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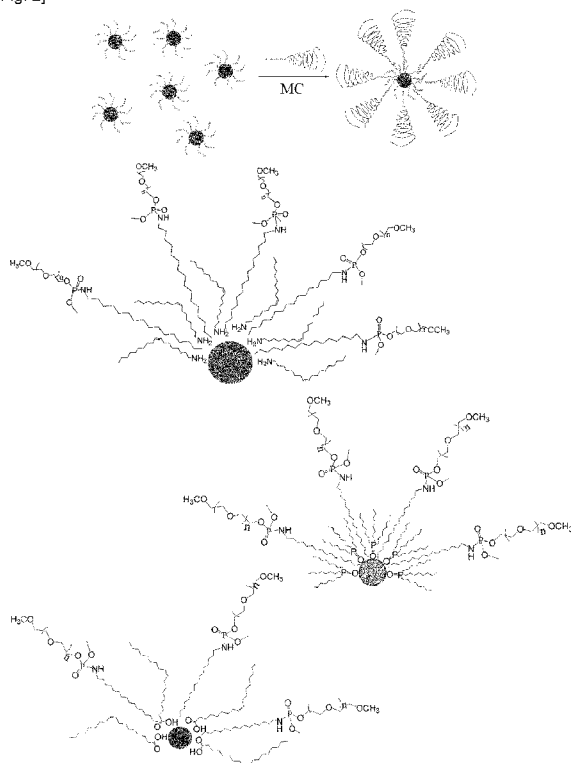
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[Continued on next page]

(54) Title: SURFACTANTS FOR WATER DISPERSING OF NANOPARTICLES

[Fig. 2]



(57) Abstract: A surfactant capable of stably dispersing nanoparticles in water is disclosed. The disclosed surfactant is capable of stably dispersing a variety of nanoparticles in water while maintaining their physical properties. It is applicable to various nanoparticles such as metals, metal oxides, quantum dots, and so forth.



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Description

Title of Invention: SURFACTANTS FOR WATER DISPERSING OF NANOPARTICLES

Technical Field

[0001] The present disclosure relates to a surfactant capable of stably dispersing nanoparticles in water.

[0002]

Background Art

[0003] Nanoparticles have a high surface area to volume ratio and exhibit properties quite different from those of the bulk material due to the quantum confinement effect [Alivisatos, A. P. *Science*, 271: 933 (1996)]. Among various nanoparticles, fluorescent quantum dots and magnetic iron oxide nanoparticles may be used for biological imaging applications. For this, the nanoparticles need to have uniform size and be water-soluble [Gao, X. et al., *S. Nat. Biotechnol.*, 22: 969-976 (2004); Bruchez, J. M. et al., *A. P. Science*, 281: 2013-2016 (1998); Chan, W. C. W. et al., *S. Science*, 281: 2016-2018 (1998); and Weissleder, R. et al., *L. Nat. Biotechnol.*, 23: 1418 (1998)]. In this context, the most pertinent way may be to produce the nanoparticles in water. However, it is impossible to form uniform nanoparticles in water with the synthesis method known thus far. As for the quantum dots, they give too low a quantum yield when they are synthesized in water, making them inapplicable to actual imaging. Also, there is no case of producing uniform iron oxide nanoparticles in water reported.

[0004] Accordingly, in general, the process of synthesizing uniform quantum dots or iron oxide nanoparticles in an organic solvent and then transferring them to water is required.

[0005] Recently, synthesis techniques for uniform quantum dots such as cadmium selenide (CdSe) and cadmium telluride (CdTe) and magnetic nanoparticles such as iron oxide, iron-platinum (FePt) and cobalt have been developed, and several surfactants for making them water-soluble have been reported.

[0006] In order to water-soluble quantum dots, water-soluble polymers, lipids or thiol ligands such as thiol dendrimers and dithiols have been used. Further, 4-(dimethylamino)pyridine has been used to transfer various metal nanoparticles to the water phase. For iron oxide, Weissleder et al. could dissolve iron oxide nanoparticles of various sizes in water using dextran and used them for magnetic resonance imaging (MRI). In addition, use of a polymer having a cyclodextran or maleic anhydride backbone to dissolve various nanoparticles in water has been reported.

[0007] Although a surfactant capable of dissolving iron oxide, quantum dots and various

metals in water was reported, there remains the problem of quantum yield and stability.

[0008] As for the quantum dots, if the quantum yield in an organic solvent is 50%, dissolution of them in water using a surfactant results in a yield only about 50 to 60% of that in the organic solvent (i.e. the final yield is only 25 to 30%).

