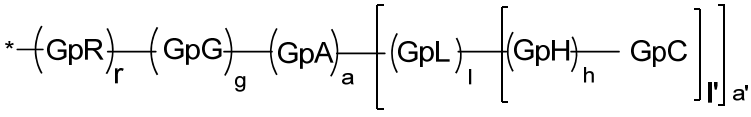
CLAIMS

1. A composition in the form of an injectable aqueous solution, for which the pH is comprised from 6.0 to 8.0, comprising at least:

a) amylin or pramlintide;

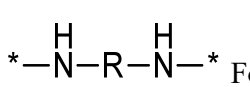
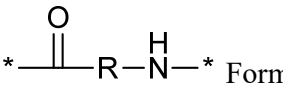
b) a co-polyamino acid bearing carboxylate charges and hydrophobic radicals Hy, the co-polyamino acid being constituted of glutamic or aspartic units and the hydrophobic radicals Hy chosen among the radicals according to formula X as defined below:

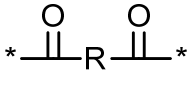


Formula X

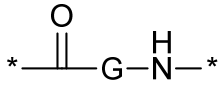
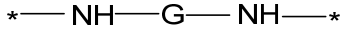
in which

GpR is chosen among the radicals according to formulas VII, VII' or VII":

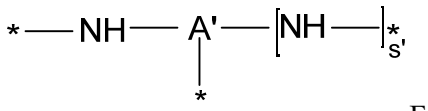

Formula VII or

Formula VII' or


Formula VII'';

– Identical or different GpG and GpH are chosen among the radicals according to formulas XI or XI';

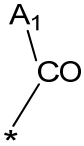

Formula XI

Formula XI'

– GpA is chosen among the radicals according to formula VIII

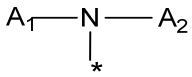


Formula VIII

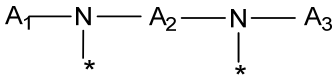
in which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''



Formula VIII'

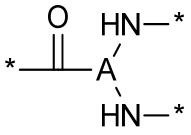


Formula VIII''



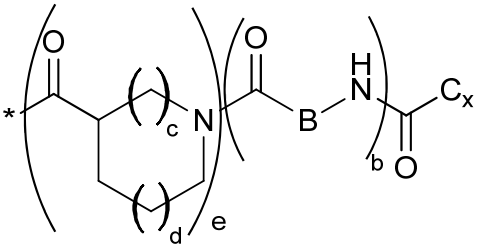
Formula VIII'''

– -GpL is chosen among the radicals according to formulas XII



Formula XII

– GpC is a radical according to formula IX:



Formula IX;

– * indicate the attachment sites of the different groups bound by amide functions;

– a is an integer equal to 0 or to 1 and a' = 1 if a = 0 and a' = 1, 2 or 3 if a =1;

- a' is an integer equal to 1, to 2 or to 3;

- b is an integer equal to 0 or to 1;
- c is an integer equal to 0 or to 1, and if c is equal to 0, then d is equal to 1 or to 2;
- d is an integer equal to 0, to 1 or to 2;
- e is an integer equal to 0 or to 1;
- g is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6;
- h is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6, and at least one of g, h or l is different from 0;
- l is an integer equal to 0 or to 1 and l' = 1 if l = 0 and l' = 2 if l =1;
- r is an integer equal to 0, 1 or to 2, and
- s' is an integer equal to 0 or to 1;
- and if e is different from 0, then at least one of g, h or l is different from 0;
- and if a = 0, then l = 0;
- A, A_1, A_2 and A_3 identical or different, are linear or branched alkyl radicals comprising from 1 to 8 carbon atoms and/or substituted by a radical from a saturated, unsaturated or aromatic ring;

- B is a radical ether or polyether, unsubstituted, comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms, or a linear or branched alkyl radical and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms;

- C_x is a monovalent, linear or branched, alkyl radical and/or comprising a cyclic part, in which x indicates the number of carbon atoms; and:

  - when the hydrophobic radical -Hy bears 1 -GpC, then $9 \leq x \leq 25$,
  - when the hydrophobic radical -Hy bears 2 -GpC, then $9 \leq x \leq 15$,
  - when the hydrophobic radical -Hy bears 3 -GpC, then $7 \leq x \leq 13$,
  - when the hydrophobic radical -Hy bears 4 -GpC, then $7 \leq x \leq 11$,

- when the hydrophobic radical -Hy bears at least 5 -GpC, then $6 \leq x \leq 11$,

– G is a linear or branched divalent alkyl radical of 1 to 8 carbon atoms, the alkyl radical bearing one or more free carboxylic acid functions;

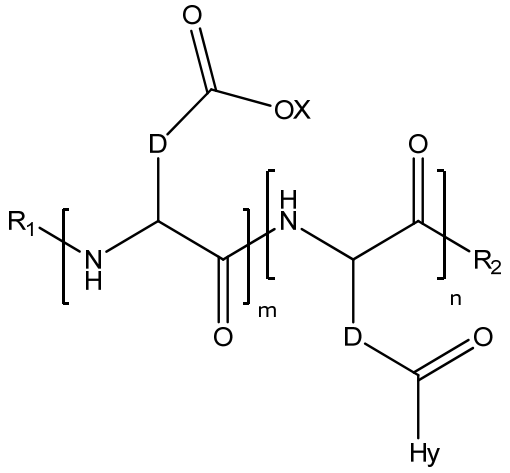
– R is a radical chosen from the group consisting of a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms, a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms bearing one or more $-CONH_2$ functions or an unsubstituted ether or polyether radical comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms;

– the hydrophobic radical(s) -Hy according to formula X being bound to the PLG:

  - via a covalent bond between a carbonyl of the hydrophobic radical -Hy and a nitrogen atom borne by the PLG, thus forming an amide function resulting from the reaction of an amine function borne by the PLG and an acid function borne by the precursor -Hy' of the hydrophobic radical -Hy, and
  - via a covalent bond between a nitrogen atom of the hydrophobic radical -Hy and a carbonyl borne by the PLG, thus forming an amide function resulting from the reaction of an amine function of the precursor -Hy' of the hydrophobic radical -Hy and an acid function borne by the PLG,

- the ratio M between the number of hydrophobic radicals and the number of glutamic or aspartic units being between $0 < M \leq 0.5$;
- when several hydrophobic radicals are borne by a co-polyamino acid, then they are identical or different,
- the degree of polymerization DP in glutamic or aspartic units for the PLG chains is comprised from 5 to 250;
- free carboxylic acids being in the form of an alkaline cation salt chosen from the group consisting of Na^+ and K^+.

2. The composition according to claim 1, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXX below:



Formula XXX

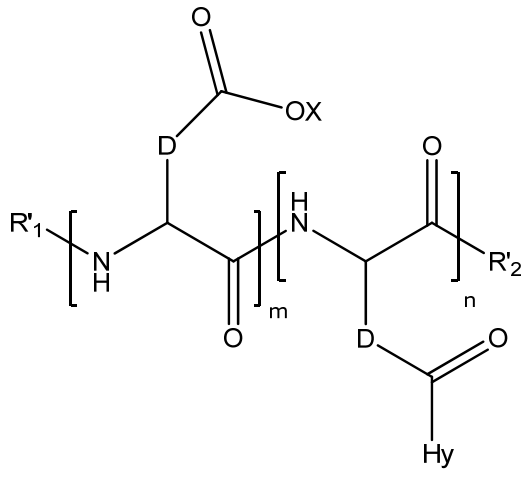
in which,

- D represents, independently, either a -CH_2- group (aspartic unit) or a -CH_2-CH_2- group (glutamic unit);
- Hy is a hydrophobic radical chosen among the hydrophobic radicals according to formulas X;
- R_1 is a hydrophobic radical chosen among the hydrophobic radicals according to formula X in which r=0 or r=1 and GpR is a radical according to formula VII' or VII'', or a radical chosen from the group consisting of a H, a linear acyl group in C2 to C10, a branched acyl group in C3 to C10, a benzyl, a terminal "amino acid" unit and a pyroglutamate;
- R_2 is a hydrophobic radical chosen among the hydrophobic radicals according to formula X or an -NR'R'' radical, R' and R'', identical or

different, being chosen from the group consisting of H, the linear, branched or cyclic alkyls in C2 to C10, benzyl and the R' and R" alkyls may together form one or more saturated, unsaturated and/or aromatic rings and/or may comprise heteroatoms, chosen from the group consisting of O, N and S;

