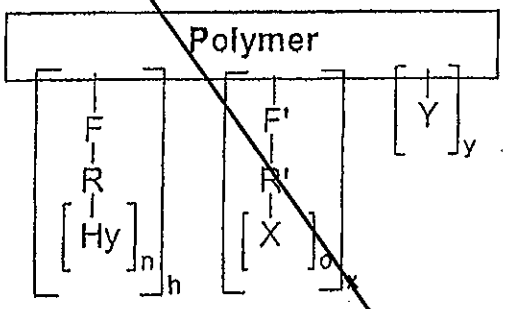
CLAIMS

1. Physically and chemically stable, water-soluble, amphiphilic polymer-PDGF complex, characterized in that:

the amphiphilic polymers consist of a hydrophilic polymeric backbone functionalized with hydrophobic substituents and hydrophilic groups according to the following general formula:



DP = m monomer units

- R and R′ being a bond or a chain comprising between 1 and 18 carbons, optionally branched and/or unsaturated comprising one or more heteroatoms, such as O, N and/or S,

  R and R′ being identical to or different from one another,

- F and F′ being an ester, a thioester, an amide, a carbonate, a carbamate, an ether, a thioether, an amine,

  F and F′ being identical to or different from one another,

- X being a hydrophilic group that may be:
  - a carboxylate
  - a sulphate
  - a sulphonate

- a phosphate
- a phosphonate,

- Y being a hydrophilic group that may be:
  - a sulphate
  - a sulphonate
  - a phosphate
  - a phosphonate,

- Hy being a hydrophobic group that may be:
  - a C_8 to C_{30} linear or branched alkyl, optionally unsaturated and/or containing one or more heteroatoms, such as O, N or S,
  - a C_8 to C_{18} linear or branched alkylaryl or arylalkyl, optionally unsaturated and/or optionally containing a heteroatom,
  - an optionally unsaturated C_8 to C_{30} polycycle,

n and o are between 1 and 3,

h represents the molar fraction of hydrophobic unit relative to a monomeric unit of between 0.01 and 0.5,

x represents the molar fraction of hydrophilic groups relative to a monomeric unit, of between 0 and 2.0,

y represents the molar fraction of hydrophilic groups relative to a monomeric unit, of between 0 and 0.5;

- the PDGF is chosen from the group of PDGFs (platelet-derived growth factors).

2. Complex according to Claim 1, characterized in that the PDGF is chosen from the group consisting of human recombinant PDGFs containing two B chains (rhPDGF-BB).

3. Complex according to either one of the preceding claims, characterized in that the polymer is chosen

from polymers in which the substituents are distributed randomly.

4. Complex according to one of Claims 1 to 3, characterized in that the polymer is chosen from polysaccharides.

5. Complex according to Claim 4, characterized in that the polysaccharides are chosen from the group consisting of hyaluronans, alginates, chitosans, galacturonans, chondroitin sulphate, dextrans and celluloses.

6. Complex according to Claim 5, characterized in that the group of celluloses consists of celluloses functionalized with acids, such as carboxymethyl-cellulose.

7. Complex according to Claim 5, characterized in that the group of dextrans consists of dextrans functionalized with acids, such as carboxymethyl

dextran.

8. Complex according to Claim 4, characterized in that the polysaccharides are chosen from the group consisting of hyaluronans, alginates and chitosans.

9. Complex according to Claim 4, characterized in that the polysaccharides are chosen from the group consisting of soluble dextran derivatives corresponding to formula (I) below:

$$DMC_aB_bSu_c \quad (I)$$

in which:

- D represents a polysaccharide chain, preferably consisting of series of glucoside units,

- MC represents methylcarboxylic groups,

- B represents N-benzylmethylenecarboxamide groups,

- Su represents sulphate groups (sulphation of the free hydroxyl functions borne by the glucoside units),

- a, b and c represent the degree of substitution (ds), respectively, of the groups MC, B and Su, with
  - i) a strictly greater than 0;
  - ii) b is such that:
    - either b is greater than or equal to 0.3 and c is between 0.1 and 0.5;
    - or b is strictly less than 0.3 and c corresponds to equation (1) below:

$$c \geq 8.5\ b^2 - 5.41\ b + 0.86 \quad (1).$$

10. Complex according to any one of the preceding claims, characterized in that the hydrophobic group Hy is chosen from the group consisting of fatty acids,

fatty alcohols, fatty amines, benzyl amines, cholesterol derivatives and phenols.

11. Complex according to any one of the preceding claims, characterized in that the formation of the amphiphilic polymer-PDGF complex is reversible.

12. Complex according to any one of the preceding claims, characterized in that it passes the tests for demonstration of the chemical and physical stabilization.

13. Complex according to Claim 12, characterized in that the tests for demonstration of the chemical and physical stabilization are chosen from the group consisting of the test for demonstration of the complex (Gel Mobility Shift Assay), the test for slowing down of the enzymatic degradation by bringing into contact with a protease and the test for physical stabilization at physiological pH carried out by SDS-Page.