[0009] As for the iron oxide nanoparticles, there are few researches about solubilization in water in spite of the necessity. In most cases, phospholipids or dextrans have been used to form vesicles and thereby dissolve them in water. However, in this case, aggregation may occur at low concentrations. This phenomenon is more distinct with magnetic nanoparticles probably because of stronger attractions between them than other nanoparticles.

[0010]

Summary of Invention

Technical Problem

[0011] The inventors have worked to improve quantum yield and stability of nanoparticles in water. As a result, they have developed a novel surfactant for dispersing in water and found out that, when the novel surfactant for dispersing in water is used, a variety of nanoparticles may be stably dispersed in water without aggregation and solvent replacement is possible at room temperature, thereby overcoming the quantum yield problem for quantum dots.

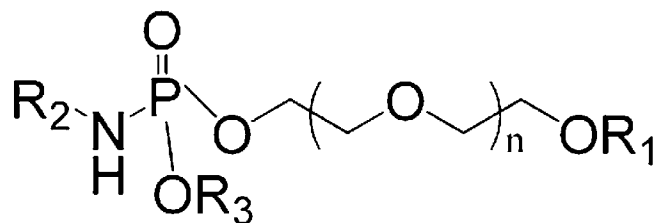
[0012] Thus, the present disclosure is directed to providing a novel surfactant for dispersing nanoparticles in water capable of solving the quantum yield and stability problems of the nanoparticles.

[0013]

Solution to Problem

[0014] In an aspect, the present disclosure provides a surfactant for dispersing nanoparticles in water represented by Chemical Formula 1:

[0015]



(1)

[0016] wherein n is from 1 to 500; R₁ is C₁-C₃₀ alkyl; R₂ is hydrogen or C₁-C₅₀ alkyl; and R₃ is hydrogen or C₁-C₃₀ alkyl.

[0017]

Advantageous Effects of Invention

- [0018] The surfactant for dispersing nanoparticles in water according to the present disclosure is capable of stably dispersing a variety of nanoparticles in water while maintaining their physical properties. Hence, it will be widely applicable to various nanoparticles including metals, metal oxides, quantum dots, and so forth.
- [0019] The quantum dots made water-soluble using the surfactant according to the present disclosure may be introduced into an organism to monitor biological metabolisms or diagnose various diseases including cancer macroscopically, and may be introduced into cells to study various cellular mechanisms microscopically. Since the surfactant can be synthesized in large scale very economically, it will be able to replace the expensive phospholipids currently used to obtain water-soluble nanoparticles.
- [0020] In addition, the magnetic nanoparticles made water-soluble may be utilized for magnetic resonance imaging (MRI).

Brief Description of Drawings

- [0021] The above and other objects, features and advantages of the present disclosure will become apparent from the following description of certain exemplary embodiments given in conjunction with the accompanying drawings, in which:
- [0022] Fig. 1 shows a result of measuring hydrated radius by gel-filtration chromatography (left) and light scattering (right);
- [0023] Fig. 2 schematically illustrates the transfer of nanoparticles from a dichloromethane (MC) solvent to water using a surfactant (top) and the transfer of nanoparticles to water using oleic acid, oleylamine or trioctylphosphine (TOP)/trioctylphosphine oxide (TOPO) as a stabilizer (bottom);
- [0024] Fig. 3 shows MALDI-TOF analysis result of polyethylene glycol methyl ether (mPEG, $M_n = 2000$), an intermediate and a final product, from top to bottom;
- [0025] Fig. 4 shows ^1H NMR analysis result of an intermediate (top) and a final product (bottom);
- [0026] In Fig. 5, (a) shows Fe_2O_3 nanoparticles dissolved in hexane, (b) shows Fe_2O_3 nanoparticles dispersed in water using a surfactant (using mPEG with $M_n = 5000$) according to an embodiment of the present disclosure, (c) shows Fe_2O_3 nanoparticles dispersed in water using a surfactant (using mPEG with $M_n = 2000$) according to another embodiment of the present disclosure, (d) shows Fe_2O_3 nanoparticles dispersed in water using a surfactant (using mPEG with $M_n = 750$) according to another embodiment of the present disclosure, (e) shows Fe_2O_3 nanoparticles dispersed in water using a di(mPEG)-monoalkyl type surfactant, and (f) shows Fe_2O_3 nanoparticles dispersed in water using a mono(mPEG)-dialkyl type surfactant;
- [0027] Fig. 6 shows nanoparticles dissolved in hexane (left) or in water (right) [(a) shows CdSe/ZnS nanoparticles observed under UV light (The image inserted at the left

bottom shows the nanoparticles observed under visible light, and the image inserted at the right bottom is a TEM image of the nanoparticles in water.), (b) shows InP/ZnS nanoparticles (The graph inserted at the right bottom shows fluorescence intensity of the nanoparticles in hexane and water.), (c) shows Au nanoparticles (The image inserted at the right top is a TEM image of the nanoparticles, and the graph inserted at the left bottom shows absorbance of the nanoparticles in water (red) or hexane (blue).), and (d) shows Fe₂O₃ nanoparticles (The image inserted at the left top is a TEM image of the nanoparticles in water, and the image inserted at the right bottom shows the nanoparticles in water under a magnetic field).];

