CLAIMS

1. A C-type natriuretic (CNP) compound comprising a CNP peptide and a modifying group;

wherein the net charge of the compound at physiological pH is 0 or negative;

wherein the amino acid sequence of the CNP peptide is:

AA_{01}- AA_{02}-AA_{03}-AA_{04}-AA_{05}-AA_{06}-AA_{07}-AA_{08}-AA_{09}-AA_{10}-AA_{11}-AA_{12}-AA_{13}-AA_{14}-AA_{15}-AA_{16}-AA_{17}-AA_{18}-AA_{19}-AA_{20}-AA_{21}-AA_{22}-AA_{23}-AA_{24}-AA_{25}-AA_{26}-AA_{27}-AA_{28}-AA_{29}-AA_{30}-AA_{31}-AA_{32}-AA_{33}-AA_{34}-AA_{35}-AA_{36}-AA_{37};

wherein:

AA_{01} is Gln or absent,

AA_{02} is Glu or absent,

AA_{03} is His or absent,

AA_{04} is Pro or absent,

AA_{05} is Asn or Gln or Glu or absent,

AA_{06} is Ala or absent,

AA_{07} is Arg or His or Ala or absent,

AA_{08} is Lys or Ser or His or absent,

AA_{09} is Tyr or Glu or absent,

AA_{10} is Lys or Glu or Gln or His or absent,

AA_{11} is Gly,

AA_{12} is Ala,

AA_{13} is Gln,

AA_{14} is Lys or His or Glu,

AA_{15} is Lys or Ser or Glu or Thr or His,

AA_{16} is Gly,

AA_{17} is Leu or Gly or Ser or Val,

AA_{18} is Ser or His,

AA_{19} is Gln or Ser,

AA_{20} is Gly,

AA_{21} is Cys,

AA_{22} is Phe,

AA_{23} is Gly,

AA_{24} is Leu,

AA_{25} is Pro,

AA_{26} is Leu,

AA_{27} is Asp or Glu,

AA_{28} is Arg,

AA_{29} is Ile,

AA_{30} is Gly,

AA_{31} is Ser,

AA_{32} is Leu,

AA_{33} is Ser,

AA_{34} is Gly,

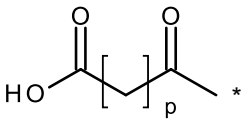
AA_{35} is Leu,

AA_{36} is Gly, and

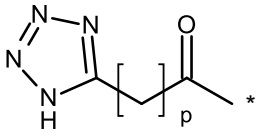
AA_{37} is Cys;

wherein the modifying group comprises Chem. A, Chem. B and Chem. C;

wherein Chem. A is:



(Chem. A1), or

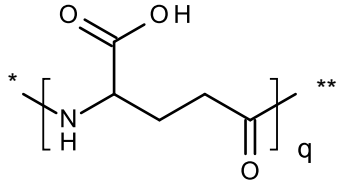


(Chem. A2)

wherein p is an integer in the range of 14-20, and

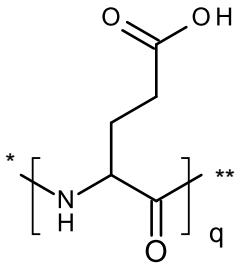
where * denotes an amide bond connecting Chem. A and Chem. B; and

wherein Chem. B is:



(Chem. B1)

or



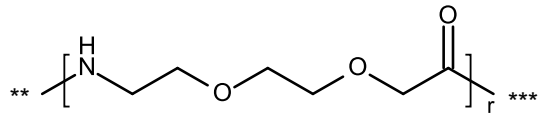
(Chem. B2)