- X represents a H or a cationic entity chosen from the group comprising the metallic cations;
- n + m represents The degree of polymerization DP of the co-polyamino acid, that is the average number of monomeric units per co-polyamino acid chain and $5 \leq n + m \leq 250$.

3. The composition according to claim 2, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXX, in which $R_1 = R'_1$ and $R_2 = R'_2$, according to formula XXXa below:



Formula XXXa

in which,

– n+m represents The degree of polymerization DP of the co-polyamino acid, that is the average number of monomeric units per co-polyamino acid chain and $5 \leq n + m \leq 250$;

– X represents a H or a cationic entity chosen from the group comprising the metallic cations;

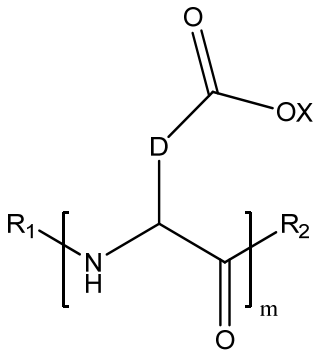
– D represents, independently, either a $-CH_2-$ group (aspartic unit) or a $-CH_2-CH_2-$ group (glutamic unit);

– Hy is a hydrophobic radical chosen among the hydrophobic radicals according to formulas X;

– R'_1 is a radical chosen from the group consisting of a H, a linear acyl group in C2 to C10, a branched acyl group in C3 to C10, a benzyl, a terminal “amino acid” unit and a pyroglutamate,

– R'_2 is a -NR’R’’ radical, R’ and R’’, identical or different, being chosen in the group consisting of H, the linear, branched or cyclic alkyls in C2 to C10, benzyl and said R’ and R” alkyls may together form one or more saturated, unsaturated and/or aromatic rings and/or may comprise heteroatoms, chosen from the group consisting of O, N and S.

4. The composition according to claim 2, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formulas XXX, in which n = 0, according to formula XXXb below:



Formula XXXb

in which

– m represents The degree of polymerization DP of the co-polyamino acid, that is the average number of monomeric units per co-polyamino acid chain and $5 \leq m \leq 250$;

– X represents a H or a cationic entity chosen from the group comprising the metallic cations;

– D represents, independently, either a $-CH_2-$ group (aspartic unit) or a $-CH_2-CH_2-$ group (glutamic unit);

– R_1 is a hydrophobic radical chosen from the hydrophobic radicals according to formula X in which r=0 or r=1 and GpR is a radical according to formula VII' or VII'', or a radical chosen from the group consisting of a H, a linear acyl group in C2 to C10, a branched acyl group in C3 to C10, a benzyl, a terminal "amino acid" unit and a pyroglutamate;

– R_2 is a hydrophobic radical chosen among the hydrophobic radicals according to formula X or an -NR'R'' radical, R' and R'', identical or different, being chosen from the group consisting of H, the linear, branched or cyclic alkyls in C2 to C10, benzyl and the R' and R" alkyls may together form one or more saturated, unsaturated and/or aromatic rings and/or may comprise heteroatoms, chosen from the group consisting of O, N and S; and

– at least R_1 or R_2 is a hydrophobic radical according to formula X.

5. The composition according to claim 1, wherein the co-polyamino acid/amylin or pramlintide molar ratio is greater than or equal to 1.

6. The composition according to claim 1, wherein the amyline or pramlintide is amylin.

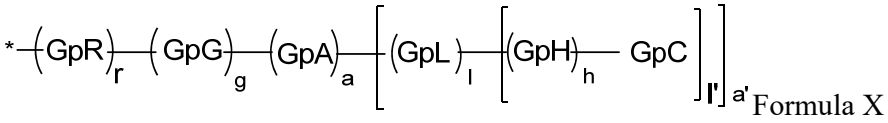
7. The composition according to claim 1, wherein the amylin or pramlintide is pramlintide.