[0028] Fig. 7 shows nanoparticles used as a magnetic resonance imaging (MRI) imaging agent dispersed in water using a surfactant according to an embodiment of the present disclosure (It can be seen that the role as the MRI imaging agent is retained.);

[0029] Fig. 8 shows absorption spectrum of Au nanoparticles synthesized in an organic solvent and then dispersed in water; and

[0030] Fig. 9 shows CdSe/ZnS, InP/ZnS, Au and Fe₂O₃ nanoparticles, from left to right, dispersed in hexane (left), and the nanoparticles dispersed in water using a surfactant according to an embodiment of the present disclosure (right) (In each image, the lower layer is a water layer and the upper layer is a hexane layer.).

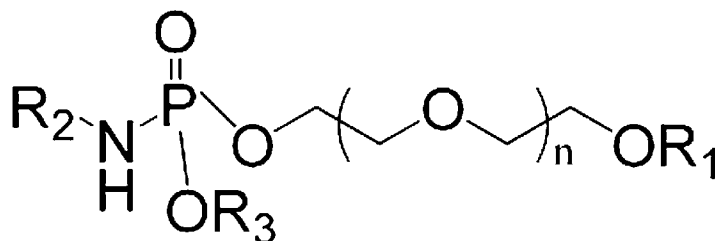
[0031]

Best Mode for Carrying out the Invention

[0032] Hereinafter, the embodiments of the present disclosure will be described in detail with reference to accompanying drawings.

[0033] The present disclosure relates to a novel surfactant for dispersing nanoparticles in water, more particularly to a surfactant for dispersing nanoparticles in water represented by Chemical Formula 1:

[0034]



(1)

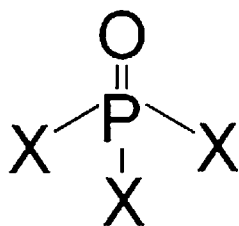
[0035] wherein n is from 1 to 500; R₁ is C₁-C₃₀ alkyl; R₂ is hydrogen or C₁-C₅₀ alkyl; and R₃ is hydrogen or C₁-C₃₀ alkyl.

[0036] In the context of the present disclosure, the nanoparticles refer to general nanoparticles, for example, metals such as gold (Au) and palladium (Pd), magnetic oxides such as Fe₂O₃ and Fe₃O₄ or quantum dots such as CdSe, InP/ZnS and CdSe/ZnS

core-shell nanoparticles.

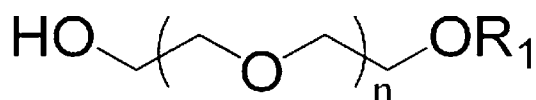
[0037] The surfactant represented by Chemical Formula 1 may be synthesized using compounds represented by Chemical Formulae 2 to 7 according to Scheme 1.

[0038]



(2)

[0039]



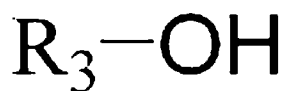
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[0040]



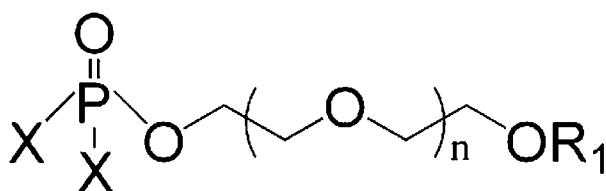
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[0041]



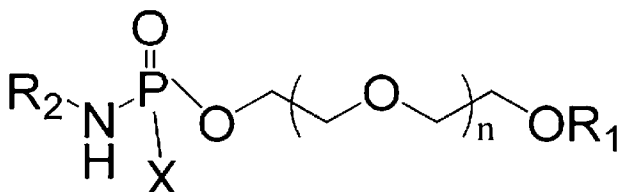
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[0042]



(6)

[0043]

