

WHAT IS CLAIMED IS:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:
AA1-Arg-Val-AA4-AA5-His-Pro-AA8-OH (I),

wherein

5 AA1 is an amino acid residue selected from the group consisting of sarcosine and ((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)glycine;

AA4 is an amino acid residue selected from the group consisting of tyrosine or *meta*-tyrosine, each of which is optionally substituted with at least one substituent selected from the group consisting of halo and hydroxyl;

10 AA5 is an amino acid residue selected from the group consisting of valine, leucine, isoleucine, glycine, alanine, phenylalanine, threonine, lysine, and tyrosine, each of which is optionally substituted with at least one substituent selected from the group consisting of C₁₋₆ alkyl, C₄₋₆ cycloalkyl, NH₂, aryl, and heteroaryl; and

15 AA8 is an amino acid residue selected from the group consisting of 1-naphthylalanine, (3-benzothienyl)alanine, and phenylalanine substituted with at least one substituent selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₄₋₆ cycloalkyl, halo, CN, aryl, and heteroaryl, in which the at least one substituent is at the 2-position on the phenyl ring of the phenylalanine;

20 wherein AA8 is a D-amino acid residue, and each of Arg, Val, AA4, AA5, His, and Pro in formula (I) is an L-amino acid residue.

2. The compound of claim 1, wherein AA4 is tyrosine optionally substituted with at least one substituent, in which the at least one substituent is at the 3-position on the phenyl ring of the tyrosine.

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3. The compound of claim 2, wherein AA4 is tyrosine, *meta*-tyrosine, 3-hydroxytyrosine, or 3-chlorotyrosine.

4. The compound of any preceding claim, wherein AA5 is an amino acid residue selected from the group consisting of valine, leucine, isoleucine, glycine, alanine, phenylalanine, threonine, lysine, and tyrosine, each of which is optionally substituted with at least one substituent selected from the group consisting of CH₃, cyclobutyl, cyclopentyl, cyclohexyl, NH₂, thienyl, and thiazolyl.

5. The compound of any preceding claim, wherein AA5 is valine, isoleucine, cyclobutylglycine, cyclopentylglycine, cyclohexylglycine, cyclohexylalanine, leucine, *o*-methyl threonine, lysine, phenylalanine, tyrosine, 4-aminophenylalanine, 3-thienylalanine, 2-thienylalanine, or 4-thiazolylalanine.

6. The compound of claim 5, wherein AA5 is valine, isoleucine, cyclopentylglycine, cyclohexylglycine, or *O*-methyl threonine.

7. The compound of any preceding claim, wherein AA8 is an amino acid residue selected from the group consisting of D-1-naphthylalanine, D-(3-benzothienyl)alanine, and D-phenylalanine substituted with at least one substituent selected from the group consisting of CH₃, CF₃, Cl, Br, CN, and phenyl.

8. The compound of any preceding claim, wherein AA8 is D-1-naphthylalanine, D-(3-benzothienyl)alanine, D-2-chlorophenylalanine, D-2-bromophenylalanine, D-2-methylphenylalanine, D-2-trifluoromethylphenylalanine, D-2-cyanophenylalanine, D-2-phenylphenylalanine, D-2,4-dichlorophenylalanine, or D-2,6-dimethylphenylalanine.

9. The compound of any preceding claim, wherein AA1 is sarcosine.

10. The compound of claim 9, wherein AA4 is tyrosine, *meta*-tyrosine, 3-hydroxytyrosine, or 3-chlorotyrosine.

11. The compound of claims 9 or 10, wherein AA5 is valine, isoleucine, lysine, tyrosine, 4-aminophenylalanine, cyclohexylalanine, cyclopentylglycine, cyclohexylglycine, phenylalanine, *O*-methyl threonine, 3-thienylalanine, 2-thienylalanine, or 4-thiazolylalanine.

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12. The compound of claims 9, 10 or 11, wherein AA8 is D-1-naphthylalanine, D-(3-benzothienyl)alanine, D-2-chlorophenylalanine, D-2-bromophenylalanine, D-2-methylphenylalanine, D-2-trifluoromethylphenylalanine, D-2-cyanophenylalanine, D-2-phenylphenylalanine, D-2,4-dichlorophenylalanine, or D-2,6-

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dimethylphenylalanine.

13. The compound of any preceding claim, wherein AA1 is ((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)glycine.

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14. The compound of claim 13, wherein AA4 is tyrosine.

15. The compound of claim 13 or 14, wherein AA5 is valine or cyclohexylglycine.

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16. The compound of claim 13, 14 or 15, wherein AA8 is D-1-naphthylalanine, D-(3-benzothienyl)alanine, D-2-chlorophenylalanine, D-2-methylphenylalanine, or D-2-phenylphenylalanine.

