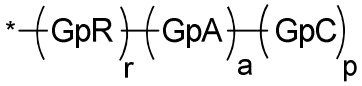
CLAIMS

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

a) one basal insulin the isoelectric point (pI) of which is from 5.8 to 8.5, and

b) a prandial insulin and/or a gastrointestinal hormone, and

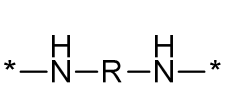
c) a co-polyamino acid consisting of glutamic or aspartic units bearing carboxylate charges and hydrophobic radicals Hy, and said hydrophobic radicals Hy being radicals of the following formula I:



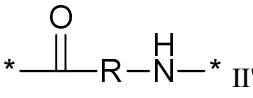
Formula I

in which

– GpR is a radical of formula II or II':

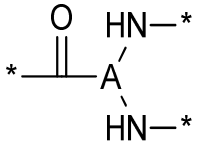


II or

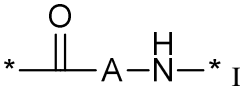


II';

– GpA is a radical of formula III or III':

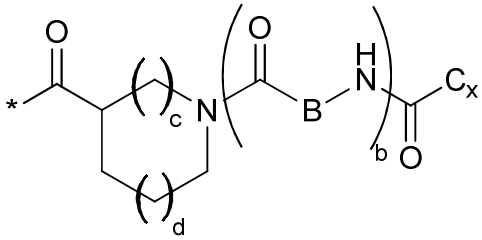


III or



III';

– GpC is a radical of formula IV:



IV;

– Hy comprises more than 30 carbon atoms,

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

– a is a whole number equal to 0 or 1;

- b is a whole number equal to 0 or 1;
- p is a whole number equal to 1 or 2, and
  - if p is equal to 1, then a is equal to 0 or 1 and GpA is a radical of formula III', and
  - if p is equal to 2, then a is equal to 1 and GpA is a radical of formula III;

- c is a whole number equal to 0 or 1, and, if c is equal to 0, then d is equal to 1 or 2;
- d is a whole number equal to 0, to 1 or 2;
- r is a whole number equal to 0 or 1, and
  - if r is equal to 0, then the hydrophobic radical of formula I is bound to the co-polyamino acid via a covalent bond between a carbonyl of the hydrophobic radical and a nitrogen atom in N-terminal position of the co-polyamino acid, thus forming an amide function, and
  - if r is equal to 1, then the hydrophobic radical of formula I is bound to the co-polyamino acid:
    - via a covalent bond between a nitrogen atom of the hydrophobic radical and a carbonyl of the co-polyamino acid, thus forming an amide function, or
    - via a covalent bond between a carbonyl of the hydrophobic radical and a nitrogen atom in N-terminal position of the co-polyamino acid, thus forming an amide function;

- R is a radical selected from the group consisting of:
  - a linear or branched divalent alkyl radical comprising, if GpR is a radical of formula II, from 2 to 12 carbon atoms, or, if GpR is a radical of formula II', from 1 to 11 carbon atoms;
  - a linear or branched divalent alkyl radical comprising, if GpR is a radical of formula II, from 2 to 11 carbon atoms, or, if GpR is a radical of formula II', from 1 to 11 carbon atoms, said alkyl radical bearing one or more -CONH2 functions, and
  - an un-substituted ether or polyether radical comprising from 4 to 14 carbon atoms and from 1 to 5 oxygen atoms;

- A is a linear or branched alkyl radical comprising from 1 to 6 carbon atoms;
- B is a linear or branched alkyl radical, optionally comprising an aromatic ring, comprising from 1 to 9 carbon atoms;
- $C_x$ is a linear or branched monovalent alkyl radical, in which x indicates the number of carbon atoms, and:
  - if p is equal to 1, x is from 11 to 25 ($11 \leq x \leq 25$);

- if p is equal to 2, x is from 9 to 15 ($9 \leq x \leq 15$),

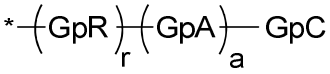
– the ratio i between the number of hydrophobic radicals and the number of glutamic or aspartic units being between $0 < i \leq 0.5$;

– 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 is from 5 to 250;

– the free acid functions being in the form of a salt of an alkaline cation selected from the group consisting of $Na^+$ and $K^+$.

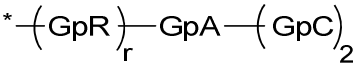
2. The composition according to Claim 1, wherein said hydrophobic radicals are selected from the hydrophobic radicals of formula I in which p = 1, represented by the following formula V:




formula V

GpR, GpA, GpC, r and a have the definitions given above.