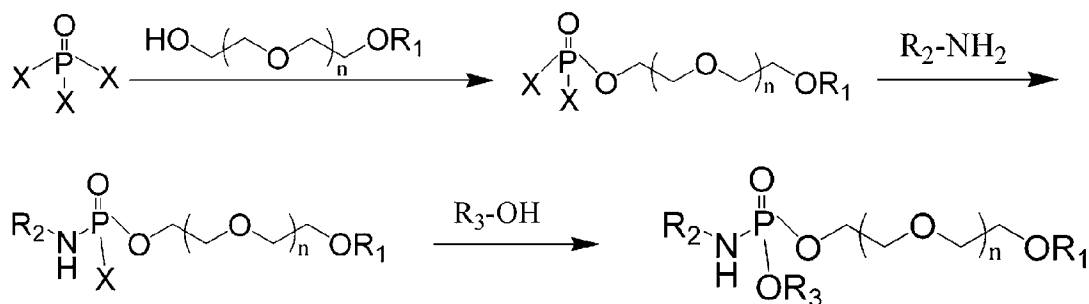


(7)

[0044]

[Scheme 1]

[0045]



[0046] In Chemical Formulae 2 to 7 and Scheme 1, n is from 1 to 500; R_1 is C_1 - C_{30} alkyl; R_2 is hydrogen or C_1 - C_{30} alkyl; R_3 is hydrogen or C_1 - C_{30} alkyl; and X is F, Cl, Br or I.

[0047] The surfactant for dispersing nanoparticles in water represented by Chemical Formula 1 may be prepared by a process including:

[0048] (a) reacting a compound represented by Chemical Formula 2 with a compound represented by Chemical Formula 3 at 10 to 200 °C for 1 to 24 hours to prepare a compound represented by Chemical Formula 6;

[0049] (b) reacting the resulting compound represented by Chemical Formula 6 with a compound represented by Chemical Formula 4 at 10 to 200 °C for 0.5 to 48 hours to prepare a compound represented by Chemical Formula 7; and

[0050] (c) reacting the resulting compound represented by Chemical Formula 7 with a compound represented by Chemical Formula 5 at 10 to 200 °C for 1 to 48 hours:

[0051] All the reactions in the above steps are nucleophilic substitution reactions.

[0052] First, in the compound represented by Chemical Formula 2 of the step (a), X may be a halogen element such as F, Cl, Br or I. Specifically, it may be Cl.

[0053] In the compound represented by Chemical Formula 3, R_1 may be C_1 - C_{30} alkyl. Specifically, it may be C_1 - C_5 alkyl. For example, the compound represented by Chemical Formula 3 may be methoxy-PEG, ethoxy-PEG, or the like. And, n may be from 1 to 500, specifically from 10 to 200.

[0054] In the step (a), the compound represented by Chemical Formula 2 may be added in excess to achieve 1 : 1 reaction. Otherwise, the compound represented by Chemical Formula 3 may be substituted with the compound represented by Chemical Formula 2 two or more times and the reaction may not proceed to the next step.

[0055] In the compound represented by Chemical Formula 4 of the step (b), R_2 may be hydrogen or C_1 - C_{50} alkyl. Specifically, it may be C_1 - C_{20} alkyl. For example, the compound represented by Chemical Formula 4 may be hexadecylamine (HDA), octadecylamine (ODA), or the like.

[0056] In the compound represented by Chemical Formula 5 of the step (c), R_3 may be hydrogen or C_1 - C_{30} alkyl. Specifically, it may be C_1 - C_5 alkyl. For example, the compound represented by Chemical Formula 5 may be methanol, ethanol, isopropanol, butanol, or the like.

- [0057] In the step (c), the halogen of the compound represented by Chemical Formula 7 is substituted with the compound represented by Chemical Formula 5, thereby resulting in a non-toxic surfactant for dispersing nanoparticles in water.
- [0058] In order to substitute the compound represented by Chemical Formula 7 with the compound represented by Chemical Formula 5 to a higher degree, the step (c) may be repeated several times. It is because the substitution with the compound represented by Chemical Formula does not occur easily if the compound represented by Chemical Formula 4 has a long alkyl chain and thus is strongly nonpolar.
- [0059] All the reactions in the above steps are carried out at 30 to 60 °C under nitrogen atmosphere. It is because the moisture included in the air may act as a nucleophile and interfere with the reactions. In the reactions, an aprotic solvent such as tetrahydrofuran (THF) may be used.
- [0060] Unlike other surfactants for dispersing in water, the surfactant for dispersing nanoparticles in water prepared in accordance with the present disclosure allows solvent replacement at room temperature. Although quantum dots generally experience decrease in quantum yield when they are transferred from an organic solvent to water, due to heating at high temperature, the surfactant according to the present disclosure experiences little change in quantum yield since the solvent can be replaced at room temperature.

