CLAIMS

1. Use of an effective amount of a relaxin analogue and a vasopressin analogue in the manufacture of a medicament for preventing or treating renal failure in an individual in need thereof.

2. The use of claim 1, wherein the renal failure is selected from the group consisting of: renal dysfunction induced by liver cirrhosis, renal dysfunction induced by liver transplantation, chronic kidney disease, and acute kidney injury.

3. The use of claim 1, wherein the relaxin analogue is an RXFP1 agonist, optionally a long-acting peptidyl RXFP1 agonist, and wherein the vasopressin analogue is a V1a receptor agonist, optionally wherein the vasopressin analogue is terlipressin or a pharmaceutically acceptable salt thereof.

4. Use of an effective amount of a relaxin analogue and a vasopressin analogue in the manufacture of a medicament for preventing or treating hepatorenal syndrome in an individual in need thereof.

5. The use of claim 4, wherein the hepatorenal syndrome is HRS-AKI (hepatorenal syndrome type 1).

6. The use of claim 4, wherein the relaxin analogue is a RXFP1 agonist, optionally wherein the relaxin analogue is a long acting peptidyl RXFP1 agonist, and wherein the vasopressin analogue is a V1a receptor agonist, optionally wherein the vasopressin analogue is terlipressin or a pharmaceutically acceptable salt thereof.

7. The use of claim 3 or claim 6, wherein said terlipressin is to be administered intravenously at a dosage of 0.5 to 2 mg per administration, optionally wherein said terlipressin is to be administered intravenously every 4 to 6 hours.

8. The use of any one of claims 1-7, wherein the relaxin analogue is to be administered at a dose of from about 0.01 mg/kg to about 0.5 mg/kg.

9. A pharmaceutical composition comprising separately or together a relaxin analogue, a vasopressin analogue, and one or more pharmaceutically acceptable excipients.

10. The composition of claim 9, wherein the vasopressin analogue is a V1a agonist, optionally wherein the vasopressin analogue is terlipressin, wherein the relaxin analogue is an RXFP1 peptidyl agonist.

11. The composition of any one of claims 9-10 or the use of any one of claims 1-8, wherein the relaxin analogue is a modified relaxin B chain peptide comprising formula (I) (SEQ ID NO: 105):

N_{ter}-Ac-X_{10}-E-G-R-E-X_{15}-V-R-X_{18}-X_{19}-I-X_{21}-X_{22}-E-G-X_{25}-S-X_{27}-X_{28}-X_{29}-X_{30}-X_{31}-X_{32}-X_{33}-NH_2-C_{ter},

wherein:

N_{ter} represents the N-terminal end of the peptide;

C_{ter} represents the C-terminal end of the peptide;

Ac represents acetyl group;

X_{10} represents an amino acid selected from the group consisting of leucine, 2-amino-isobutyric acid, Nε-acetyl-lysine and α-methyl-leucine;

E represents glutamic acid;

G represents glycine;

R represents arginine;

X_{15} represents an amino acid selected form the group consisting of lysine, arginine, homolysine, homoarginine, ornithine, glutamine, phenylalanine and leucine;

V represents valine;

X_{18} represents an amino acid selected from the group consisting of alanine, 2-amino-isobutyric acid, leucine, Nε-acetyl-lysine and glutamine;

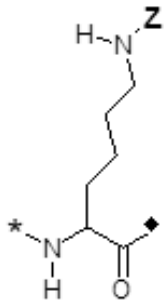
X_{19} represents an amino acid selected from the group consisting of lysine, Nε-acetyl-lysine, citrulline, glutamine, alanine and 2-amino-isobutyric acid;

I represents isoleucine;

X_{21} represents an amino acid selected from the group consisting of 2-amino-isobutyric acid and alanine;

X_{22} represents an amino acid selected from the group consisting of 2-amino-isobutyric acid and isoleucine;

X_{25} represents the following structure:



in which:

* represents a covalent bond with the glycine preceding X_{25} in formula (I);