8. The composition according to claim 1, further comprising a prandial insulin.

9. The composition according to claim 1, wherein the co-polyamino acid/insulin ratio is greater than or equal to 1.

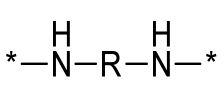
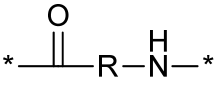
10. The composition according to claim 1, wherein the composition has a stability measured by Thioflavin T (ThT) greater than that of a reference composition comprising amylin or pramlintide but not comprising a co-polyamino acid bearing carboxylate charges and Hy hydrophobic radicals.

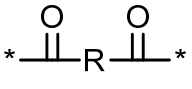
11. A co-polyamino acid bearing carboxylate charges and hydrophobic radicals Hy, the co-polyamino acid being constituted of glutamic or aspartic units and the hydrophobic radicals Hy chosen among the radicals according to formula X as defined below:


Formula X

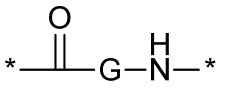
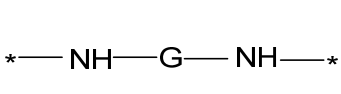
in which

GpR is chosen among the radicals according to formulas VII, VII' or VII'':

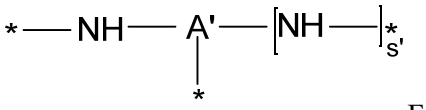

Formula VII or 
Formula VII' or


Formula VII'';

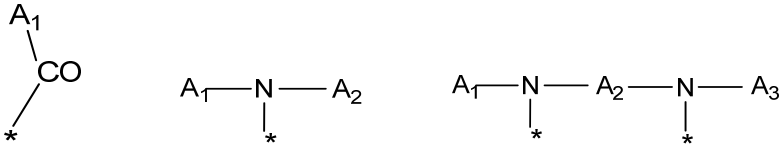
- Identical or different GpG and GpH are chosen among the radicals according to formulas XI or XI';


Formula XI 
Formula XI'

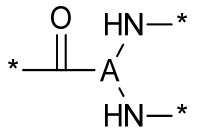
- GpA is chosen among the radicals according to formula VIII


Formula VIII

in which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''

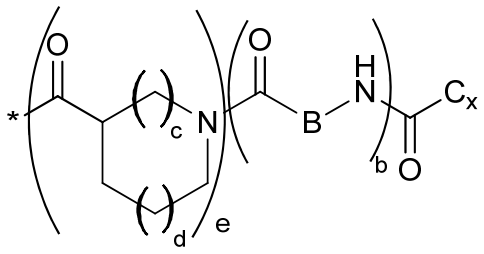

Formula VIII' or Formula VIII'' or Formula VIII'''

– -GpL is chosen among the radicals according to formulas XII



Formula XII,

– GpC is a radical according to formula IX:



Formula IX;

– * indicate the attachment sites of the different groups bound by amide functions;

– a is an integer equal to 0 or to 1 and a' = 1 if a = 0 and a' = 1, 2 or 3 if a =1;

- a' is an integer equal to 1, to 2 or to 3;

- b is an integer equal to 0 or to 1;

- c is an integer equal to 0 or to 1, and if c is equal to 0, then d is equal to 1 or to 2;

– d is an integer equal to 0, to 1 or to 2;

– e is an integer equal to 0 or to 1;

– g is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6;

- h is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6, and at least one of g, h or l is different from 0;

- l is an integer equal to 0 or to 1 and l' = 1 if l = 0 and l' = 2 if l =1;

- r is an integer equal to 0, 1 or to 2, and

- s' is an integer equal to 0 or to 1;

- and if e is different from 0, then at least one of g, h or l is different from 0;
- and if a = 0, then l = 0;
- A, A_1, A_2 and A_3 identical or different, are linear or branched alkyl radicals comprising from 1 to 8 carbon atoms and/or substituted by a radical from a saturated, unsaturated or aromatic ring;

