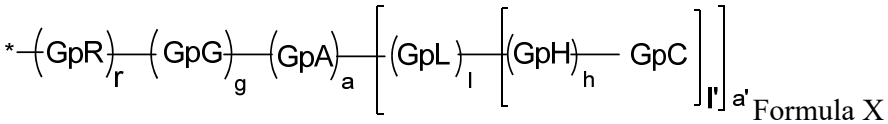
CLAIMS

1. A ~~Composition~~ 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) human glucagon;

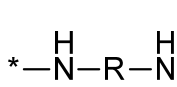
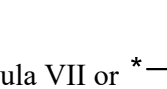
b) a co-polyamino acid bearing carboxylate charges and hydrophobic radicals Hy, said co-polyamino acid being constituted of glutamic or aspartic units and said hydrophobic radicals Hy chosen according to formula X as defined below:

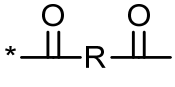


Formula X

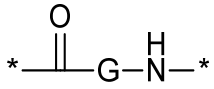
in which

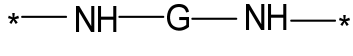
– GpR is chosen among the radicals ~~according to formulas~~according to formulas VII, VII' or VII'':


Formula VII or  Formula VII' or

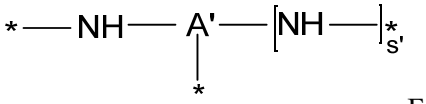
 Formula VII'';

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

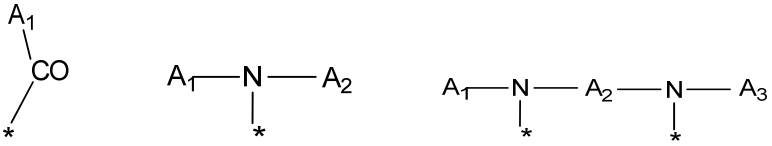

Formula XI


Formula XI'

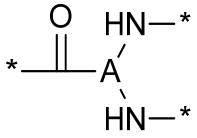
– GpA is chosen among the radicals according to formula VIII


Formula VIII

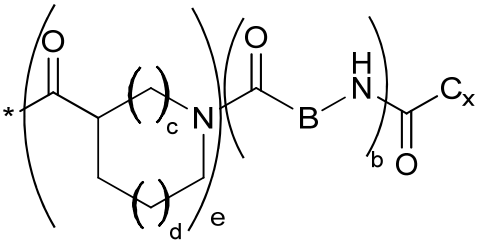
In which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''


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

– -GpL is chosen among the radicals according to formula 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;
  - 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;
  - 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, ~~optionally,~~ 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 from 1 to 5 oxygen atoms, or a linear or branched alkyl radical, ~~optionally~~ and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms~~.~~;
- C_x is a linear or branched, monovalent alkyl radical ~~optionally~~ 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; $6 \leq x \leq 11$;

– G is a branched alkyl radical of 1 to 8 carbon atoms, said alkyl radical bears 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 from 1 to 5 oxygen atoms;

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

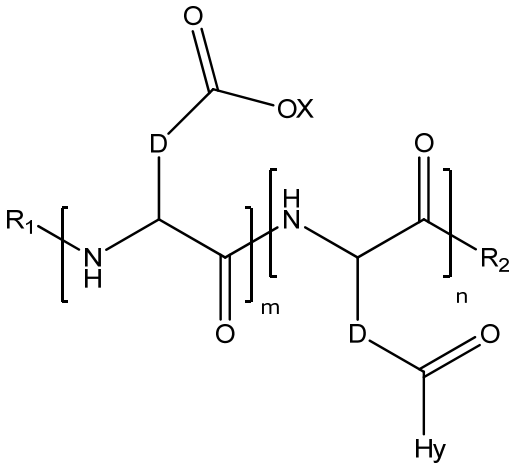
o via a covalent bond between a carbonyl of hydrophobic radical -Hy and a nitrogen atom borne by the PLG, thus forming an amide function resulting from the reaction of an amine function borne by the PLG and an acid function borne by the precursor Hy' of the hydrophobic radical -Hy, and

o 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 unites 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~~ composition according to claim 1, ~~characterized in that~~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

