the delivery of gases. Hollow core particles would therefore be desirable that can encapsulate gas molecules and are functionalized in a way that they can take up and release gases upon a stimulus or in a delayed release pattern.

Therefore, there is a need to provide hollow core-shell particles that overcome, or at least ameliorate, one or more of the disadvantages described above.

There is also a need to provide hollow core-shell particles which provide a solution to the insolubility of gases in applications where gas delivery, especially oxygen delivery, is needed.

There is also a need to provide a process for preparing these hollow core-shell particles.

Summary

There is provided a hollow core-shell particle having pores extending through its shell and a plurality of polymer chains that are grafted to the outer surface of the shell, wherein the polymer backbone of said polymer chains comprises monomer units that are functionalized with a group selected from amidines, guanidines, amino acid derivatives and heteroaromatic or non heteroaromatic heterocyclic groups, wherein the heterocycles comprise 1 to 3 nitrogen atoms.

According to a first aspect, there is provided a hollow core-shell particle having pores extending through its shell and a plurality of polymer chains that are grafted to the outer surface of the shell, wherein the polymer backbone of said polymer chains comprises monomer units that are functionalized with a group selected from amidines, guanidines, amino acid derivatives and heteroaromatic or non heteroaromatic heterocylic groups, wherein the heterocycles comprise 1 to 3 nitrogen atoms, wherein the particle is a hollow silica sphere

Advantageously, the polymer backbone may contain functionalities selected from either aminocarbonyls, amidines, guanidines, indoles or imidazoles. These nitrogen-containing functionalities may elicit a response to an external agent, for example to an increased concentration of carbon dioxide. This response may lead to the opening of the above mentioned core-shell particle.

Further advantageously, the hollow core may be filled with releasable gas molecules. These may be released upon the opening of the core-shell particle. They may also be released by diffusion from the particle core depending on the particle's environment.

Further advantageously, the releasable gas molecule may be oxygen.

According to a second aspect, there is provided a process for making a particle as disclosed above, comprising the steps of

a) modifying the surface of a hollow particle with an amino, halogen, epoxide or thio-carbonyl thioester group;

b) reacting the modified particle with a methacrylate monomer functionalized with a group selected from amidines, guanidines, amino acid derivatives and heteroaromatic or non heteroaromatic heterocylic groups; and

c) further polymerizing the obtained grafted hollow particle with the monomer of step b).

According to a third aspect, there is provided a process for making a particle as disclosed above, comprising the steps of

a) modifying the surface of a hollow particle with an amino, halogen, epoxide or thio-carbonyl thioester group;

b) reacting the modified particle with an optionally substituted acrylonitrile;

c) further polymerizing the obtained grafted hollow particle with an acrylonitrile; and

d) reacting the obtained cyano groups of the polymer backbone to amidine groups.

According to a fourth aspect, there is provided a process for loading the particle as disclosed above with a gas, comprising exposing the above mentioned polymer particle with a selected gas and allowing the gas to permeate into the hollow particle.

According to a fifth aspect, there is provided use of a loaded particle as disclosed above for the encapsulation and delivery of gases. Advantageously, the loaded particle may be used as a delivery means for oxygen in paramedic emergencies.

According to a sixth aspect, there is provided a delivery means comprising a plurality of particles as disclosed above, wherein the hollow core is filled with gas molecules. Advantageously, the delivery means functions as a carrier for the loaded particle and may deliver oxygen site-specific to oxygen-deprived tissues.

According to a seventh aspect, there is provided use of the delivery means as disclosed above to provide oxygen in cosmetic skin care applications.

According to an eighth aspect, there is provided a non-therapeutic use of the delivery means as disclosed above to deliver oxygen site-specific to an oxygen-deprived tissue or cell.

Definitions

The following words and terms used herein shall have the meaning indicated below:

The term 'hollow silica sphere' is to be interpreted broadly to include a hollow container which may consist of silica. The container contains a void. The void may refer to a partially enclosed space.

In the definitions of a number of substituents below it is stated that "the group may be a terminal group or a bridging group". This is intended to signify that the use of the term is intended to encompass the situation where the group is a linker between two other portions of the molecule as well as where it is a terminal moiety. Using the term alkyl as an example, some publications would use the term "alkylene" for a bridging group and hence in these other publications there is a distinction between the terms "alkyl" (terminal group) and "alkylene" (bridging group). In the present application no such distinction is made and most groups may be either a bridging group or a terminal group.

The term "aliphatic" is one that includes only carbon and hydrogen and possibly having monovalent and divalent straight or branched chain saturated or unsaturated hydrocarbon groups from 1 to 50 carbon atoms, preferably 1 to 30, e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms or the likes. In cases where there is at least one double bond, either the E, Z, cis or trans stereochemistry may exist, where applicable, at any location along the carbon chain. An aliphatic group as used herein may be a terminal or bridging group.

The term "hetero-aliphatic" is one that includes "aliphatic" groups as mentioned above wherein the chains of the hydrocarbon groups may include hetero atoms such N, O or S.