3. The composition according to Claim 1, wherein said hydrophobic radicals are selected from the hydrophobic radicals of formula I in which a = 1 and p = 2, represented by the following formula VI:

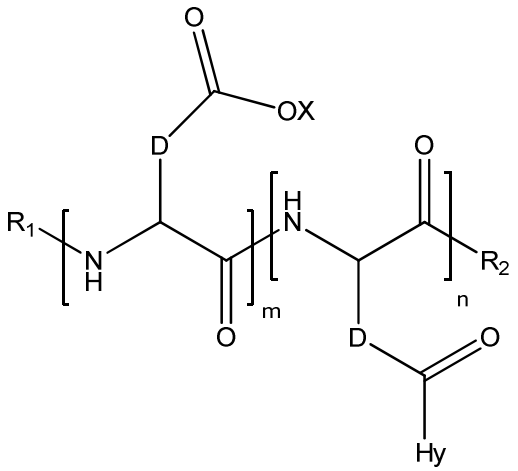



Formula VI

in which

GpR, GpA, GpC, r and a have the definitions given above.

4. The composition according to Claim 1, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of the following formula VII:

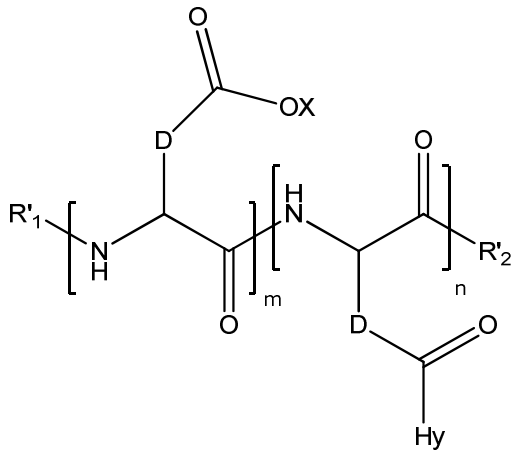



formula VII

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 selected from the hydrophobic radicals of formula I, V or VI, in which r = 1 and GpR is a radical of Formula II,
- $R_1$ is a hydrophobic radical selected from the hydrophobic radicals of formula I, V or VI in which r = 0 or r = 1 and GpR is a radical of Formula II', or a radical selected from the group consisting of H, a C2 to C10 linear acyl group, a C4 to C10 branched acyl group, benzyl, a terminal "amino acid" unit and a pyroglutamate,
- $R_2$ is a hydrophobic radical selected from the hydrophobic radicals of formula I, V or VI in which r = 1 and GpR is a radical of Formula II, or an -NR'R" radical, R' and R" which are identical or different being selected from the group consisting of H, the C2 to C10 linear or branched or cyclic alkyls, benzyl, and said alkyl R' and R" together optionally forming one or more saturated, unsaturated and/or aromatic carbon rings and/or optionally comprising heteroatoms selected from the group consisting of O, N and S;
- X represents a cationic entity selected from the group comprising the alkaline cations;
- n + m represents the degree of polymerization DP of the co-polyamino acid, that is to say the average number of monomer units per co-polyamino acid chain, and $5 \leq n + m \leq 250$.

5. The composition according to Claim 4, wherein co-polyamino acid bearing carboxylate charges and hydrophobic charges is selected from the co-polyamino acids of formula VII, in which $R_1 = R'_1$ and $R_2 = R'_2$, of the following formula VIIa:



Formula VIIa

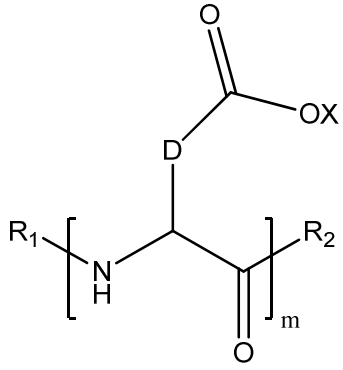
in which

– m, n, X, D and Hy have the definitions given above,

– $R'_1$ is a radical selected from the group consisting of H, a C2 to C10 linear acyl group, a C4 to C10 branched acyl group, benzyl, a terminal "amino acid" unit and a pyroglutamate,

– $R'_2$ is a -NR'R" radical, R' and R" which are identical or different being selected from the group consisting of H, the C2 to C10 linear or branched or cyclic alkyls, benzyl, and said alkyl R' and R" together optionally forming one or more saturated, unsaturated and/or aromatic carbon rings and/or optionally comprising heteroatoms selected from the group consisting of O, N and S.

6. The composition according to Claim 4, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of formula VII, in which n = 0, of the following formula VIIb:



Formula VIIb

in which m, X, D, $R_1$ and $R_2$ have the definitions given above, and at least one $R_1$ or $R_2$ is a hydrophobic radical of formula I, V or VI.

7. The composition according to Claim 6, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of formula VII, in which n = 0, of formula VIIb, and $R_1$ or $R_2$ is a hydrophobic radical of formula I, V or VI.

8. The composition according to Claim 6, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of formula VIIb, in which $R_2$ is a hydrophobic radical of formula I, V or VI, in which r = 1 and GpR is of formula II.

9. The composition according to Claim 4, wherein $R_1$ is a radical selected from the group consisting of a $C_2$ to $C_{10}$ linear acyl group, a $C_4$ to $C_{10}$ branched acyl group, benzyl, a terminal "amino acid" unit and a pyroglutamate.

10. The composition according to Claim 9, wherein $R_1$ is a radical selected from the group consisting of a $C_2$ to $C_{10}$ linear acyl group or a $C_4$ to $C_{10}$ branched acyl group.