wherein q is an integer in the range of 1-8,

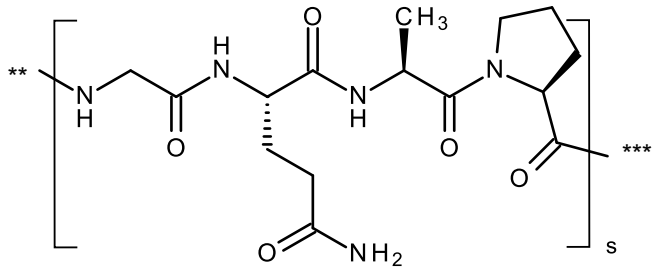
wherein * denotes an amide bond connecting Chem. A- and Chem. B-,

wherein ** denotes an amide bond connecting Chem. B- and Chem. C-; and

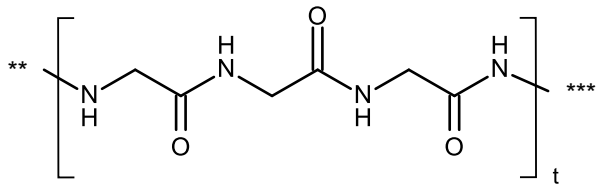
wherein Chem. C is



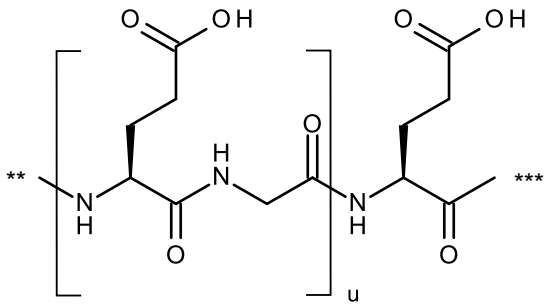
(Chem. C1),



(Chem. C2),



(Chem. C3), or



(Chem C4),

wherein r is an integer in the range of 0-4,
wherein s is an integer in the range of 0-3,
wherein t is an integer in the range of 0-1,
wherein u is an integer in the range of 0-3,
wherein ** denotes an amide bond connecting Chem. B- and Chem. C-, and
wherein *** denotes an amide bond connecting Chem. C- and the N-terminal alpha-amine on the CNP peptide.

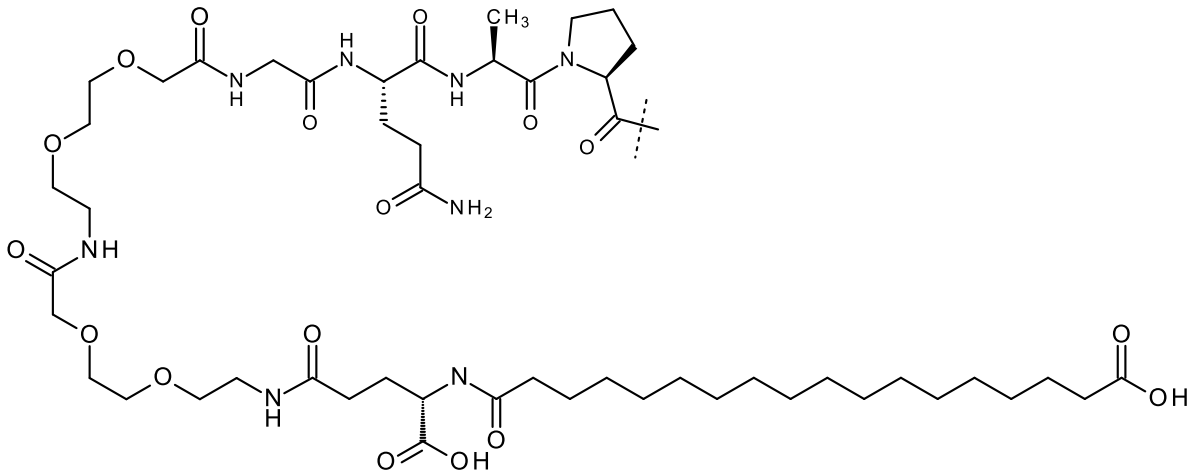
2. The CNP compound according to claim 1, wherein AA_5 of the CNP peptide is Gln.