◆ represents a covalent bond with the serine following X_{25} in formula (I); and

Z represents a group of formula (II):

$$–[(PEG_{xx})_b(gE)_cC_d],$$

b and c independently represent 1, 2, 3, 4 or 5;

PEG_{xx} independently represents a polyethylene glycol derivative selected from the group consisting of PEG_2, PEG_2DGA, and TTDS;

gE represents γ-glutamic acid; and

C_d represents a linear saturated C_{12}-C_{22} acyl group;

S represents serine;

X_{27} represents an amino acid selected from the group consisting of threonine, lysine, arginine and glutamine;

X_{28} represents an amino acid selected from the group consisting of tryptophan, phenylalanine, 5-fluoro-tryptophan, 5-chloro-tryptophan, 5-methoxy-

tryptophan, tyrosine, 4-fluoro-phenylalanine, 1-naphtylalanine, 2-naphtylalanine, α-methyl-tryptophan, α-methyl-phenylalanine and 5-hydroxy-tryptophan;

X_{29} represents an amino acid selected from the group consisting of serine, D-serine,
2-amino-isobutyric acid, threonine, α-methyl-serine, Nε-acetyl-lysine and valine;

X_{30} represents an amino acid selected from the group consisting of 2-amino-isobutyric acid, α-methyl-lysine, D-lysine, lysine, homolysine, ornithine, arginine and α-methyl-arginine;

X_{31} represents an amino acid selected from the group consisting of arginine, Nω–methyl-arginine, alanine, Nω,Nω'-dimethyl-arginine and citrulline;

X_{32} represents an amino acid selected from the group consisting of lysine, alanine, arginine, Nε-acetyl-lysine and Nε,Nε,Nε-tri-methyl-lysine; and

X_{33} represents an amino acid selected from lysine, Nε-acetyl-lysine, leucine, arginine and alanine;

or a salt or solvate thereof.

12. The composition of any one of claims 9-10 or the use of any one of claims 1-8, wherein the relaxin analogue comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 1 to 97, optionally wherein the relaxin analogue comprises the amino acid sequence of SEQ ID NO: 3.

13. The use of any one of claims 1-6, wherein the relaxin analogue is to be co-administered at a dose from about 1.0 mg to about 10.0 mg, optionally from about 1.0 mg to about 3.0 mg, with the vasopressin analogue.

14. The use of claim 13, wherein the relaxin analogue is to be administered intravenously over from about 1 hour to about 10 hours, optionally from about 3 hours to about 6 hours.

15. The use of claim 13, wherein the relaxin analogue is to be further administered at an additional dose between 5 hours and 18 hours after administration, optionally between

10 hours and 13 hours after administration of the about 1.0 mg to about 10.0 mg of the relaxin analogue.

16. The use of claim 15, wherein the additional dose of the relaxin analogue is to be administered subcutaneously to the individual, wherein the additional dose comprises from about 1 mg to about 50 mg of the relaxin analogue, optionally from about 5 mg to about 15 mg of the relaxin analogue.

17. The use of claim 15, wherein the relaxin analogue is to be further administered at a yet additional dose administered between 18 hours and 30 hours after administration, optionally between 20 hours and 26 hours after administration, of the about 1.0 mg to about 10.0 mg of the relaxin analogue.

18. The use of claim 17, wherein the yet additional dose of the relaxin analogue is to be administered subcutaneously to the individual, wherein the yet additional dose of the relaxin analogue comprises from about 1 mg to about 50 mg of the relaxin analogue.

19. The use of any one of claims 13-18, wherein the vasopressin analogue is terlipressin or a pharmaceutically acceptable salt thereof, wherein the terlipressin is to be administered intravenously at a dosage from about 0.5 to about 10 mg, optionally at a dosage of about 1 mg, 4 mg, 6 mg, 8 mg every 6 hours.

20. Use of an effective amount of a relaxin analogue in the manufacture of a medicament for treating renal failure or hepatorenal syndrome in an individual in need thereof, wherein the individual previously has been administered a vasopressin analogue.