

## CLAIMS

1. A process for the preparation of a citrate-coated amorphous calcium phosphate nanoparticle which comprises the following steps:
  - 1) providing a first solution of a salt of calcium and a citrate salt wherein the molar  
5 ratio of citrate ion to calcium ion is in the range from 1 to 2 thus obtaining a clear first solution;
  - 2) providing a second solution of a salt capable to give phosphate anion and a carbonate salt;
  - 3) mixing together the clear first solution and the second solution at a pH in the  
10 range from 8 to 11;
  - 4) precipitating the nanoparticle; and
  - 5) drying the nanoparticle obtained from step 4).
2. The process according to claim 1, wherein the salt of calcium is made of an anion selected from the group consisting of chloride, nitrate, hydroxide, acetate,  
15 oxalate, lactate, preferably the anion is chloride.
3. The process according to claim 1 or claim 2, wherein the salt of citrate is made of a cation selected from the group consisting of sodium and potassium, preferably the cation is sodium.
4. The process according to anyone of claims 1-3, wherein the molar ratio of  
20 citrate ion to calcium ion is about 2.
5. The process according to anyone of claims 1-4, wherein the first solution of step 1) comprises at least one further salt selected from the group of: strontium salt, and magnesium salt.
6. The process according to anyone of claims 1-5, wherein the salt capable to give  
25 phosphate anion is a salt of phosphate, hydrogen phosphate or hydrogen phosphate, preferably made of a cation selected from the group consisting of sodium, potassium and ammonium.
7. The process according to anyone of claims 1-6, wherein the pH of step 3) is in the range from 8.5-10.7.
- 30 8. The process according to anyone of claims 1-7, wherein in the mixing step 3) the second solution is added to the clear first solution.
9. The process according to anyone of claims 1-8, wherein in step 4) the

precipitation is carried out by providing sedimentation cycles by centrifugation removal of supernatant, collecting and washing the precipitate.

10. The process according to anyone of claims 1-9, wherein the drying step 5) is selected from freeze-drying, spray-drying and ventilated oven drying.

5 11. The process according to anyone of claim 1-10, wherein in step 1) a fluoride compound is added.

12. The process according to claim 11, wherein the fluoride compound is a fluoride of a cation selected from the group consisting of sodium and potassium.

13. A citrate-coated amorphous calcium phosphate nanoparticle obtainable by the  
10 process according to anyone of claims 1-10, wherein the drying step 5) is a freeze-drying step, being said nanoparticle characterized by a superficial area from  $250 \text{ m}^2\text{g}^{-1}$  to  $360 \text{ m}^2\text{g}^{-1}$  as measured with Brunauer-Emmett-Teller (BET) gas adsorption method and having a round-shaped morphology with a diameter in the range from 30 to 80 nm as measured by transmission electron microscopy (TEM)  
15 images.

14. A citrate-coated amorphous calcium phosphate nanoparticle agglomerate obtainable by the process according to anyone of claims 1-10, wherein the drying step 5) is a spray-drying step, being said nanoparticle agglomerate characterized by a superficial area from  $2 \text{ m}^2\text{g}^{-1}$  to  $10 \text{ m}^2\text{g}^{-1}$  as measured with Brunauer-Emmett-  
20 Teller (BET) gas adsorption method and having a round shaped morphology with a diameter in the range from 2 to  $25 \text{ }\mu\text{m}$  as measured by scanning electron microscopy (SEM).

15. A fluorine-doped citrate-coated amorphous calcium phosphate nanoparticle obtainable by the process according to anyone of claims 1-12, wherein the drying  
25 step 5) is a freeze-drying step, being said nanoparticle characterized by a superficial area from  $250 \text{ m}^2\text{g}^{-1}$  to  $370 \text{ m}^2\text{g}^{-1}$  as measured with Brunauer-Emmett-Teller (BET) gas adsorption method and having a round shaped morphology with a diameter in the range from 30 to 80 nm as measured by transmission electron microscopy (TEM) images.

30 16. A fluorine-doped citrate-coated amorphous calcium phosphate nanoparticle agglomerate obtainable by the process according to anyone of claims 1-12, wherein the drying step 5) is a spray-drying step, being said nanoparticle

agglomerate characterized by a superficial area from 3 m<sup>2</sup>g<sup>-1</sup> to 10 m<sup>2</sup>g<sup>-1</sup>—as measured with Brunauer-Emmett-Teller (BET) gas adsorption method and having a round shape morphology with a diameter in the range from 2 to 25 μm as measured by scanning electron microscopy (SEM).

- 5 17. A nanoparticle or a nanoparticle agglomerate according to anyone of claims 13-16 as a biomaterial for use in dentistry application.
18. The nanoparticle as biomaterial for use according to claim 17 wherein the biomaterial is used as remineralization agent or as dentin desensitizer.