3. The CNP compound according to claim 1, wherein the amino acid sequence of the CNP peptide is selected from the group consisting of:
GAQKKGSSQGCFGLPLDRIGSLSGLGC (SEQ ID NO: 136),
ARKYKGAQKKGLSQGCFGLPLDRIGSLSGLGC (SEQ ID NO: 77),
YKGAQKKGGSQGCFGLPLDRIGSLSGLGC (SEQ ID NO: 88),
YKGAQKKGLSQGCFGLPLDRIGSLSGLGC (SEQ ID NO: 103),
QEHPQARKYKGAQKKGLSSGCFGLPLDRIGSLSGLGC (SEQ ID NO: 67), and
QEHPQARKYKGAQKKGLSSGCFGLPLERIGSLSGLGC (SEQ ID NO: 104).

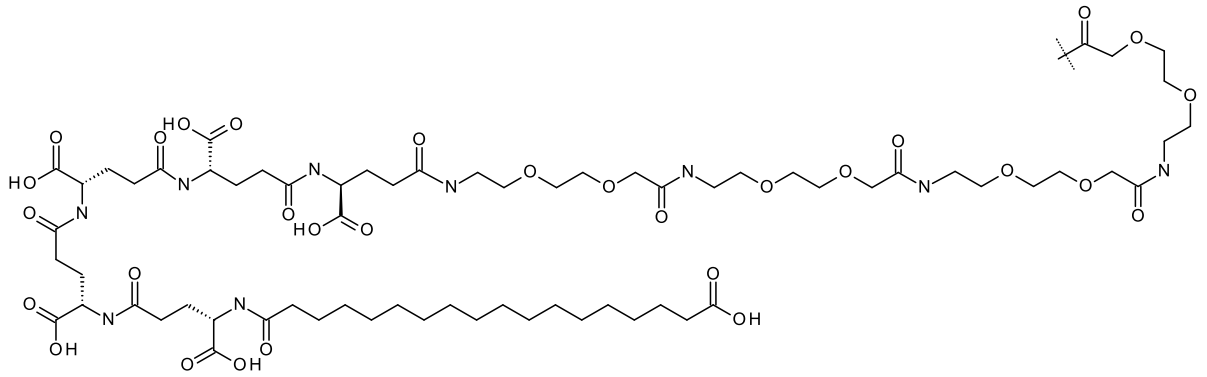
4. The CNP compound according to claim 3, wherein the amino acid sequence of the CNP peptide is QEHPQARKYKGAQKKGLSSGCFGLPLDRIGSLSGLGC (SEQ ID NO: 67).

5. The CNP compound according to claim 1, wherein q is in the range of 1-5.

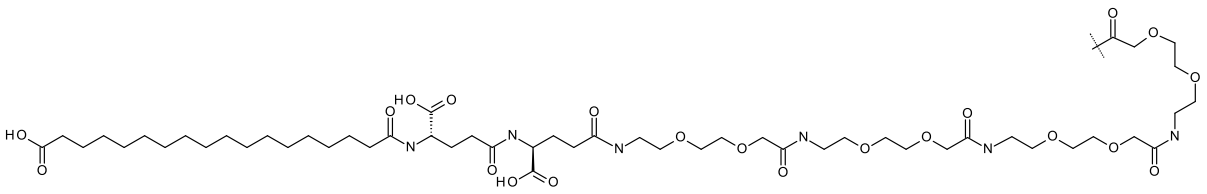
6. The CNP compound according to claim 1, wherein the modifying group is selected from the group consisting of:



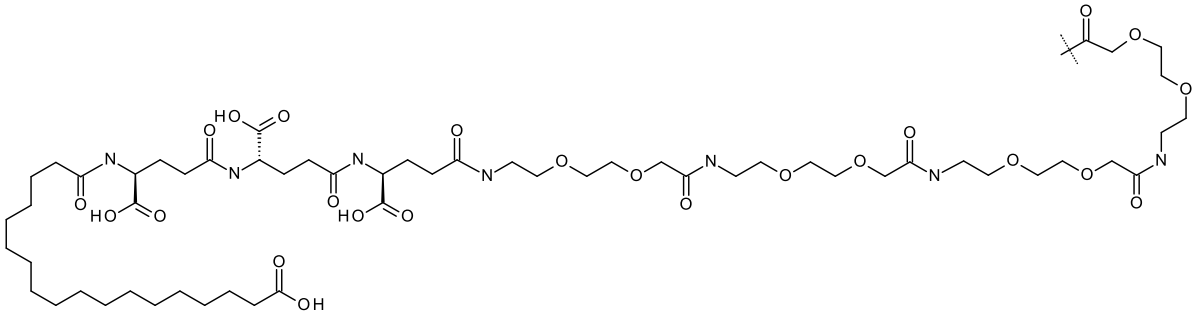
(Chem. E),



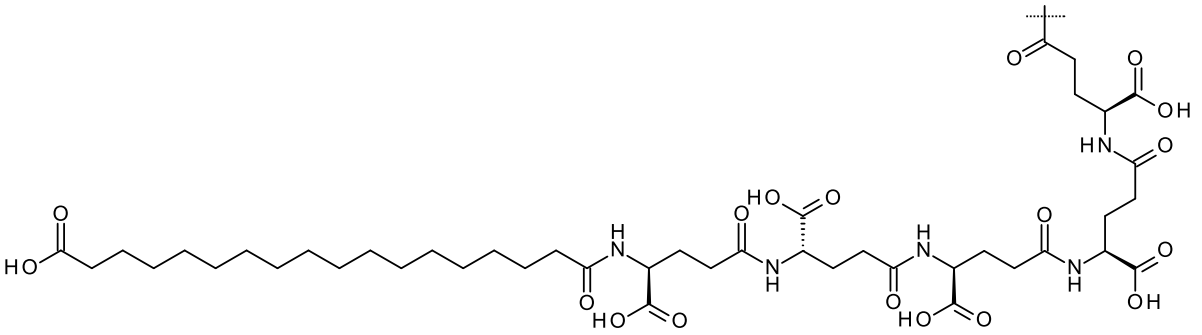
(Chem. F),



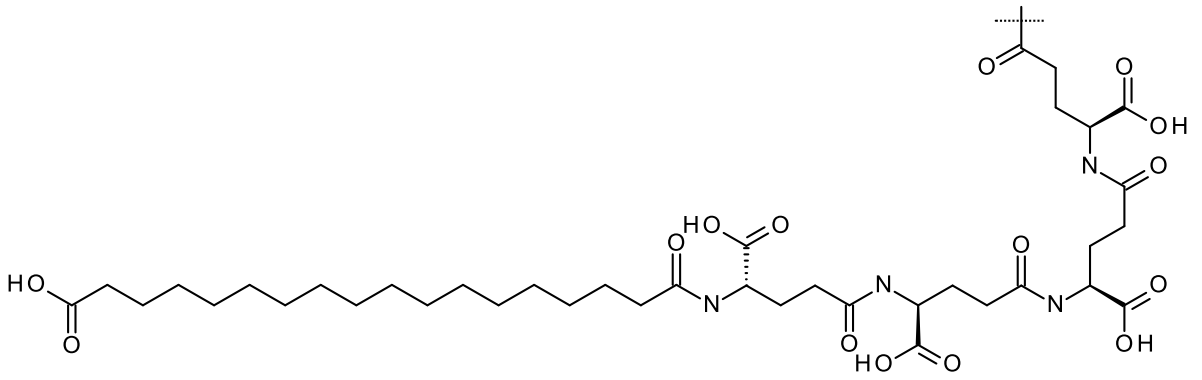
(Chem. G),



(Chem. H),



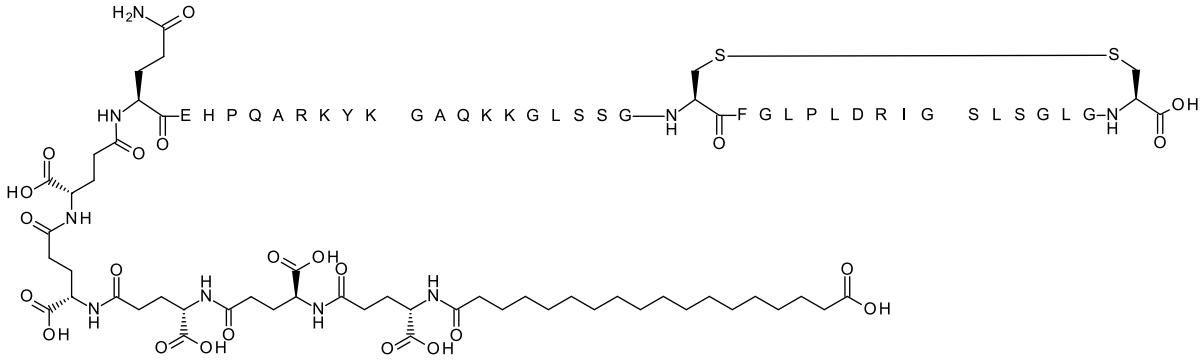
(Chem. I), and



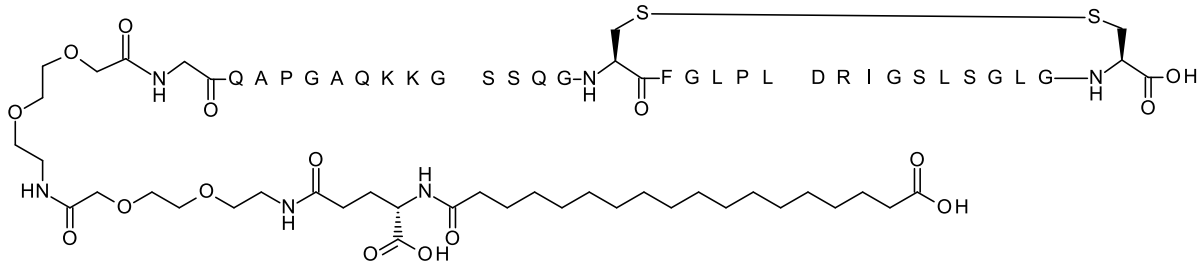
(Chem. J),

