

CLAIMS

1. A method for the preparation of a gel-forming composition for parenteral administration, said method comprises the steps of admixing a mixture of mammalian derived plasma and hyaluronic acid or a salt or ester thereof with a source of calcium, characterized in that said calcium source is added to said mixture such that the calcium concentration is between 0.2 and 1.4 mg/ml.
2. The method according to claim 1, characterized in that said calcium source is a calcium chloride solution.
3. The method according to claim 1 or 2, characterized in that said calcium chloride solution has an acidic pH.
4. The method according to any one of the preceding claims 1-3, characterized in that said plasma and hyaluronic acid mixture is freeze-dried prior to the addition of said calcium source.
5. The method according to any one of the preceding claims 1-4, characterized in that said plasma comprises lipids and/or phospholipids, wherein said lipids and/or phospholipids are present at a total concentration of between 0.2 and 7 mg/l.
6. The method according to any one of the preceding claims 1-5, characterized in that said lipids comprises minor plasma lipids, wherein said minor plasma lipids are preferably chosen from the group of palmitoyl ethanolamide (PEA), stearoyl ethanolamide (SEA), arachidonoyl ethanolamide (AEA), and wherein a total concentration of minor plasma lipids is between 5 and 50 nmol/l.
7. The method according to any one of the preceding claims 1-6, characterized in that said plasma has a concentration of white blood cells (WBCs) of less than 200 mil/l, preferably a concentration of WBCs of between 3 and 145 mil/l, more preferably between 5 and 85 mil/l.
8. The method according to any one of the preceding claims 1-7, characterized in that said plasma has a concentration of blood platelets (BPs) of less than 50,000 mil/l, preferably a concentration of BPs of between 1,000 and 35,000 mil/l, more preferably a concentration of BPs of between 2,000 and 20,000 mil/l.
9. The method according to any one of the preceding claims 1-8, characterized in that the hyaluronic acid or a derivative thereof has a molecular weight less than 1,800 kDa, more preferably between 700 and 1,600 kDa, more preferably 700 and 1,000 kDa.
10. The method according to any one of the preceding claims 1-9, characterized in that said plasma and hyaluronic acid mixture further comprise one or more pharmaceutical compounds chosen from the group of an active pharmaceutical

ingredient, an antibiotic agent, a cell composition, a small organic molecule, a protein, and a peptide.

11. The method according to any of the preceding claims 1-10, characterized in that said active pharmaceutical ingredient is an alpha-2 adrenergic receptor agonist, preferably clonidine or a derivative thereof, preferably clonidine.
12. The method according to any one of the preceding claims 1-11, characterized in that said small organic molecule is a scaffold or matrix component with osteoconductive properties, preferably tricalcium phosphate particles (TCP).
13. The method according to any of the preceding claims 1-12, characterized in that said gel-forming formulation is configured for parenteral administration, preferably for intraosseous, periosteous, intraarticular, periarticular administration, or for intratendon, peritendon, intraligament, or periligament administration.
14. A composition obtained by the method according to any one of the preceding claims 1 to 13.
15. The composition according to claim 14 for use in the treatment of musculoskeletal diseases in a subject, wherein the musculoskeletal disease is preferably a bone disease or a joint disease.
16. The composition according to claim 15 for use in the treatment of osteoarthritis.
17. The composition according to claim 15 for use in the treatment or prevention of cranial cruciate ligament rupture.
18. The composition according to claim 15 for use in the treatment of tendinopathies.