Summary

In one aspect of the present disclosure, there is provided a hybrid nanodot made by a process comprising a step of reacting a mixture of poly(ethylene imine) (PEI) and an amino acid selected from the group consisting of serine, threonine, cysteine, tyrosine, asparagine, glutamine, lysine, aspartic acid, glutamic acid and mixtures thereof, under hydrothermal reaction conditions.

In another aspect of the present disclosure, there is provided a process for producing a hybrid nanoparticle disclosed herein, comprising the process steps of:

(a) dissolving the amino acid and polycationic polymer in an aqueous medium;

(b) heating the obtained solution at elevated temperature and increased pressure; and

(c) separating the hybrid nanoparticles that have formed from the reaction mixture.

In a further aspect of the present disclosure, there is provided a hybrid nanodot disclosed herein for combating bacteria.

In another aspect of the present disclosure, there is provided an antimicrobial composition comprising a hybrid nanodots disclosed herein, optionally together with customary solvents, additives or fillers.

In a further aspect of the present disclosure, there is provided a use of the antimicrobial composition of disclosed herein to combat gram-positive and/or gram-negative bacteria in hygiene applications, preferably surface disinfection.

In one example of the present disclosure, there is provided a hybrid nanodot made by a process comprising a step of reacting a mixture of an amino acid and a polymer selected from polycationic polymers or any copolymers or derivatives of these polymers under hydrothermal reaction conditions.

Advantageously, the hybrid nanodots of the present disclosure may possess tunable photoluminescent, antimicrobial and bacteria-staining properties. Further advantageously, the hybrid nanodots of the present disclosure may be able to disrupt bacterial membrane, release intracellular proteins, thus allowing for potent antibacterial effects. The antibacterial effects of the hybrid nanodots of the present disclosure may be towards broad-spectrum bacteria (both gram-positive and gram-negative) and they may be advantageously effective against multidrug-resistant superbugs, such as *Pseudomonas aeruginosa*.

Also advantageously, the hybrid nanodots of the present disclosure may have small sizes and spherical shapes which may lead to fast interaction between the hybrid nandot and bacteria, which may thus achieve bacterial inhibition almost instantaneously.

Further advantageously, the hybrid nanodots of the present disclosure may have excitation-dependent fluorescent properties which may allow for simultaneous staining of bacteria.

Also advantageously, the hybrid nanodot as defined herein may possess many unique properties such as small size, near neutral charge, bright fluorescence, and abundant functional groups.

Further advantageously, the abundant functional groups on the surface of said hybrid nanodot may be facile for conjugation with biomolecules such as aptamers or antibodies for selective detection of a particular bacteria of interest.

In another example of the present disclosure, there is provided a process for producing a hybrid nanoparticle as defined herein, comprising the process steps of:

(a) dissolving the amino acid and polycationic polymer in an aqueous medium;

(b) heating the obtained solution at elevated temperature and increased pressure; and

(c) separating the hybrid nanoparticles that have formed from the reaction mixture.

Advantageously, the synthesis process defined herein may be a simple scalable one-step hydrothermal reaction from amino acids and selected polymers. Hence, advantageously, said synthesis process may be scaled-up in a straightforward approach.

Also advantageously, the formulation (amino acid-to-polymer ratio) of the hybrid nanodot as defined example may be finely tuned to control the surface properties, such as zeta potential to be near neutral. Therefore, advantageously, said hybrid nanodot may preferentially disrupt membranes of bacteria cells but not mammalian cells, and thus lead to potent antimicrobial activity while improving mammalian cell biocompatibility to achieve a satisfactory therapeutic index.

In yet another example of the present disclosure, there is provided a hybrid particle as defined herein, obtained by any of the processes as defined herein.

In a further example of the present disclosure, there is provided a hybrid nanodot as defined herein for fluorescence-based imaging of cells, preferably bacteria.

Advantageously, the hybrid nanodot as defined herein may possess excitation-dependent fluorescence with high quantum yield. Further advantageously, said hybrid nanodot may possess small size and spherical shape and can undergo fast interaction with the bacteria. When used, said hybrid nanodot may undergo efficient uptake by the bacteria into intracellular compartments, and may be an efficient staining agent for potential bacterial detection applications. Therefore, advantageously, said hybrid nanodot has high potential for simultaneous multicolor bacteria imaging and detection.

In another example of the present disclosure, there is provided a hybrid nanodot as defined herein for combating bacteria.

Advantageously, the hybrid nanodot as defined herein may possess small size and spherical shape and can undergo fast interaction with the bacteria membranes. When used, said hybrid nanodot may demonstrate strong bacteria membrane disruption capability.