wherein the dotted line denotes the attachment of the modifying group to the N-terminal alpha-amine of the CNP peptide via an amide bond.

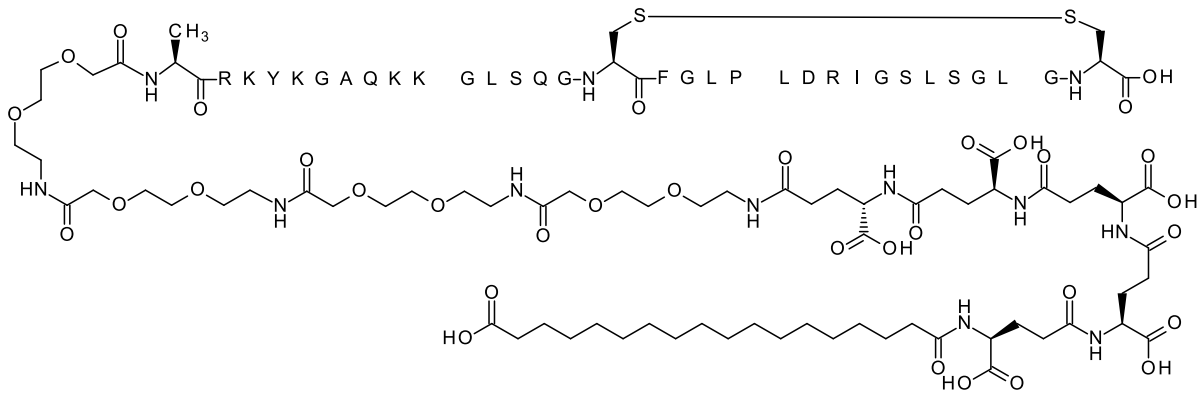
7. The CNP compound according claim 1, wherein the CNP compound is selected from the group consisting of:



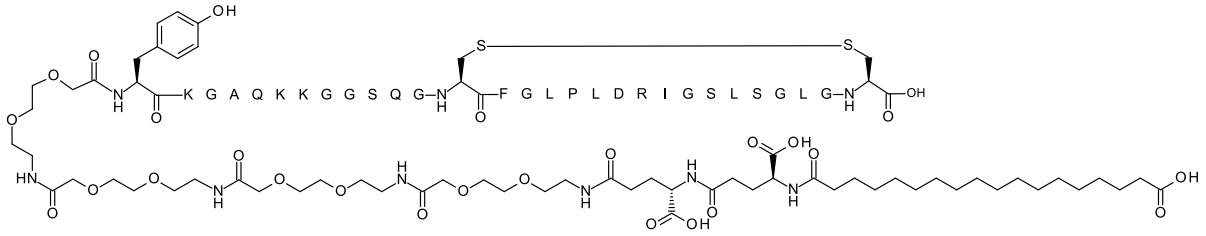
(Formula II),



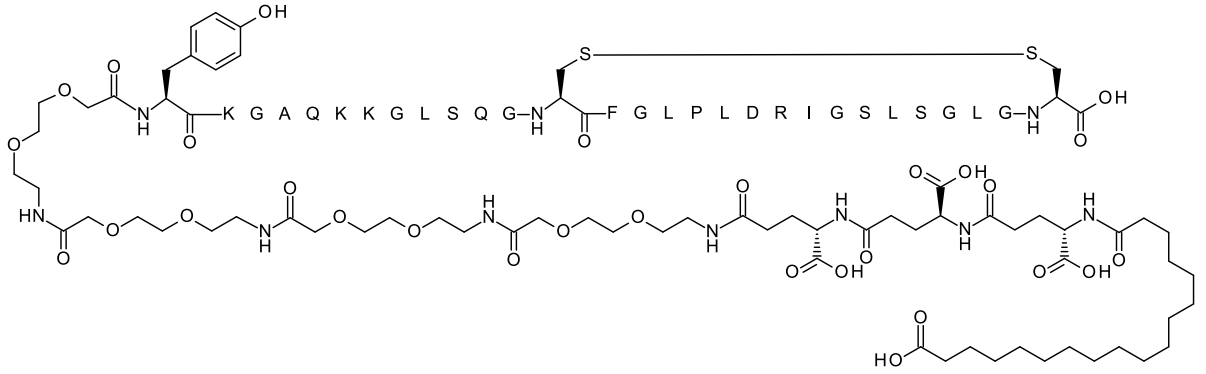
(Formula III),



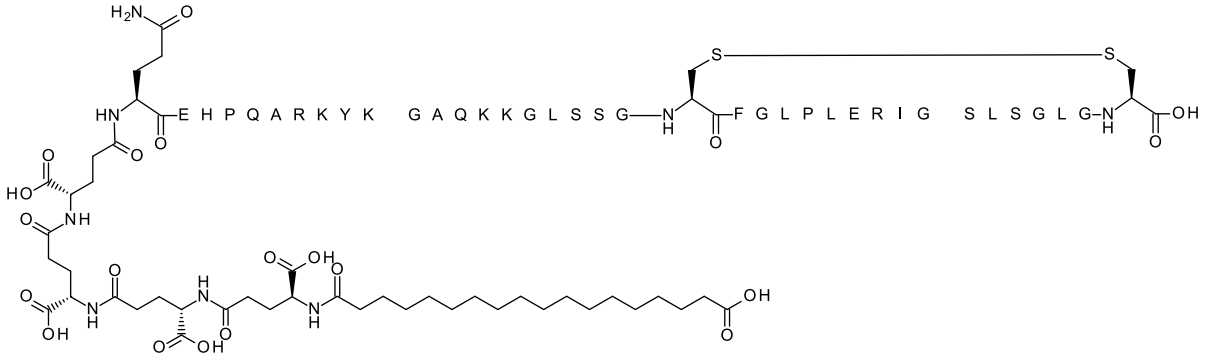
(Formula IV),



(Formula V),