11. The composition according to Claim 4, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of formula VII, VIIa or VIIb, in which the co-polyamino acid is selected from the co-polyamino acids in which group D is a $–CH_2-$ group (aspartic unit).

12. The composition according to Claim 4, wherein the co-polyamino acid bearing carboxylate charges and hydrophobic radicals is selected from the co-polyamino acids of formula VII, VIIa or VIIb, in which the co-polyamino acid is selected from the co-polyamino acids in which group D is a $–CH_2-CH_2-$ group (glutamic unit).

13. The composition according to Claim 1, wherein the basal insulin of which the isoelectric point is from 5.8 to 8.5 is insulin glargine.

14. The composition according to Claim 1, wherein it comprises from 40 to 500 U/mL of basal insulin of which the isoelectric point is from 5.8 to 8.5.

15. The composition according to Claim 1, wherein the concentration of co-polyamino acid bearing carboxylate charges and hydrophobic radicals is at most 60 mg/mL.

16. The composition according to Claim 1, wherein the concentration of co-polyamino acid bearing carboxylate charges and hydrophobic radicals is at most 40 mg/mL.

17. The composition according to Claim 1, wherein the concentration of co-polyamino acid bearing carboxylate charges and hydrophobic radicals is at most 20 mg/mL.

18. The composition according to Claim 1, wherein the concentration of co-polyamino acid bearing carboxylate charges and hydrophobic radicals is at most 10 mg/mL.

19. A composition according to Claim 1, comprising at least

a) one basal insulin the isoelectric point (pI) of which is from 5.8 to 8.5,

b) a prandial insulin, and

c) a co-polyamino acid bearing carboxylate charges and at least one hydrophobic radical of formula I.

20. The composition according to Claim 19, wherein the prandial insulin is human insulin.

21. The composition according to Claim 19, wherein it comprises in total from 40 to 500 U/mL of insulin with a combination of prandial insulin and of basal insulin of which the isoelectric point is from 5.8 to 8.5.

22. The composition according to Claim 19, wherein the proportions between the basal insulin of which the isoelectric point is from 5.8 to 8.5 and the prandial insulin are, expressed in percentage, 25/75, 30/70, 40/60, 50/50, 60/40, 70/30, 80/20 or 90/10.

23. A compositionaccording to Claim 1, comprising at least:

a) one basal insulin the isoelectric point (pI) of which is from 5.8 to 8.5,

b) a gastrointestinal hormone, and

c) a co-polyamino acid bearing carboxylate charges and at least one hydrophobic radical of formula I.

24. A composition according to Claim 1, comprising at least:

a) one basal insulin the isoelectric point (pI) of which is from 5.8 to 8.5,

b) a prandial insulin and a gastrointestinal hormone, and

c) a co-polyamino acid bearing carboxylate charges and at least one hydrophobic radical of formula I.

25. The composition according to Claim 24, wherein the gastrointestinal hormone is selected from the group consisting of exenatide, liraglutide, lixisenatide, albiglutide and dulaglutide, the analogs or derivatives thereof, and the pharmaceutically acceptable salts thereof.

26. The composition according to Claim 23, wherein the gastrointestinal hormone is dulaglutide, the analogs or derivatives thereof, and the pharmaceutically acceptable salts thereof.

27. The composition according to Claim 23, wwherein the gastrointestinal hormone is exenatide, the analogs or derivatives thereof, and the pharmaceutically acceptable salts thereof.

28. The composition according to Claim 23, wherein the gastrointestinal hormone is liraglutide, the analogs or derivatives thereof, and the pharmaceutically acceptable salts thereof.

29. The composition according to Claim 23, wherein the gastrointestinal hormone is lixisenatide, the analogs or derivatives thereof, and the pharmaceutically acceptable salts thereof.

30. The composition according to Claim 23, wherein the concentration of gastrointestinal hormone is within an interval of 0.01 to 10 mg/mL.

31. The composition according to Claim 24, wherein it comprises from 40 U/mL to 500 U/mL of basal insulin of which the isoelectric point is from 5.8 to 8.5, and from 0.05 to 0.5 mg/mL of exenatide.

32. The composition according to Claim 24, wherein it comprises from 40 U/mL to 500 U/mL of basal insulin of which the isoelectric point is from 5.8 to 8.5, and from 1 to 10 mg/mL of liraglutide.

33. The composition according to Claim 24, wherein it comprises from 40 U/mL to 500 U/mL of basal insulin of which the isoelectric point is from 5.8 to 8.5, and from 0.01 to 1 mg/mL of lixisenatide.

34. A single-dose formulation at a pH from 7 to 7.8, comprising a basal insulin of which the isoelectric point is from 5.8 to 8.5, and a prandial insulin.

35. A single-dose formulation at a pH from 7 to 7.8, comprising a basal insulin of which the isoelectric point is from 5.8 to 8.5, and a gastrointestinal hormone.

36. A single-dose formulation at a pH from 7 to 7.8, comprising a basal insulin of which the isoelectric point from 5.8 to 8.5, a prandial insulin, and a gastrointestinal hormone.