The term "alicyclic" refers to a group that is both aliphatic and cyclic having from 3 to 30, preferably 6 to 30, carbon atoms and any other number of carbon atoms falling within this range. They contain one or more all-carbon rings which may be either saturated or unsaturated, but do not have aromatic character. Examples may include monocyclic cycloalkanes such as cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane,

Claims

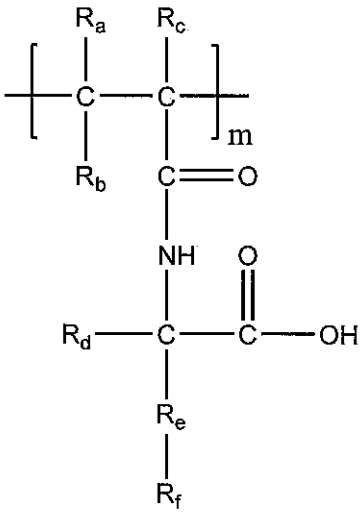
1. A hollow core-shell particle having pores extending through its shell and a plurality of polymer chains that are grafted to the outer surface of the shell, wherein the polymer backbone of said polymer chains comprises monomer units that are functionalized with a group selected from amidines, guanidines, amino acid derivatives and heteroaromatic or non heteroaromatic heterocylic groups, wherein the heterocycles comprise 1 to 3 nitrogen atoms, wherein the particle is a hollow silica sphere.

2. The particle of claim 1, wherein the polymer backbone comprises functionalities selected from either aminocarbonyls, amidines, guanidines, indoles or imidazoles.

3. The particle of claim 1, wherein the polymer is selected from poly(histidine methacrylamide) , poly(arginine methacrylamide) or poly(amidine).

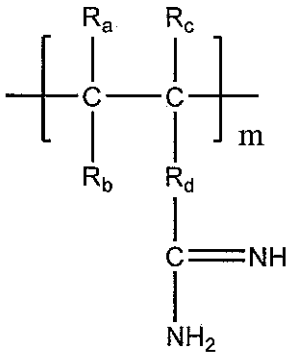
4. The particle of any of the preceding claims wherein the terminal end of the polymer chains comprises a halogen moiety.

5. The particle of any of claim 1 or 2, wherein the polymer comprises at least one repeating monomer unit of formula (Ia) or (Ib)



(Ia)

or



(Ib)

wherein

m is an integer selected in an way that the polymer has a molecular weight selected from the range of 2 kDa to 500 kDa;

R_a, R_b, and R_c represent a group that is independently selected from the group consisting of hydrogen, amine, optionally substituted aliphatic, optionally substituted hetero-aliphatic and optionally substituted carbocyclyl;

R_d represents hydrogen or a direct bond, or R_d represents optionally substituted C_1-C_6-alkyl or optionally substituted C_1-C_6-alkylidene.

R_e represents optionally substituted C_1-C_6-alkylidene;

R_f represents amino, optionally substituted heterocyclyl or an optionally substituted guanidinium group.

6. The particle of claim 5, wherein

R_a, and R_b represent hydrogen;

R_c represents hydrogen, methyl or ethyl;

R_d represents hydrogen or a direct bond;

R_e represents C_1-C_6-alkylene;

R_f represents an amino, aminocarbonyl, amidine, guanidine, indole or imidazole group.

7. The particle of any of the preceding claims, wherein the hydrodynamic diameter of the particle is between about 10 nm to 100 μm.

8. The particle of any of the preceding claims, wherein the diameter of the particle shell is between about 10 nm to 100 μm.

9. The particle of any of the preceding claims, wherein said particle contains 10 % to 90 % (w/w) of the polymer.

10. The particle of any one of the preceding claims, wherein said hollow-core shell particle has a shell that is microporous, mesoporous or macroporous.

11. The particle according to any one of the preceding claims, wherein the pores on the particle shell have an average diameter between 0.1 Å to 50 nm.

12. The particle according to any one of the preceding claims, wherein the hollow core is filled with releasable gas molecules.

13. The particle of claim 12 wherein the gas is oxygen.

14. The particle according to any of the preceding claims which shows an interaction upon exposure to an agent in the environment of the particle or upon temperature changes.

15. The particle according to claim 14, wherein the interaction is a change in particle size or pore size.

16. The particle according to claim 15 wherein the interaction leads to the release of the gas from the hollow core.

17. The particle of any of claims 14 to 16 wherein the agent in the environment is carbon dioxide.

18. A process for making a particle of any of the preceding claims, comprising the steps of

a) modifying the surface of a hollow particle with an amino, halogen, epoxide or thio-carbonyl thioester group;

b) reacting the modified particle with a methacrylate monomer functionalized with a group selected from amidines, guanidines, amino acid derivatives and heteroaromatic or non heteroaromatic heterocyclic groups; and

c) further polymerizing the obtained grafted hollow particle with the monomer of step b).

19. A process for making a particle of any of claims 1 to 17, comprising the steps of

a) modifying the surface of a hollow particle with an amino, halogen, epoxide or thio-carbonyl thioester group;

b) reacting the modified particle with an optionally substituted acrylonitrile;

c) further polymerizing the obtained grafted hollow particle with an acrylonitrile; and

d) reacting the obtained cyano groups of the polymer backbone to amidine groups.

20. A process for loading the particle of any of claims 1 to 17 with a gas, comprising exposing said polymer particle with said gas and allowing the gas to permeate into the hollow particle.

21. Use of a loaded particle prepared by the process of claim 20 for the encapsulation and delivery of gases.

22. A delivery means comprising a plurality of particles according to any of claims 1 to 17, wherein the hollow core is filled with gas molecules.

23. Use of the delivery means of claim 22 to provide oxygen in cosmetic skin care applications.

24. A non-therapeutic use of the delivery means of claim 22 to deliver oxygen site-specific to an oxygen-deprived tissue or cell.