AA¹² is a residue selected from:



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Chemical structures of five heterocyclic aromatic rings, each with a dashed line indicating the attachment point:

- 4-fluorophenyl
- phenyl
- pyridin-2-yl
- 1,2,4-triazol-5-yl
- 1,2,4-triazol-3-yl

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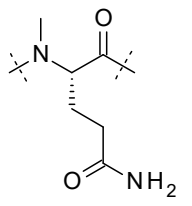
Cc1c[nH]cn1

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8. The compound according to any one of claims 1 to 6, wherein X is a bond.

9. The compound according to any one of claims 1 to 8, wherein AA¹ is a glutamine residue, a D-glutamine residue, a homophenylalanine residue or an N-methyl glutamine residue of the formula:



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10. The compound according to claim 9, wherein AA¹ is a glutamine residue.

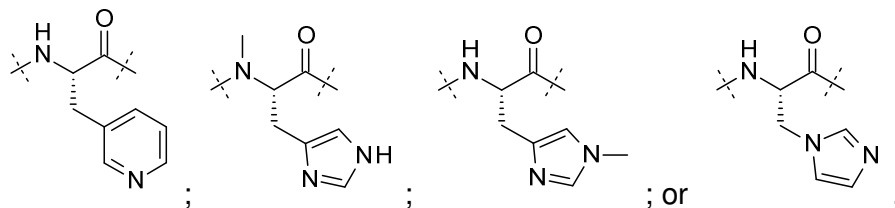
11. The compound according to any one of claims 1 to 10, wherein AA⁵ is a leucine residue, a D-leucine residue, a *tert*-butylalanine residue, a cyclobutylalanine residue or an N-methyl leucine residue.

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12. The compound according to claim 11, wherein AA⁵ is a leucine residue.

13. The compound according to any one of claims 1 to 12, wherein AA⁷ is a 2-aminoisobutyric acid residue, a histidine residue, a 4-bromophenylalanine residue or is a residue selected from:

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14. The compound according to claim 13, wherein AA⁷ is a histidine residue.

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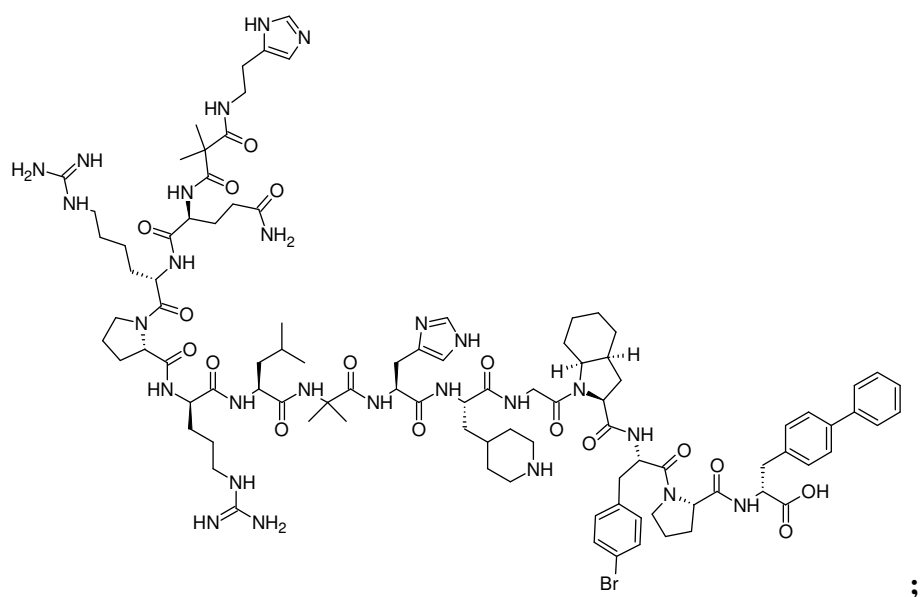
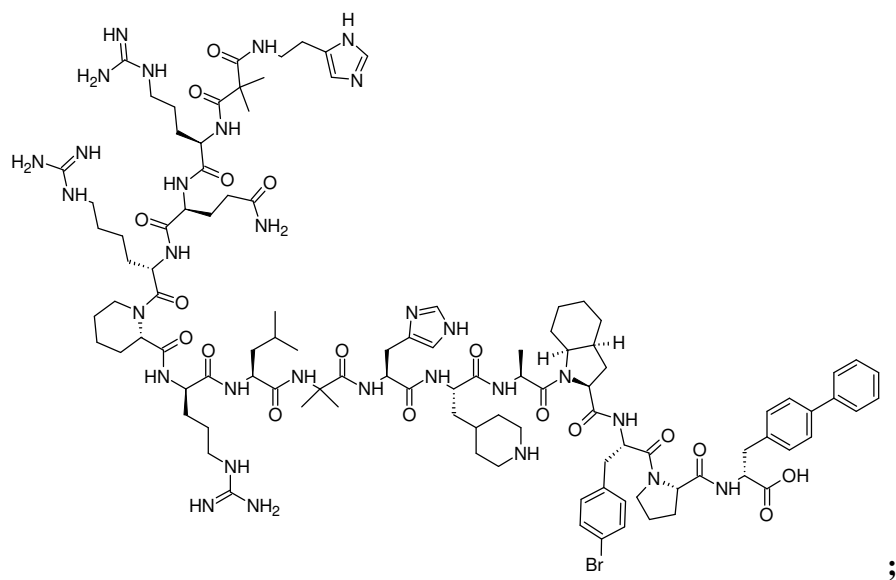
15. The compound according to any one of claims 1 to 14, wherein AA¹¹ is a phenylalanine residue, a 2-naphthylalanine residue, a 3-chlorophenylalanine residue, a 4-bromophenylalanine residue, a 4-chlorophenylalanine residue, a norleucine residue or a 4-phenylphenylalanine residue.