17. The compound of claim 1, wherein the compound is

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- (1) Sar-Arg-Val-Tyr-Val-His-Pro-(D-1Nal)-OH;
- (2) Sar-Arg-Val-Tyr-Lys-His-Pro-(D-1Nal)-OH;
- (3) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-CF₃))-OH;
- (4) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Cl))-OH;
- (5) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-CN))-OH;
- (6) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Ph))-OH;

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- (7) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2,4-diCl))-OH;
(8) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2,6-diMe))-OH;
(9) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Me))-OH;
(10) Sar-Arg-Val-Tyr-Val-His-Pro-(D-(3-benzothienyl)alanine)-OH;
5 (11) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Br))-OH;
(12) Sar-Arg-Val-Tyr-Tyr-His-Pro-(D-1Nal)-OH;
(13) Sar-Arg-Val-Tyr-Aph-His-Pro-(D-1Nal)-OH;
(14) Sar-Arg-Val-Tyr-Cha-His-Pro-(D-1Nal)-OH;
(15) Sar-Arg-Val-Tyr-Cpg-His-Pro-(D-1Nal)-OH;
10 (16) Sar-Arg-Val-Tyr-Phe-His-Pro-(D-1Nal)-OH;
(17) Sar-Arg-Val-Tyr-Thr(Me)-His-Pro-(D-1Nal)-OH;
(18) Sar-Arg-Val-Tyr-Cpg-His-Pro-(D-Phe(2-Cl))-OH;
(19) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Cl))-OH;
(20) Sar-Arg-Val-Tyr-Aph-His-Pro-(D-Phe(2-Cl))-OH;
15 (21) Sar-Arg-Val-Tyr-Thr(Me)-His-Pro-(D-Phe(2-Cl))-OH;
(22) Sar-Arg-Val-Tyr-(3-Thi)-His-Pro-(D-Phe(2-Cl))-OH;
(23) Sar-Arg-Val-Tyr-(2-Thi)-His-Pro-(D-Phe(2-Cl))-OH;
(24) Sar-Arg-Val-Tyr-(Ala(4-Thz))-His-Pro-(D-Phe(2-Cl))-OH;
(25) Sar-Arg-Val-Tyr-Ile-His-Pro-(D-Phe(2-Cl))-OH;
20 (26) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-CF₃))-OH;
(27) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Me))-OH;
(28) Sar-Arg-Val-Tyr(3-Cl)-Val-His-Pro-(D-Phe(2-Cl))-OH;
(29) Glac-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Cl))-OH;
(30) Sar-Arg-Val-(*m*-Tyr)-Val-His-Pro-(D-Phe(2-Cl))-OH;
25 (31) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Cl))-OH;
(32) Sar-Arg-Val-DOPA-Val-His-Pro-(D-Phe(2-Cl))-OH;
(33) Sar-Arg-Val-Aph-Val-His-Pro-(D-Phe(2-Cl))-OH;
(34) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-1Nal)-OH;
(35) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-(3-benzothienyl)alanine)-OH;
30 (36) Sar-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Ph))-OH;

- (37) Glac-Arg-Val-Tyr-Val-His-Pro-(D-1Nal)-OH;
(38) Glac-Arg-Val-Tyr-Val-His-Pro-(D-(3-benzothienyl)alanine)-OH;
(39) Glac-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Ph))-OH;
(40) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-1Nal)-OH;
5 (41) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-(3-benzothienyl)alanine)-OH;
(42) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Ph))-OH;
(43) Glac-Arg-Val-Tyr-Cpg-His-Pro-(D-Phe(2-Cl))-OH;
(44) Glac-Arg-Val-Tyr-Cpg-His-Pro-(D-Phe(2-Me))-OH;
(45) Glac-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Me))-OH; or
10 (46) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Me))-OH.

18. The compound of claim 1, wherein the compound is:

- (4) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Cl))-OH;
(9) Sar-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Me))-OH;
15 (29) Glac-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Cl))-OH;
(31) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Cl))-OH;
(45) Glac-Arg-Val-Tyr-Val-His-Pro-(D-Phe(2-Me))-OH; or
(46) Glac-Arg-Val-Tyr-Chg-His-Pro-(D-Phe(2-Me))-OH.

- 20 19. A pharmaceutical composition, comprising the compound of any of claims 1-18 and a pharmaceutically acceptable carrier.

20. A method of treating hypertension, comprising administering to a patient in need thereof an effective amount of the pharmaceutical composition of claim 19.

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21. The method of claim 20, wherein the hypertension is induced by pregnancy.

22. A method of treating preeclampsia or a renal disease induced by pregnancy, comprising administering to a patient in need thereof an effective amount of the pharmaceutical composition of claim 19.

5 23. A pharmaceutical composition according to claim 19 for use in treating hypertension.

24. A pharmaceutical composition for use according to claim 23, wherein the hypertension is induced by pregnancy, preeclampsia or renal disease.

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25. A pharmaceutical composition according to claim 19 for use in treating preeclampsia or a renal disease induced by pregnancy.

26. Use of a compound according to any of claims 1-18 in the manufacture of a medicament for the treatment of hypertension.

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27. Use of a compound according to claim 26, wherein the hypertension is induced by pregnancy, preeclampsia or renal disease.

20 28. Use of a compound according to any of claims 1-18 in the manufacture of a medicament for the treatment of preeclampsia or a renal disease induced by pregnancy.