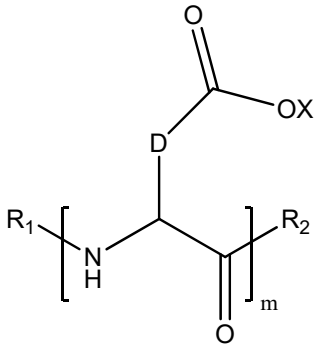
in which,

- D represents, independently, either a -CH_2- group (aspartic unit) of a -CH_2-CH_2- group (glutamic unit),
- Hy is a hydrophobic radical chosen among the hydrophobic radicals according to formula X, in which r = 1 and GpR is a radical according to formula VII-2,
- 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 a radical chosen from the group consisting of an H, a linear acyl group in C2 to C10, a branched acyl group in C3 to C10, a benzyl, an end "amino acid" unit and a pyroglutamate,

- R_2 is a hydrophobic radical chosen among the hydrophobic radicals according to formula X in which r = 1 and GpR is a radical according to formula VII or an -NR'R'', R' and R'' radical, identical or different, being chosen from the group consisting of H, the linear, branched or cyclic alkyls in C2 to C10, benzyl and said R' and R" alkyls being able to together form one or more saturated, unsaturated and/or aromatic rings and/or being able to 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 $5 \leq n + m \leq 250$;
- ~~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~~ composition according to ~~any one of the preceding claims~~claim 2, ~~characterized in that~~wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXX, in which n = 0 according to formula XXXb below:

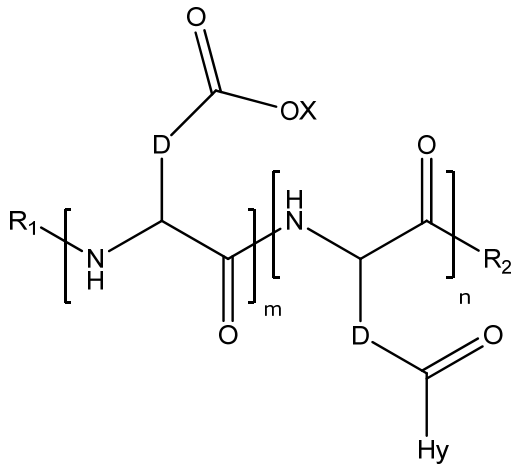


Formula XXXb

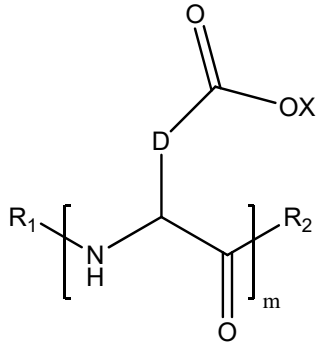
in which m, X, D, R_1 and R_2 have the definitions given above and at least R_1 or R_2 is a hydrophobic radical according to formula X.

4. The ~~Composition~~ composition according to claim 3, ~~characterized in that~~wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXXb, in which R_2 is a hydrophobic radical according to formula X in which r = 1 and GpR is according to formula VII'.

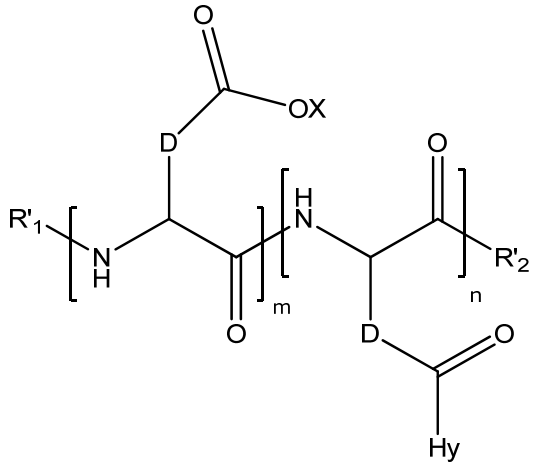
5. The ~~Composition~~ composition according to ~~any one of claims 1 to 4~~claim 1, ~~characterized in that~~wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXX, XXXb, XXXa:



Formula XXX



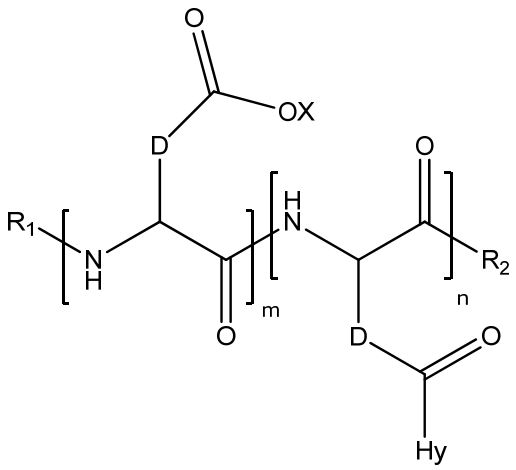
Formula XXXb



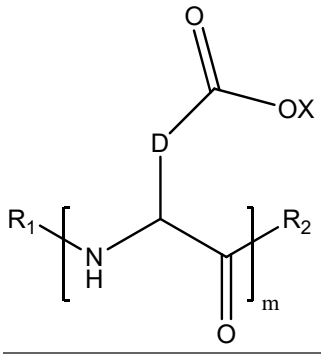
Formula XXXa

in which at least one co-polyamino acid is chosen among the co-polyamino acids in which the D group is a $–CH_2-$ group (aspartic unit).

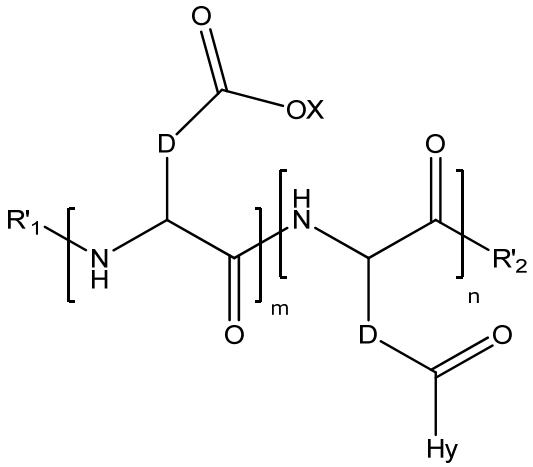
6. The ~~Composition~~ composition according to ~~any one of claims 1 to 4~~claim 1, ~~characterized in that~~wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is chosen among the co-polyamino acids according to formula XXX, XXXb, XXXa:



Formula XXX



Formula XXXb



Formula XXXa

in which at least one co-polyamino acid is chosen among the co-polyamino acids in which the D group is a $–CH_2-CH_2-$ group (glutamic unit).

7. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein the concentration of co-polyamino acid bearing carboxylate charges and hydrophobic radicals is at most of 40 mg/mL.

8. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein the concentration of human glucagon is comprised from 0.25 to 5 mg/mL.

9. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein the[hydrophobic radical]/[human glucagon] molar ratio is greater than or equal to 15.

10. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein it also comprises a polyanionic compound.

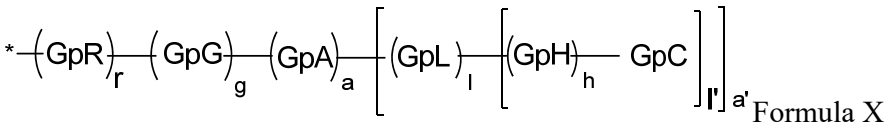
11. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein it also comprises a zinc salt.