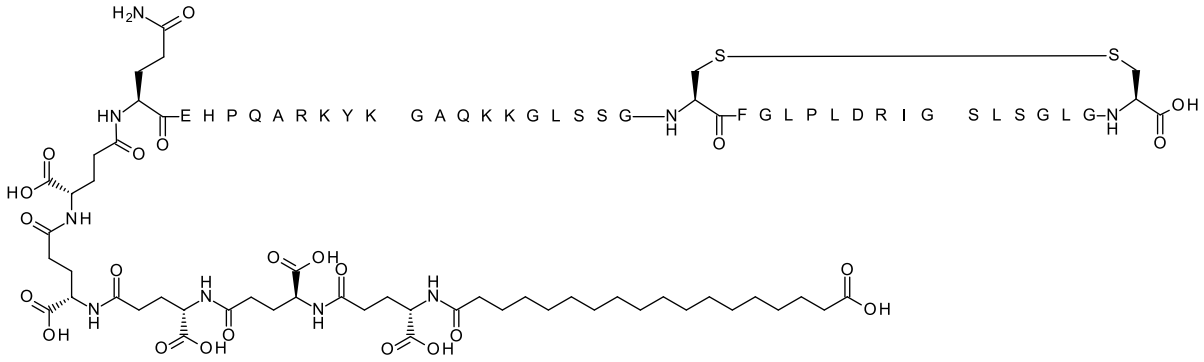


(Formula VI), and



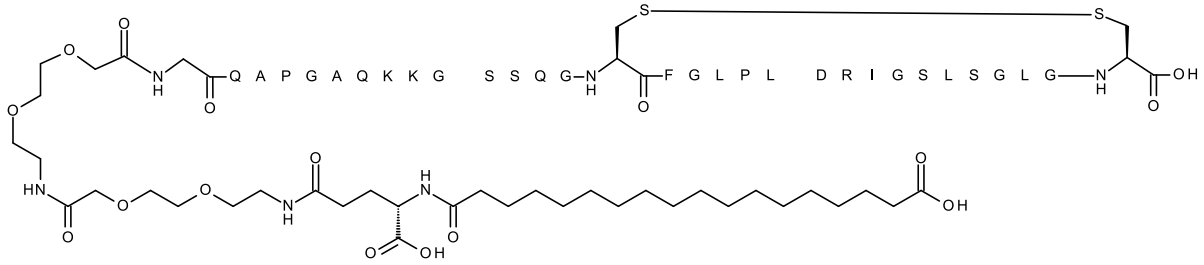
(Formula VII).

8. A CNP peptide that is



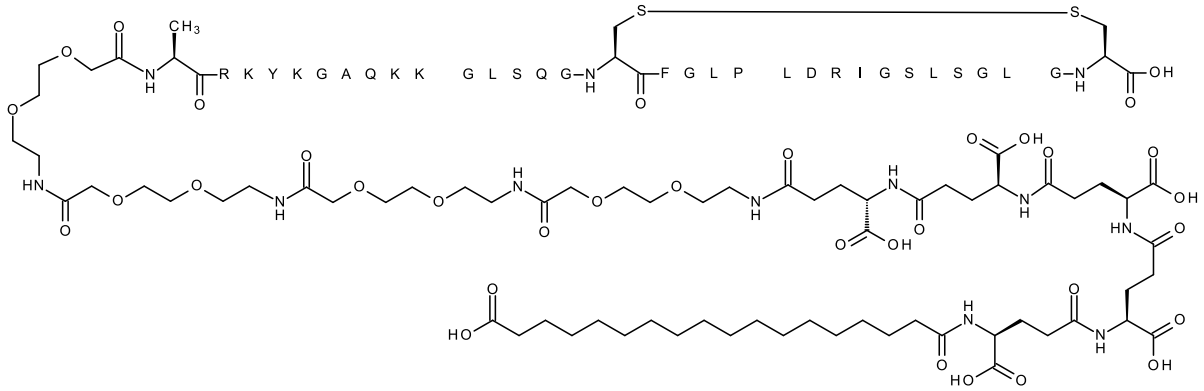
(Formula II).