14. Complex according to any one of the preceding claims, characterized in that the PDGF/amphiphilic polymer ratio is between 1/5 and 1/5000.

15. Complex according to any one of the preceding claims, characterized in that the PDGF/amphiphilic polymer ratio is between 1/100 and 1/5000.

16. Complex according to any one of the preceding claims, characterized in that the PDGF/amphiphilic polymer ratio is between 1/300 and 1/700.

17. Method of preparing the amphiphilic polymer/PDGF complex according to any one of the preceding claims, characterized in that this polymer/PDGF-BB complex is prepared in aqueous media and in the absence of any organic solvent that may denature the protein.

18. Therapeutic composition, characterized in that it comprises an amphiphilic polymer-PDGF complex according to any one of Claims 1 to 17.

19. Therapeutic composition according to Claim 15, characterized in that it allows an administration of 100 µg per ml of PDGF.

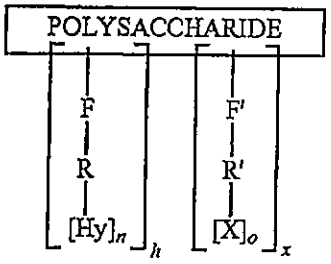
20. Use of an amphiphilic polymer-PDGF complex according to any one of Claims 1 to 17, for the preparation of a therapeutic composition with healing action, for use in the treatment of ulcers by topical application.

21. Method of therapeutic treatment for human or veterinary use, characterized in that it consists in administering, at the site of treatment, a therapeutic composition comprising an amphiphilic polymer-PDGF complex according to any one of Claims 1 to 17.

The invention claimed is:

1. A composition comprising an amphiphilic polysaccharide-PDGF complex solubilized in an aqueous medium, wherein:

the amphiphilic polysaccharide comprises a hydrophilic polysaccharide backbone functionalized with hydrophobic substituents and hydrophilic substituents according to the following general formula:



R and R' being a bond or a chain comprising between 1 and 18 carbons, optionally branched, unsaturated, and/or containing one or more heteroatoms,

R and R' being identical to or different from one another,

F and F' being selected from the group consisting of an ester, an amide, a carbamate, and an ether,

F and F' being identical to or different from one another,

X being a hydrophilic group that is a carboxylate,

Hy being a hydrophobic group that is selected from the group consisting of:

a C_8 to C_{30} linear or branched alkyl, optionally unsaturated and/or containing one or more heteroatoms,

a C_8 to C_{18} linear or branched alkylaryl or arylalkyl, optionally unsaturated and/or containing one or more heteroatoms, and

an optionally unsaturated C_8 to C_{30} polycycle,

n and o are between 1 and 3,

h represents the molar fraction of hydrophobic groups to saccharide units and is between 0.01 and 0.5,

x represents the molar fraction of hydrophilic groups to saccharide units and is between 0 and 2.0, and

the PDGF is a platelet-derived growth factor.

2. The composition according to claim 1, wherein PDGF is a human recombinant PDGF containing two B chains.

3. The composition according to claim 1, wherein the polysaccharide substituents are distributed randomly.

4. The composition according to claim 1, wherein the polysaccharide is selected from the group consisting of hyaluronans, alginates, chitosans, galacturonans, chondroitin sulphate, dextrans and celluloses.

5. The composition according to claim 1, wherein the polysaccharide is carboxymethylcellulose.

6. The composition according to claim 1, wherein the polysaccharide is a dextran functionalized with a carboxylate.

7. The composition according to claim 1, wherein the polysaccharide is selected from the group consisting of hyaluronans, alginates and chitosans.

8. The composition according to claim 1, wherein the hydrophobic group Hy is selected from the group consisting of fatty acids, fatty alcohols, fatty amines, benzyl amines, cholesterols and phenols.

9. The composition according to claim 1, wherein the amphiphilic polysaccharide-PDGF complex is reversibly formed.

10. The composition according to claim 1, wherein a weight ratio of PDGF to amphiphilic polysaccharide is between 1/5 and 1/5000.

11. The composition according to claim 1, wherein a weight ratio of PDGF to amphiphilic polysaccharide is between 1/100 and 1/5000.

12. The composition according to claim 1, wherein a weight ratio of PDGF to amphiphilic polysaccharide is between 1/300 and 1/700.

13. A method of preparing the composition according to claim 1, comprising combining the polysaccharide, PDGF, and the aqueous medium in the absence of an organic solvent that may denature the protein.

14. The composition according to claim 1, wherein the composition comprises 100 µg per ml of PDGF.

15. The composition according to claim 1, wherein the hydrophobic group Hy is tryptophan or an ester or salt of tryptophan.

16. The composition according to claim 1, wherein the composition is formulated as a spray.