12. The ~~Composition~~ composition according to ~~any one of the preceding claims~~claim 1, ~~characterized in that~~wherein it also comprises a gastro-intestinal hormone.

13. The ~~Composition~~ composition according to claim 12, ~~characterized in that~~wherein the gastro-intestinal hormone is chosen from the group consisting of ~~exentide~~exanatide, liraglutide, lixisenatide, albiglutide and dulaglutide, their analogues or derivatives and their pharmaceutically acceptable salts.

14. The ~~Composition~~ composition according to ~~any one of claims 12 and 13~~claim 12, ~~characterized in that~~wherein the concentration of gastro-intestinal hormone is comprised in an interval from 0.01 to 10 mg/mL~~.~~.

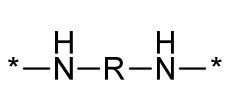
~~[000760]~~ Co-polyamino acid bearing carboxylate charges and hydrophobic radicals Hy, chosen among the radicals according to formula X as defined below:



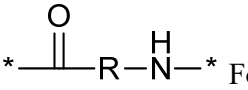
Formula X

in which

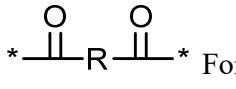
– GpR is chosen among the radicals according to formulas VII, VII' or VII":



Formula VII or

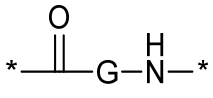


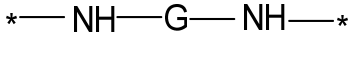
Formula VII' or



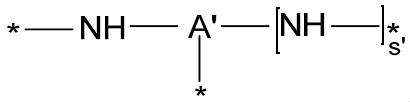
Formula VII'';

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

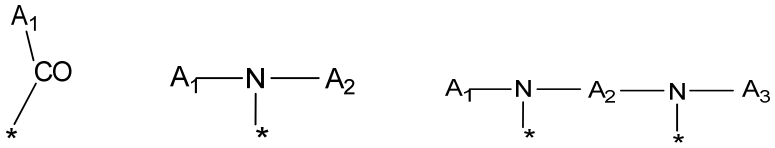

Formula XI


Formula XI'

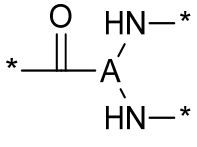
– - GpA is chosen among the radicals according to formulas VIII


Formula VIII

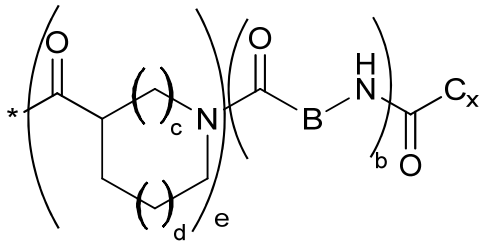
In which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''


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

– GpL is chosen among the radicals according to formula 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;

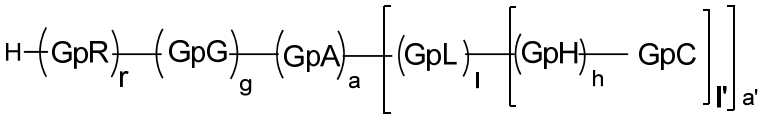
- h is an integer equal to 0, to 1, to 2, to 3, to 4, to 5 or to 6;
- l is an integer equal to 0 or to 1 and l' = 1 if l = 0 and l' = 2 if l =1;
- r is an integer equal to 0, 1 or to 2;
- s' is an integer equal to 0 or to 1;
- And if e is different from 0, then at least one of g, h or l is different 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, ~~optionally,~~ 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 from 1 to 5 oxygen atoms, or a linear or branched alkyl radical, ~~optionally~~ and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms~~.~~;
- C_x is a linear or branched, monovalent alkyl radical ~~optionally~~ 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; $6 \leq x \leq 11$;
- G is a branched alkyl radical of 1 to 8 carbon atoms, said alkyl radical bears 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 from 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 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 unites 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^+.