Advantageously, said hybrid nanodot may effectively inhibit a broad spectrum of bacteria growth (both gram-positive and gram-negative). Further advantageously, the inhibition may occur immediately upon simple mixing. When used, said hybrid nanodot may be able to kill more than 99% of bacteria species within 60 minutes.

Advantageously, the hybrid nanodot as defined herein may also be effective against multidrug-resistant bacteria.

In yet another example of the present disclosure, there is provided an antimicrobial composition comprising a hybrid nanodot as defined herein, optionally together with customary solvents, additives or fillers.

In a further example of the present disclosure, there is provided a use of the antimicrobial composition as defined herein to combat gram-positive and/or gram-negative bacteria in hygiene applications, preferably surface disinfection.

In another example of the present disclosure, there is provided a method of combating bacteria by exposing the bacteria with a hybrid nanodot as defined herein.

Claims

1. A hybrid nanodot made by a process comprising a step of reacting a mixture of poly(ethylene imine) (PEI) and an amino acid selected from the group consisting of serine, threonine, cysteine, tyrosine, asparagine, glutamine, lysine, aspartic acid, glutamic acid and mixtures thereof, under hydrothermal reaction conditions.

2. The hybrid nanodot of claim 1, wherein the PEI has an average molecular weight of about 200 to 50,000 g/mol, preferably about 1,000 to 5,000 g/mol and most preferably about 1,500 to 2,100 g/mol determined by light scattering.

3. The hybrid nanodot of claim 1 or 2, wherein the PEI has an average molecular weight of about 1200 to 1800 g/mol determined by light scattering.

4. The hybrid nanodot of any of claims 1 to 3, wherein the PEI has an average molecular weight of about 1800 g/mol determined by light scattering.

5. The hybrid nanodot of any one of claims 1 to 4, wherein the amino acid is selected from the group consisting of serine, threonine, and lysine.

6. The hybrid nanodot of any one of claims 1 to 5, wherein the weight ratio of amino acid to PEI is about 10:1 to 1:2, preferably 5:1 to 1:1, more preferably 3:1 to 1.25:1 and most preferably 2.5:1 to 1.5:1.

7. The hybrid nanodot of any one of claims 1 to 6, wherein the weight ratio of amino acid to PEI is about 3:1 to about 1:1.

8. The hybrid nanodot of any one of claims 1 to 7, wherein the particle size of the hybrid nanodot is about 1 to 100 nm, preferably 2 to 50 nm, more preferably 5 to 40 nm and most preferably 7 to 20 nm.

9. The hybrid nanodot of any of claims 1 to 8, wherein the nanodots exhibit excitation-dependent fluorescence emission.

10. The hybrid nanodot of any one of claims 1 to 9 for fluorescence-based imaging of cells, preferably bacteria.

11. The hybrid nanodot of any one of claims 1 to 10, which substantially consists of a hydrophobic sp^2 carbon network with hydrophilic functional groups on the surface.

12. A process for producing a hybrid nanoparticle according to any one of claims 1 to 11, comprising the process steps of:

(a) dissolving the amino acid and polycationic polymer in an aqueous medium;

(b) heating the obtained solution at elevated temperature and increased pressure; and

(c) separating the hybrid nanoparticles that have formed from the reaction mixture.

13. The process of claim 12, wherein the temperature of step (b) is between about 120 to 250 °C, preferably 150 to 210 °C and more preferably 170 to 190 °C.

14. The process according to claim 12 or 13, wherein the increased pressure in step (b) is achieved by hydrothermal reaction in an autoclave.

15. The process according to any one of claims 12 to 14, wherein the reaction in step (b) is run for 1 to 48 hours, preferably 2 to 36 hours, more preferably 20 to 30 hours and most preferably about 23 to 25 hours.

16. The process according to any one of claims 12 to 15, wherein the separation step (c) comprises one, several or all of the following steps:

(a) centrifugation to remove precipitate;

(b) filtration to remove precipitate;

(c) dialysis with a given weight cut off against purified water, preferably a weight cut off of about 3,000 g/mol; and

(d) lyophilizing and re-suspending the obtained product in ultrapure water.

17. A hybrid nanodot according to any of claims 1 to 11 for combating bacteria.

18. An antimicrobial composition comprising a hybrid nanodots according to any of claims 1 to 11, optionally together with customary solvents, additives or fillers.

19. The antimicrobial composition according to claim 18, wherein the hybrid nanodots are dispersed in an aqueous medium at a concentration of at least about 50 µg/mL, preferably of about 100 µg/mL to 10 mg/L, more preferably 150 µg/mL to 1 mg/L.

20. Use of the antimicrobial composition of claim 19 to combat gram-positive and/or gram-negative bacteria in hygiene applications, preferably surface disinfection.