In this approach, the quasi-concomitant injection of the inactive agent and of the active one is required to increase the global amount of agents present in the blood and consequently to prolong their blood half-life. Such strategy, which expressly relies on a probability-based approach, necessarily requires the association of the active agent with a targeting agent in order to achieve its successful accumulation on the target site by conferring said active agent an advantage over the inactive one. In addition, due to the quasi-concomitant injection, a specific design of the inactive carrier may be required depending on the intended use of the active composition.

As apparent from the prior art and despite of a long medical need, the improvement of compounds (including therapeutic, prophylactic as well as diagnostic compounds) which cannot be efficiently used in patients due to their unacceptable toxicity or to their unfavorable pharmacokinetics parameters remains a concern.

SUMMARY

In one aspect, there is provided a use of a combination of (i) a biocompatible nanoparticle having a longest dimension of between about 4 nm and about 500 nm and an absolute surface charge value of at least 10 mV (|10 mV|) and of (ii) a pharmaceutical compound of interest in the manufacture of a medicament, for use in a therapeutic, prophylactic or diagnostic method in a subject in need thereof, wherein the nanoparticle and the pharmaceutical compound of interest are to be administered in the subject sequentially, and wherein the nanoparticle is to be administered to the subject between more than 5 minutes and about 72 hours before or after the pharmaceutical compound of interest.

In an embodiment, the disclosure relates to a pharmaceutical composition comprising the combination of (i) a biocompatible nanoparticle and of (ii) a pharmaceutical compound of interest, wherein the longest dimension of the biocompatible nanoparticle is between about 4 nm and about 500 nm, and the absolute surface charge value of the biocompatible nanoparticle is of at least 10 mV (|10 mV|) for use in a therapeutic, prophylactic or diagnostic method in a subject in need thereof, the therapeutic, prophylactic or diagnostic method comprising a step of administering the pharmaceutical compound of interest to the subject and a distinct step of administering the nanoparticle, said nanoparticle being

administered to the subject between more than 5 minutes and about 72 hours before or after the pharmaceutical compound of interest.

DETAILED DESCRIPTION

The present invention now allows optimization of the efficiency of a compound of interest (herein also simply identified as "the compound") whatever its intended use in the context of therapy, prophylaxis or diagnostic. The composition herein described which is a combination of (i) a biocompatible nanoparticle and of (ii) at least one compound of interest, optimize the at least one compound of interest pharmacokinetic parameters, and, as a consequence, now renders possible the development of therapeutic compounds which could not have been developed otherwise due for example to their unacceptable toxicity.

A typical composition of the invention (herein generally identified as "pharmaceutical composition") is a composition comprising the combination of (i) a biocompatible nanoparticle and (ii) at least one compound ("the compound of interest"), wherein the longest dimension of the biocompatible nanoparticle is typically between about 4 nm and about 500 nm, and the absolute surface charge value of the biocompatible nanoparticle is of at least 10 mV.

A preferred object of the invention is a pharmaceutical composition comprising the combination of (i) a biocompatible nanoparticle and of (ii) a pharmaceutical compound of

In this approach, the quasi-concomitant injection of the inactive agent and of the active one is required to increase the global amount of agents present in the blood and consequently to prolong their blood half-life. Such strategy, which expressly relies on a probability-based approach, necessarily requires the association of the active agent with a targeting agent in order to achieve its successful accumulation on the target site by conferring said active agent an advantage over the inactive one. In addition, due to the quasi-concomitant injection, a specific design of the inactive carrier may be required depending on the intended use of the active composition.

As apparent from the prior art and despite of a long medical need, the improvement of compounds (including therapeutic, prophylactic as well as diagnostic compounds) which cannot be efficiently used in patients due to their unacceptable toxicity or to their unfavorable pharmacokinetics parameters remains a concern.

SUMMARY

In one aspect, there is provided a pharmaceutical composition comprising the combination of (i) a biocompatible nanoparticle and of (ii) a pharmaceutical compound of interest, wherein the longest dimension of the biocompatible nanoparticle is between about 4 nm and about 500 nm, and the absolute surface charge value of the biocompatible nanoparticle is of at least 10 mV (|10 mV|) for use in a therapeutic, prophylactic or diagnostic method in a subject in need thereof, the therapeutic, prophylactic or diagnostic method comprising a step of administering the pharmaceutical compound of interest to the subject and a distinct step of administering the nanoparticle, said nanoparticle being administered to the subject between more than 5 minutes and about 72 hours before or after the pharmaceutical compound of interest.

DETAILED DESCRIPTION

The present invention now allows optimization of the efficiency of a compound of interest (herein also simply identified as "the compound") whatever its intended use in the context of therapy, prophylaxis or diagnostic. The composition herein described which is a combination of (i) a biocompatible nanoparticle and of (ii) at least one compound of

interest, optimize the at least one compound of interest pharmacokinetic parameters, and, as a consequence, now renders possible the development of therapeutic compounds which could not have been developed otherwise due for example to their unacceptable toxicity.