[0061]

Mode for the Invention

- [0062] The examples and experiments will now be described. The following examples and experiments are for illustrative purposes only and not intended to limit the scope of the present disclosure.
- [0063] Example 1: Preparation of surfactant for dispersing nanoparticles in water
- [0064] Dried polyethylene glycol methyl ether (mPEG, $M_n = 2000$, 2 g, 1 mmol) and POCl_3 (0.5 mL) were dissolved in anhydrous THF (20 mL) in a 250 mL flask. Then, reaction was performed at 40 °C for 12 hours. 1 mmol of mPEG was reacted with 5 mmol of POCl_3 in order to achieve 1:1 reaction. In order to remove unreacted POCl_3 and HCl resulting from the reaction, the reaction mixture was dried in vacuum at 40 °C for 2 hours and then dissolved in anhydrous THF (15 mL).
- [0065] Hexadecylamine (HDA, 0.241 g, 1 mmol) was dried in vacuum at 120 °C for 2 hours, dissolved in THF (3 mL), and then added to the 250 mL flask containing the reaction mixture. After reaction for 24 hours, HCl and THF were removed by drying in vacuum for 2 hours. Then, addition of MeOH (5 mL), reaction at 60 °C for 1 hour and removal of MeOH was repeated 3 times to accomplish complete substitution with MeOH. It is because, since the alkyl chain of HDA is nonpolar, a complete substitution with MeOH

is not easy. Finally, in order to remove HCl, ethylenediamine (EDA, 1 mL) was added and stirred for 30 minutes to form salt. Then, THF and EDA were removed by drying in vacuum. After dissolving in dichloromethane (MC), which is less polar than THF, HCl salt was removed by centrifugation and only the final product dissolved in the supernatant was collected. Structure analysis was carried out by ^{31}P NMR, ^1H NMR and MALDI-TOF.

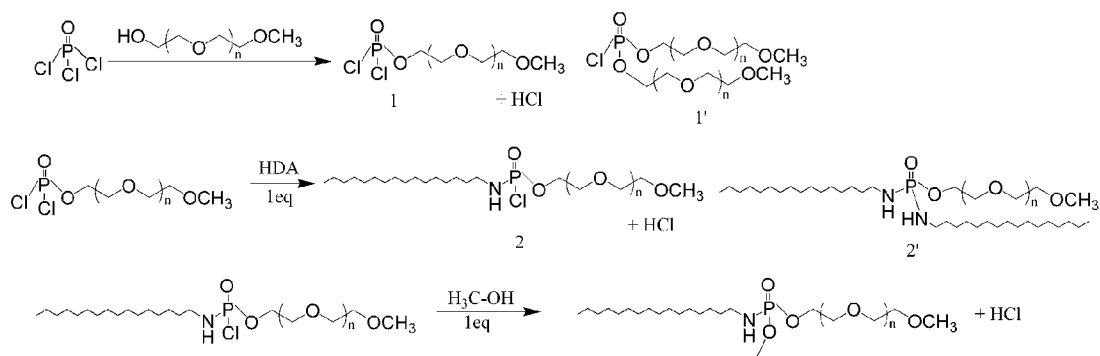
[0066] The reaction procedure is summarized in Scheme 2 below. MALDI-TOF result is shown in Fig. 3, and ^1H NMR result is shown in Fig. 4. Fig. 3 shows MALDI-TOF analysis result of mPEG ($M_n = 2000$), an intermediate formed from the reaction of mPEG with POCl_3 and a final product, from top to bottom. The shift of mass peaks reveals that the substitution reaction occurred successfully. In the early stage of the reaction, mono-mPEG-substituted intermediate was produced because POCl_3 was used in excess of mPEG. In the later stage of the reaction, only monoalkyl-substituted, not dialkyl-substituted, intermediate was produced, because of low reactivity of Cl.

[0067] ^1H NMR analysis result of the final product shown in Fig. 4 confirms the presence of mono-mPEG- and monoalkyl-substituted compounds. The ethylene peak of mPEG was observed at 3.6 ppm and the terminal $-\text{OCH}_3$ peak of mPEG was identified at 3.382 ppm. The three broad peaks at 1.76 ppm, 1.23 ppm and 0.88 ppm are due to $-\text{CH}_2\text{NHP}-$, $-\text{CH}_2-$ and terminal $-\text{CH}_3$ of HDA.

[0068] ^{31}P NMR data also confirms the successful reaction.