9. The CNP compound according to claim 7, wherein the CNP compound is



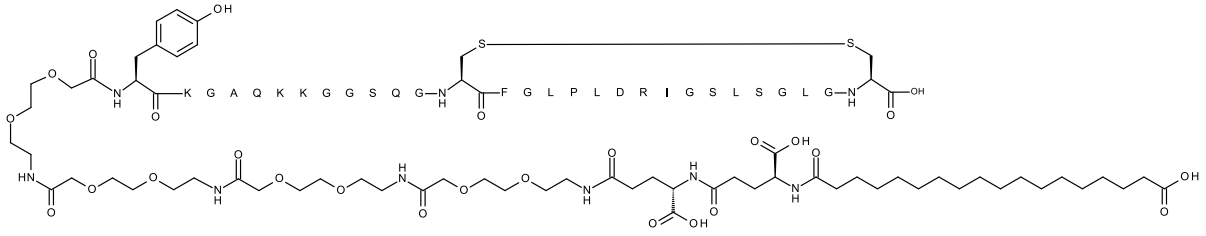
(Formula III).

10. The CNP compound according to claim 7, wherein the CNP compound is



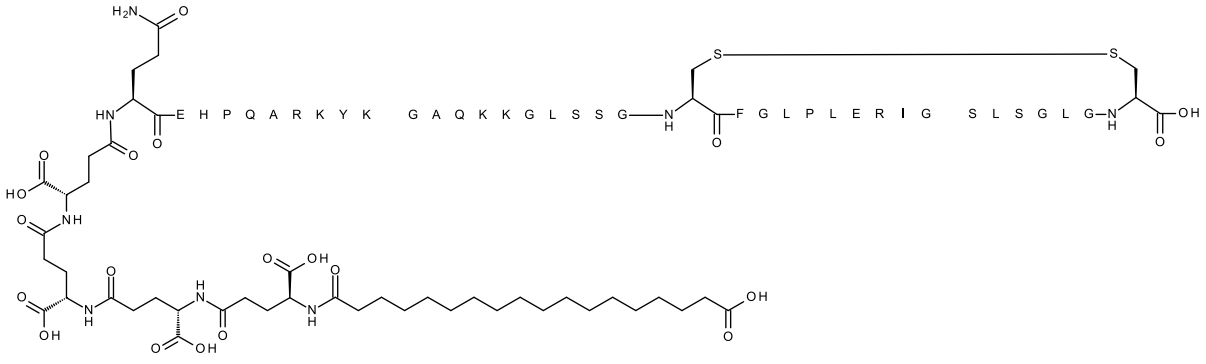
(Formula IV).

11. The CNP compound according to claim 7, wherein the CNP compound is



(Formula V).

13. The CNP compound according to claim 7, wherein the CNP compound is



(Formula VII).

14. A pharmaceutical composition comprising a CNP compound according to any one of claims 1-13, and one or more pharmaceutically acceptable excipients.

15. The CNP compound according to any one of claims 1-13, or a pharmaceutical composition according to claim 14, for use in the treatment or prevention of cardio-renal-metabolic diseases including heart failure, and growth disorders including achondroplasia.

16. Use of an effective amount of a CNP compound according to any one of claims 1-13, optionally in combination with one or more additional therapeutically active compounds in the manufacture of a medicament for the treatment or prevention of heart failure in a patient in need thereof.