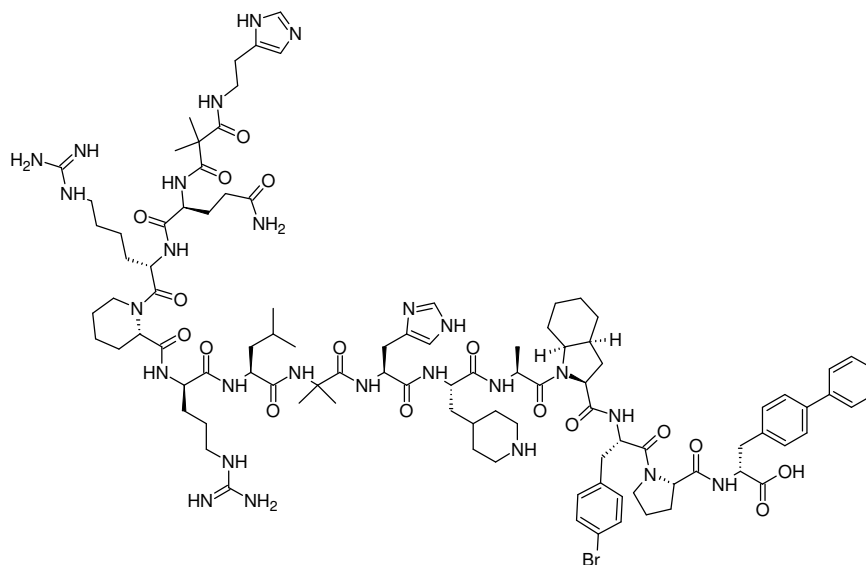
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21. The compound according to any one of claims 1 to 20 having apelin receptor agonist activity.

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22. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 21 and a pharmaceutically acceptable excipient.

23. The compound according to any one of claims 1 to 22 for use in medicine.

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24. Use of ~~the~~ the compound or composition according to any one of claims 1 to 23 for use in the manufacture of a medicament for the treatment of cardiovascular disease, acute decompensated heart failure, congestive heart failure, myocardial infarction, cardiomyopathy, ischemia, ischemia/reperfusion injury, pulmonary hypertension, diabetes, obesity, cancer, metastatic disease, fluid homeostasis, pathological angiogenesis, retinopathy, HIV infection, treatment of pulmonary arterial hypertension (PAH) increasing cardiac output, reducing pulmonary vessel hypertension, reducing inflammation, improve pulmonary tissue remodelling, preserving right heart ventricular function, heart failure, congestive heart failure, cardiomyopathy, ischemia, ischemia/reperfusion injury, fluid homeostasis, kidney failure, hypertension, pulmonary hypertension, polycystic kidney disease, hyponatremia, SIADH, platelet function are associated with a range of thrombotic diseases such as peripheral arterial

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5 disease (PAD), acute coronary syndrome (ACS), myocardial infarction (MI), heart attacks (HA), stroke, atherosclerosis, treatment and management of diabetes and associated related metabolic conditions, diabetic complications (for example diabetic nephropathy, retinopathy, neuropathy, non-alcoholic fatty liver disease, non-alcoholic steatosis, portal hypertension) and conditions where stimulation and/or growth and/or endurance of muscle mass may be considered beneficial.