[0069] [Scheme 2]

[0070]



[0071] Example 2: Comparison of performance of surfactant for dispersing nanoparticles in water depending on molecular weight of mPEG

[0072] In order to find a surfactant for dispersing nanoparticles in water with optimized performance, experiment was carried out while changing the molecular weight of mPEG. Performance of the surfactants synthesized using mPEG with a molecular weight of 750, 2000 and 5000 was compared. For mPEG with a molecular weight of 750 (mPEG 750), the surfactant was synthesized by dissolving dried mPEG ($M_n = 750$, 0.75 g, 1 mmol) and POCl_3 (0.5 mL) in anhydrous THF (10 mL) in a 250 mL flask and reacting at room temperature for 12 hours, with the remaining procedure being identical to that

of Example 1. For mPEG with a molecular weight of 2000 (mPEG 2000), the surfactant was synthesized in the same manner as Example 1. For mPEG with a molecular weight of 5000 (mPEG 5000), the surfactant was synthesized by dissolving dried mPEG ($M_n = 5000$, 5 g, 1 mmol) and POCl_3 (0.5 mL) in anhydrous THF (20 mL) in a 250 mL flask and reacting at 60 °C for 12 hours, with the remaining procedure being identical to that of Example 1. Fe_2O_3 nanoparticles of the same amount (5 equivalents) were mixed in dichloromethane with each of the surfactants. After completely evaporating the solvent at room temperature for 15 to 20 minutes, the remaining mixture was dispersed again in water. The nanoparticles were dispersed well in water when mPEG 5000 or mPEG 2000 was used. But, they were not dispersed well when mPEG 750 was used.

[0073] The result is shown in Fig. 5 [(b) $M_n = 5000$, (c) $M_n = 2000$, (d) $M_n = 750$].

[0074] The Fe content in each sample was measured using inductively coupled plasma (ICP). The contents were 0.203 mg/mL, 0.148 mg/mL and 0.010 mg/mL for (b), (c) and (d), respectively. I.e., the amount of the Fe_2O_3 nanoparticles dispersed in water increased as the molecular weight of mPEG increased. Thus, it can be concluded that a long hydrophilic group is required to disperse nanoparticles in water.

[0075] [Table 1]

Comparison of performance of surfactant for dispersing nanoparticles in water depending on molecular weight of mPEG	
Molecular weight of mPEG	Fe content measured using ICP (mg/mL)
$M_n = 5000$	0.203
$M_n = 2000$	0.148
$M_n = 750$	0.010

[0076]

[0077] Example 3: Comparison of performance of surfactant for dispersing nanoparticles in water depending on structure

[0078] In order to study the performance depending on the surfactant structure, di(mPEG)-monoalkyl and mono(mPEG)-dialkyl type surfactants were synthesized and tested, rather than the common mono(mPEG)-monoalkyl-substituted surfactant. mPEG 2000 was used and each surfactant was prepared in the same manner as Example 1. Fe_2O_3 nanoparticles of the same amount (5 equivalents) were mixed in dichloromethane with each of the surfactants. After completely evaporating the solvent at room temperature for 15 to 20 minutes, the remaining mixture was dispersed again in water.

[0079] The result is shown in Fig. 5 (c), (e) and (f). (e) and (f) showed very poor ability to disperse the nanoparticles in water.

[0080] [Table 2]

Comparison of performance of surfactant for dispersing nanoparticles in water depending on structure	
Surfactant structure	Ability to disperse nanoparticles in water
Mono(mPEG)-monoalkyl [Fig. 5 (c)]	Good
Di(mPEG)-monoalkyl [Fig. 5 (e)]	Poor
Mono(mPEG)-dialkyl [Fig. 5 (f)]	Poor

[0081]

[0082] From Examples 2 and 3, it can be concluded that a mono(mPEG)-monoalkyl-substituted surfactant using mPEG with $M_n = 5000$ has the best ability to disperse nanoparticles in water.

[0083] Example 4: Comparison of performance of surfactant for dispersing nanoparticles in water depending on original stabilizer of nanoparticles

[0084] ^{31}P -NMR reveals that the surfactant forms micelles around the nanoparticles - (*the same phosphate peaks are found both in water and hexane*). This is due to the attraction with the original stabilizer - (*the original stabilizer refers to the stabilizer on the surface of the nanoparticles. Nanoparticles tend to aggregate because of large surface energy. The stabilizer stabilizes the surface of the nanoparticles in solvents and thereby prevents aggregation.*) - oleic acid, oleylamine or trioctylphosphine oxide (TOPO), which are used to stabilize the alkyl moiety of the surfactant and the nanoparticles in solvents. Accordingly, the versatility of the surfactant depends on the structure of the original stabilizer.

