binding between diagnostic/therapeutic compounds and CaP-NP can mainly occur through formation of electrostatic interactions.

One or more therapeutic/diagnostic compounds are preferably selected from the groups consisting of nucleic acids, peptides, synthetic compounds and diagnostic probes.

The presence in step a) of the solution of one or more diagnostic/therapeutic compounds of interest allows obtaining, at the end of step c), CaP-NP that have the therapeutic/diagnostic compound(s) encapsulated in the structure.

Therefore, surprisingly, the product of the invention obtainable according to the preferred and advantageous aspect of the invention comprises one or more CaP-NP encapsulating one or more diagnostic/therapeutic compounds and/or comprises one or more surface-functionalized therapeutic/diagnostic compounds.

The product of the invention encapsulating one or more diagnostic/therapeutic compounds has surprisingly proved to comprise one or more negatively charged CaP-NP with ζ-potential in the range from -41.0 mV to -27.0 mV and with Z-average in the range from 150 to 231 nm. The product of the invention with the therapeutic/diagnostic compound(s) encapsulated in the structure has proved to be advantageously in the form of CaP-NP with spheroidal morphology.

In another aspect thereof, the invention relates to a product obtainable with the process of the invention for use as vehicle in the treatment of cardiovascular diseases through inhalation administration.

In a preferred embodiment, the invention relates to the product for use of claim 17, wherein the treatment is carried out through ad administration route selected from inhalation administration, enteral administration, parenteral administration, intravenous administration, intraperitoneal administration, oral administration, sublingual administration, spray administration, rectal administration, intraocular administration, topical administration and transdermal administration.

Cardiovascular diseases in the present invention comprise heart failure, decreased myocardial contraction, fibrillation, diabetic cardiomyopathy, dilated cardiomyopathy, genetic diseases (such as Brugada syndrome, Timothy syndrome, or short QT syndrome, muscular dystrophy), cardiac hypertrophy, hypotension, hyperthyroidism, hypothyroidism, acute heart failure, chronic heart failure, myocardial infarction.

In a further and advantageous aspect thereof, the invention relates to a product obtainable with the process of invention in its preferred and advantageous embodiment with one or more compounds encapsulated in the one or more CaP-NP for use in the treatment of cardiovascular diseases through inhalation administration, as explained above and shown in the experimental part. In

CLAIMS

1. A process for the preparation of a product comprising one or more nanoparticles of calcium phosphate (CaP-NP) with a negative surface charge having a ζ-potential in the range from -41.0 mV to -27.0 mV, comprising the steps of:

a) maintaining a mixture having a pH in the range from 7 to 10 and comprising an aqueous solution of calcium, an aqueous solution of phosphate and a solution of citrate ions at a temperature in the range from 20°C to 40°C for a time in the range from 30 seconds to 10 minutes;

b) removing non-reacted ions from the obtained solution of step a), thus obtaining a suspension of one or more nanoparticles of calcium phosphate (CaP-NP);

c) recovering the product of one or more nanoparticles of calcium phosphate (CaP-NP) from the suspension of step b).

2. The process according to claim 1, wherein in the mixture of step a) an aqueous solution of one or more therapeutic/diagnostic compounds is also present.

3. The process according to claim 1, wherein the one or more nanoparticles of calcium phosphate (CaP-NP) recovered from step c) are surface functionalized with one or more therapeutic/diagnostic compounds.

4. The process according to any one of claims 1-3, wherein the aqueous solution of calcium in the mixture of step a) is a solution of Calcium Chloride having a molarity in the range from 20 to 200 mM.

5. The process according to any one of claims 1-4, wherein the aqueous solution of phosphate in the mixture of step a) is a solution of Na_2HPO_4 with

molarity in the range from 24 to 240 mM.

6. The process according to anyone of claims 1-5, wherein the temperature of step a) is in the range from 35 to 40°C, more preferably it is about 37°C.

7. The process according to anyone of claims 1-6, wherein the maintenance time of the mixture of step a) is about 5 minutes.

8. The process according to any one of claims 1-7, wherein the solution of citrate ions is an aqueous solution of sodium citrate having a molarity in the range from 40 to 800 mM.

9. The process according to any one of claims 1-8, wherein the mixture of step a) has a pH of about 10.

10. The process according to any one of claims 1-9, wherein the step b) of removing the non-reacted ions is carried out through a dialysis membrane.

11. The process according to claim 10, wherein the dialysis membrane is a cellulose membrane having a cut-off of 3500 Dalton.

12. The process according to claim 11, wherein the removal step b), carried out with a dialysis membrane, occurs for a time from 5 to 24 hours, preferably for 6 hours.

13. The process according to any one of claims 1-12, wherein the recovery step c) of the nanoparticles of calcium phosphate (CaP-NP) is carried out by freezing drying.

14. A product comprising one or more CaP-NP obtainable by the process

according to any one of claims 1, 4-13, wherein:

- the NPs have negative surface charge having ζ-potential in the range from -41.0 mV to -27.0 mV and having a splitting factor (SF), calculated from the FT-IR spectra of the NP according to Weiner S. and Bar-Yosef O. (1990), of at most 1.76, or
- in the mixture of step a) an aqueous solution of one or more therapeutic/diagnostic compounds is also present and wherein the NPs encapsulate one or more therapeutic/diagnostic compounds, have negative surface charge having ζ-potential in the range from -41.0 mV to -27.0 mV, and Z-average determined by Dynamic Light Scattering (DLS) in the range from 150 to 231 nm.

15. The product of claim 14 when having negative surface charge having ζ-potential in the range from -41.0 mV to -27.0 mV and having a splitting factor (SF) of at most 1.76, wherein the one or more CaP-NP comprises/comprise one or more surface-functionalized therapeutic/diagnostic compounds.

16. The product of claim 14 or claim 15, wherein one or more therapeutic/diagnostic compounds are selected from the groups consisting of nucleic acids, peptides, synthetic compounds and diagnostic probes.

17. A product of any one of claims 15-16 for use in the treatment of cardiovascular diseases.

18. The product for use of claim 17, wherein the treatment is carried out through an administration route selected from inhalation administration, enteral administration, parenteral administration, intravenous administration, intraperitoneal administration, oral administration, sublingual administration, spray administration, rectal administration, intraocular administration, topical administration and transdermal administration.

19. Use of a product of any one of claims 15-16 in the manufacture of a medicament for the treatment of cardiovascular diseases.

20. The use of claim 19, wherein the treatment is carried out through an administration route selected from inhalation administration, enteral administration, parenteral administration, intravenous administration, intraperitoneal administration, oral administration, sublingual administration, spray administration, rectal administration, intraocular administration, topical administration and transdermal administration.