– B is a radical ether or polyether, unsubstituted, comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms, or a linear or branched alkyl radical and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms,

– C_x is a monovalent, linear or branched, alkyl radical and/or comprising a cyclic part, in which x indicates the number of carbon atoms, and:

  - When the hydrophobic radical -Hy bears 1 -GpC, then $9 \leq x \leq 25$,
  - When the hydrophobic radical -Hy bears 2 -GpC, then $9 \leq x \leq 15$,
  - When the hydrophobic radical -Hy bears 3 -GpC, then $7 \leq x \leq 13$,
  - When the hydrophobic radical -Hy bears 4 -GpC, then $7 \leq x \leq 11$,
  - When the hydrophobic radical -Hy bears at least 5 -GpC, then $6 \leq x \leq 11$,

– G is a linear or branched divalent alkyl radical of 1 to 8 carbon atoms, the alkyl radical bearing one or more free carboxylic acid functions;

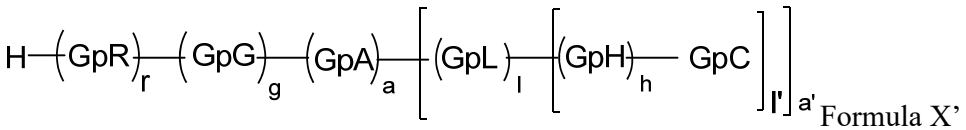
– R is a radical chosen from the group consisting of a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms, a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms bearing one or more -$CONH_2$ functions or an unsubstituted ether or polyether radical comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms;

– the hydrophobic radicals -Hy according to formula X being bound to the PLG:

- via a covalent bond between a carbonyl of the hydrophobic radical -Hy and a nitrogen atom borne by the PLG, thus forming an amide function resulting from the reaction of an amine function borne by the PLG and an acid function borne by the precursor -Hy' of the hydrophobic radical -Hy, and
- via a covalent bond between a nitrogen atom of the hydrophobic radical -Hy and a carbonyl borne by the PLG, thus forming an amide function resulting from the reaction of an amine function of the precursor -Hy' of the hydrophobic radical -Hy and an acid function borne by the PLG,

- the ratio M between the number of hydrophobic radicals and the number of glutamic or aspartic units being between $0 < M \leq 0.5$;
- when several hydrophobic radicals are borne by a co-polyamino acid, then they are identical or different,
- the degree of polymerization DP in glutamic or aspartic units for the PLG chains is comprised from 5 to 250; and
- free carboxylic acids being in the form of an alkaline cation salt chosen from the group consisting of Na^+ and K^+.

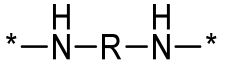
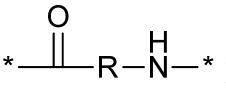
12. A hydrophobic radical precursor Hy' of the hydrophobic radical -Hy according to formula X' as defined below:

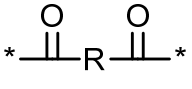


Formula X'

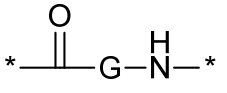
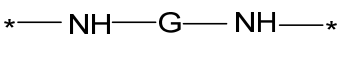
in which

GpR is chosen among the radicals according to formulas VII, VII' or VII":

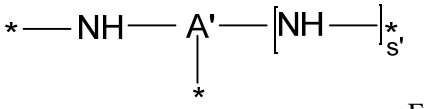
 Formula VII or  Formula VII' or

 Formula VII'';

– identical or different GpG and GpH are chosen among the radicals according to formulas XI or XI';

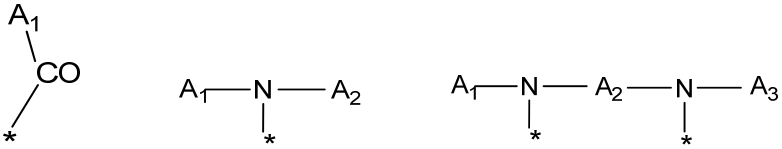
 Formula XI  Formula XI'