A typical composition of the invention (herein generally identified as "pharmaceutical composition") is a composition comprising the combination of (i) a biocompatible nanoparticle and (ii) at least one compound ("the compound of interest"), wherein the longest dimension of the biocompatible nanoparticle is typically between about 4 nm and about 500 nm, and the absolute surface charge value of the biocompatible nanoparticle is of at least 10 mV.

A preferred object of the invention is a pharmaceutical composition comprising the combination of (i) a biocompatible nanoparticle and of (ii) a pharmaceutical compound of

CLAIMS

1. Use of aA ~~pharmaceutical composition comprising the~~ combination of (i) a biocompatible nanoparticle having a longest dimension of between about 4 nm and about 500 nm and an absolute surface charge value of at least 10 mV (|10 mV|) and of (ii) a pharmaceutical compound of interest in the manufacture of a medicament, for use in a therapeutic, prophylactic or diagnostic method in a subject in need thereof, wherein ~~the longest dimension of the biocompatible nanoparticle is between about 4 nm and about 500 nm, and the absolute surface charge value of the biocompatible nanoparticle is of at least 10 mV (|10 mV|) for use in a therapeutic, prophylactic or diagnostic method in a subject in need thereof, the therapeutic, prophylactic or diagnostic method comprising a step of administering the pharmaceutical compound of interest to the subject and a distinct step of administering the nanoparticle,~~ the nanoparticle and the pharmaceutical compound of interest are to be administered in the subject sequentially, and wherein said nanoparticle ~~being~~ is to be administered to the subject between more than 5 minutes and about 72 hours before or after the pharmaceutical compound of interest.

2. The ~~pharmaceutical composition~~use according to claim 1, wherein the nanoparticle has an absolute surface charge value of more than |10 mV|, said charge being a negative charge.

3. The ~~pharmaceutical composition~~use according to claim 1 or 2, wherein the nanoparticle is an organic nanoparticle.

4. The ~~pharmaceutical composition~~use according to claim 3, wherein the nanoparticle is selected from a lipid-based nanoparticle, a protein-based nanoparticle, a polymer-based nanoparticle, a co-polymer-based nanoparticle, a carbon-based nanoparticle, and a virus-like nanoparticle.

5. The ~~pharmaceutical composition~~use according to claim 1 or 2, wherein the nanoparticle is any inorganic nanoparticle and the longest dimension of said nanoparticle is below about 7 nm.

6. The ~~pharmaceutical composition~~use according to claim 1 or 2, wherein the nanoparticle is an inorganic nanoparticle, the longest dimension of said nanoparticle is of at least 10 nm, and the inorganic material of the nanoparticle is selected from (i) one or more divalent

7. The ~~pharmaceutical composition~~use according to claim 6, wherein the inorganic material is selected from calcium carbonate ($CaCO_3$), magnesium carbonate ($MgCO_3$), magnesium hydroxide ($Mg(OH)_2$), iron hydroxide ($Fe(OH)_2$), iron oxyhydroxide (FeOOH), iron oxide (Fe_3O_4 or Fe_2O_3), aluminium oxide (Al_3O_4), aluminium hydroxide ($Al(OH)_3$), aluminium oxyhydroxide (AlOOH) and silicium oxide (SiO_2).

8. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 7, wherein the nanoparticle is further covered with a biocompatible coating.

9. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 8, wherein the ~~combined~~ sequential administration of the biocompatible nanoparticle and of the compound maintains the therapeutic benefit of the compound for a reduced toxicity, or increases the therapeutic benefit of the compound for an equivalent or reduced toxicity, for the subject, when compared to therapeutic benefit and toxicity induced by the standard therapeutic dose of said compound.

10. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 8, wherein the ~~combined~~ sequential administration of the biocompatible nanoparticle and of the compound allows a reduction of at least 10% of the administered compound therapeutic dose when compared to the standard therapeutic dose of said compound while maintaining the same therapeutic benefit for an equivalent toxicity or a reduced toxicity for the subject or while increasing the therapeutic benefit for an equivalent or reduced toxicity for the subject.

11. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 10, wherein the nanoparticle is cleared from the subject to whom it has been administered within one hour and six weeks after its administration to a subject in need of the pharmaceutical compound of interest referred to in claim 1.

12. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 11, wherein the compound is an organic compound preferably selected from a biological compound, a small molecule targeted therapeutic, and a cytotoxic compound.

13. The ~~pharmaceutical composition~~use according to claim 12, wherein the compound is selected from an antibody, an oligonucleotide, and a synthesized peptide.

14. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 11, wherein the compound is an inorganic compound selected from a metallic nanoparticle, a metal oxide nanoparticle, a metal sulfide nanoparticle and any mixture thereof.

15. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 14, wherein the compound of interest is encapsulated in a carrier.

16. The ~~pharmaceutical composition~~use according to anyone of claims 1 to 14, wherein the compound of interest is bound to a carrier.