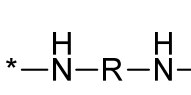
15. A hydrophobic radical precursor Hy' precursor of the hydrophobic radical -Hy ~~hydrophobic radical~~ according to formula X':



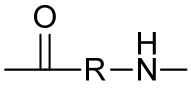
Formula X'

in which

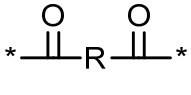
–GpR is chosen among the radicals according to formulas VII, VII' or VII'':



Formula VII or

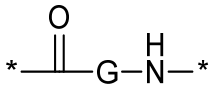


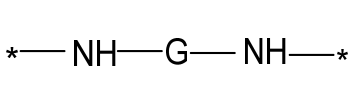
Formula VII' or



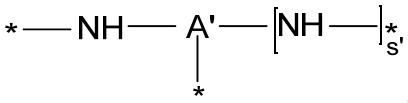
Formula VII'';

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

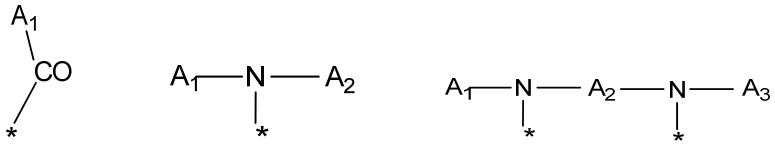

Formula XI


Formula XI'

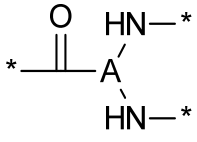
– - GpA is chosen among the radicals according to formulas VIII


Formula VIII

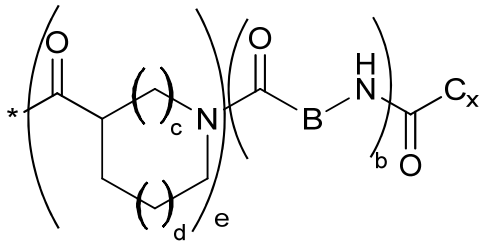
In which A' is chosen among the radicals according to formulas VIII', VIII'' or VIII'''


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 linked 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;
- 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;
- 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, ~~optionally,~~ substituted by a radical from a saturated, unsaturated or aromatic ring;

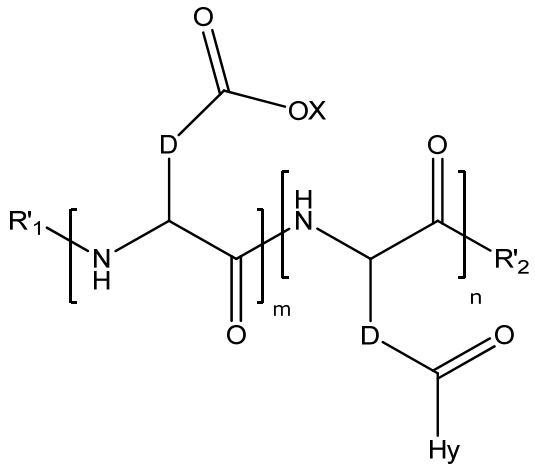
- B is a radical ether or polyether, unsubstituted, comprising from 4 to 14 carbon atoms and from 1 to 5 oxygen atoms, or a linear or branched alkyl radical, ~~optionally~~ and/or comprising an aromatic ring, comprising from 1 to 9 carbon atoms~~.~~;
- C_x is a linear or branched, monovalent alkyl radical ~~optionally~~ 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; $6 \leq x \leq 11$;
- G is a branched alkyl radical of 1 to 8 carbon atoms, said alkyl radical bears 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 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 from 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 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 unites being comprised from $0 < M \leq 0.5$;
- 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^+.

16. Use of ionic species chosen from the group of anions, cations and/or zwitterions to improve the physical chemical stability of the compositionsA 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.

17. 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 R1=R'1 and R2=R'2, according to formula XXXa below:



Formula XXXa

in which,

m, n, X, D and Hy as defined in claim 2,

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