– GpA is chosen among the radicals according to formula VIII



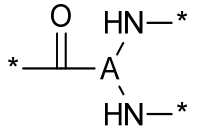
Formula VIII

in which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''



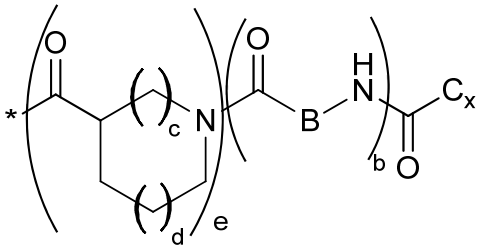
Formula VIII' or Formula VIII'' or Formula VIII'''

-GpL is chosen among the radicals according to formulas XII



Formula XII,

– GpC is a radical according to formula IX:



Formula IX;

* indicate the attachment sites of the different groups bound by amide functions;

a is an integer equal to 0 or to 1 and a' = 1 if a = 0 and a' = 1, 2 or 3 if a =1;

- a' is an integer equal to 1, to 2 or to 3;
- b is an integer equal to 0 or to 1;
- c is an integer equal to 0 or to 1, and if c is equal to 0, then d is equal to 1 or to 2;

d is an integer equal to 0, to 1 or to 2;

e is an integer equal to 0 or to 1;

g is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6;

- h is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6, and at least one of g, h or l is different from 0;
- l is an integer equal to 0 or to 1 and l' = 1 if l = 0 and l' = 2 if l =1;
- r is an integer equal to 0, 1 or to 2, and
- s' is an integer equal to 0 or to 1;
- and if e is different from 0, then at least one of g, h or l is different from 0;
- and if a = 0, then l = 0;

- A, A_1, A_2 and A_3 identical or different, are linear or branched alkyl radicals comprising from 1 to 8 carbon atoms and/or substituted by a radical from a saturated, unsaturated or aromatic ring;
- B is a radical ether or polyether, unsubstituted, comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms, or a linear or branched alkyl radical and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms;
- C_x is a monovalent, linear or branched, alkyl radical and/or comprising a cyclic part, in which x indicates the number of carbon atoms, and:
    - When the hydrophobic radical -Hy bears 1 -GpC, then $9 \leq x \leq 25$,
    - When the hydrophobic radical -Hy bears 2 -GpC, then $9 \leq x \leq 15$,
    - When the hydrophobic radical -Hy bears 3 -GpC, then $7 \leq x \leq 13$,
    - When the hydrophobic radical -Hy bears 4 -GpC, then $7 \leq x \leq 11$,
    - When the hydrophobic radical -Hy bears at least 5 -GpC, then $6 \leq x \leq 11$,
- G is a linear or branched divalent alkyl radical of 1 to 8 carbon atoms, the alkyl radical bearing one or more free carboxylic acid functions;
- R is a radical chosen from the group consisting of a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms, a divalent, linear or branched alkyl radical comprising from 1 to 12 carbon atoms bearing one or more $-CONH_2$ functions or an unsubstituted ether or polyether radical comprising from 4 to 14 carbon atoms and 1 to 5 oxygen atoms;
- the hydrophobic radical(s) -Hy according to formula X being bound to the PLG:
    - via a covalent bond between a carbonyl of the hydrophobic radical -Hy and a nitrogen atom borne by the PLG, thus forming an amide function resulting

from the reaction of an amine function borne by the PLG and an acid function borne by the precursor -Hy' of the hydrophobic radical -Hy, and

- via a covalent bond between a nitrogen atom of the hydrophobic radical -Hy and a carbonyl borne by the PLG, thus forming an amide function resulting from the reaction of an amine function of the precursor -Hy' of the hydrophobic radical -Hy and an acid function borne by the PLG,

- the ratio M between the number of hydrophobic radicals and the number of glutamic or aspartic units being between $0 < M \leq 0.5$;
- when several hydrophobic radicals are borne by a co-polyamino acid, then they are identical or different; and
- free carboxylic acids being in the form of an alkaline cation salt chosen from the group consisting of Na^+ and K^+.

13. A method for improving the physical chemical stability of a composition according to claim 1 by adding ionic species chosen from the group of anions, cations and/or zwitterions.