[0085] Three commonly used stabilizers oleic acid, oleylamine and TOP/TOPO were tested. In general, oleic acid is used for Pd, Fe_2O_3 and InP/ZnS nanoparticles, oleylamine is used for Au nanoparticles, and TOP/TOPO is used for CdSe/ZnS nanoparticles. They were synthesized referring to the following literatures [(a) N. R. Jana, Y. Chen and X. Peng, *Chem. Mater.*, 2004, 16, 3931; (b) J. Park, K. An, Y. Hwang, J.-G. Park, H.-J. Noh, J.-Y. Kim, J.-H. Park, N.-M. Hwang and T. Hyeon, *Nat. Mater.*, 2004, 3, 891; (c) F. X. Redl, C. T. Black, G. C. Papaefthymiou, R. L. Sandstrom, M. Yin, H. Zeng, C. B. Murray and S. P. O'Brien, *J. Am. Chem. Soc.*, 2004, 126, 14583]. The individual nanoparticles were transferred from the organic solvent to water in the same manner as Example 2. The result is shown in Fig. 6. Fig. 6 shows that the nanoparticles were successfully transferred from hexane to water. The nanoparticles were dispersed well in water, with no change in physical properties. In case of Fig. 6 (a) and (b), the photoluminescence peak did not change after transfer to water. The quantum yield in water was about 65% of that in hexane. When a surfactant with mPEG 5000 was used, the

quantum yield was as high as about 70%.

- [0086] The quantum yield was calculated from the absorption spectrum and fluorescence spectrum of CdSe/ZnS nanoparticles when they were dispersed in hexane or water. The absorption spectrum was measured using a UV-Vis spectrophotometer, and the fluorescence spectrum was measured using a fluorescence spectrophotometer. Rhodamine 590 was used as a reference organic dye. The quantum yield of the dye in ethanol was 95%. The quantum yield was calculated according to the following equation (Q = quantum yield, A = area under fluorescence peak, I = absorbance at excitation wavelength, n = refractive index of solvent, a = CdSe/ZnS, b = organic dye).

[0087]

$$Q_a = Q_b \times \frac{I_a \times A_b \times n_a^2}{I_b \times A_a \times n_b^2}$$

- [0088] The graph inserted in Fig. 6 (c) shows optical absorption of Au nanoparticles in water (red) or in hexane (blue). Both exhibit the same surface plasmon resonance at 530 nm. Fig. 6 (d) shows that Fe₂O₃ nanoparticles dispersed in water at high concentration exhibits a ferrofluid state and thus is applicable to various fields.

- [0089] Example 5: Measurement of quantum yield when surfactant for dispersing nanoparticles in water was used

- [0090] Fe₂O₃ nanoparticles of the same amount (5 equivalents) were mixed in dichloromethane with each of the synthesized surfactants. After completely evaporating the solvent at room temperature for 15 to 20 minutes, the remaining mixture was dispersed again in water. The quantum yield was calculated from the absorption spectrum and fluorescence spectrum of CdSe/ZnS nanoparticles when they were dispersed in hexane or water. The absorption spectrum was measured using a UV-Vis spectrophotometer, and the fluorescence spectrum was measured using a fluorescence spectrophotometer. Rhodamine 590 was used as a reference organic dye. The quantum yield of the dye in ethanol was 95%. The quantum yield was calculated according to the following equation [Q = quantum yield, A = area under fluorescence peak, I = absorbance at excitation wavelength, n = refractive index of solvent, a = CdSe/ZnS, b = organic dye (Rhodamine 590)]. The quantum yield was about 70-80% of that in hexane.

[0091]

$$Q_a = Q_b \times \frac{I_a \times A_b \times n_a^2}{I_b \times A_a \times n_b^2}$$

- [0092] When mercaptopropionic acid or phospholipid, which is commonly used to disperse nanoparticles in water, is used, the quantum yield is only about 50% of that in hexanes.

In contrast, when the surfactant according to the present disclosure was used, the quantum yield was about 70-80% of that in hexane. This is because the dispersing in water is performed at room temperature without heating.

[0093] Example 6: Test of applicability of surfactant for dispersing nanoparticles in water for nanoimaging

[0094] In order to test whether the surfactant for dispersing nanoparticles in water according to the present disclosure is applicable to nanobioimaging, hydrated radius was measured by light scattering and gel-filtration chromatography. As seen in Fig. 1, hydrated radius was measured as 12 nm by gel-filtration chromatography, and as 15 nm by light scattering. For nanoimaging, the hydrated radius is a very important factor. For example, in sentinel lymph node mapping, if the hydrated radius is smaller than 5 nm, the nanoparticles diffuse into the blood vessels. If the hydrated radius is 5 to 10 nm, they do not stop at the sentinel lymph node but pass by to the next lymph node. Meanwhile, if the hydrated radius is larger than 300 nm, the nanoparticles cannot move. In MRI imaging, a hydrated radius which is smaller than 30 nm is required for introduction into cells. The hydrated radius is not the simple addition of the size of the nanoparticle with that of the surfactant in water, but depends on relative binding and 3-dimensional structure.

[0095] Fig. 7 shows nanoparticles used as an MRI imaging agent dispersed in water using the surfactant according to the present disclosure. It can be seen that the role as the MRI imaging agent is retained. The images are T₂-weighted images actually used for clinical diagnosis and treatment, obtained at room temperature with 1.5 T.

[0096] The present application contains subject matter related to Korean Patent Application No. 10-2010-0032851, filed in the Korean Intellectual Property Office on April 9, 2010, the entire contents of which is incorporated herein by reference.

[0097] Those skilled in the art will appreciate that the conceptions and specific embodiments disclosed in the foregoing description may be readily utilized as a basis for modifying or designing other embodiments for carrying out the same purposes of the present disclosure. Those skilled in the art will also appreciate that such equivalent embodiments do not depart from the spirit and scope of the disclosure as set forth in the appended claims.

[0098]

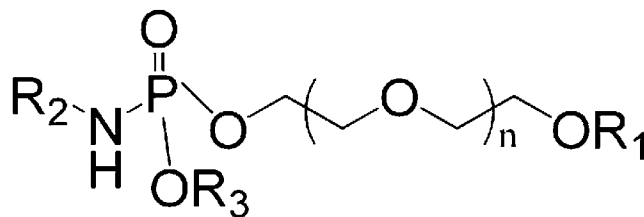
Industrial Applicability

[0099] The surfactant for dispersing nanoparticles in water according to the present disclosure will be useful in nanobioimaging applications, for example, as an MRI imaging agent.

[0100]

Claims

[Claim 1] A surfactant for dispersing nanoparticles in water represented by Chemical Formula 1:



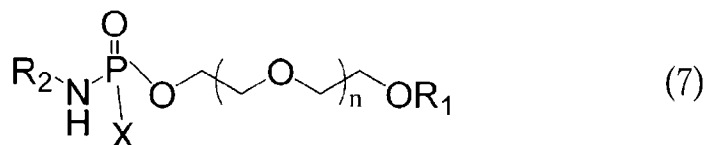
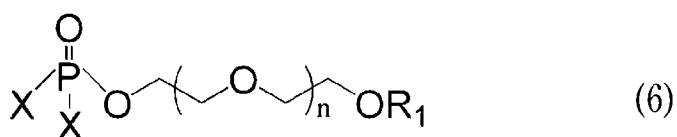
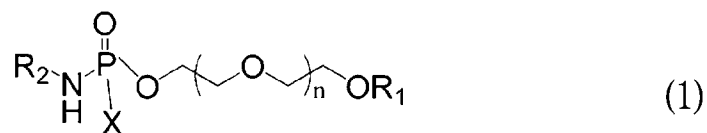
(1)

wherein n is from 1 to 500; R₁ is C₁-C₃₀ alkyl; R₂ is hydrogen or C₁-C₅₀ alkyl; and R₃ is hydrogen or C₁-C₃₀ alkyl.

[Claim 2] The surfactant for dispersing nanoparticles in water according to claim 1, wherein the nanoparticles are gold (Au) nanoparticles, palladium (Pd) nanoparticles, Fe₂O₃ nanoparticles, Fe₃O₄ nanoparticles, CdSe nanoparticles, InP/ZnS nanoparticles or CdSe/ZnS nanoparticles.

[Claim 3] The surfactant for dispersing nanoparticles in water according to claim 1, wherein, in Chemical Formula 1, n is from 10 to 200; R₁ is C₁-C₅ alkyl; R₂ is C₁-C₂₀ alkyl; and R₃ is C₁-C₅ alkyl.

[Claim 4] A method for preparing a surfactant for dispersing nanoparticles in water represented by Chemical Formula 1, comprising:
 reacting a compound represented by Chemical Formula 2 with a compound represented by Chemical Formula 3 at 10 to 200 °C for 1 to 24 hours to prepare a compound represented by Chemical Formula 6;
 reacting the resulting compound represented by Chemical Formula 6 with a compound represented by Chemical Formula 4 at 10 to 200 °C for 0.5 to 48 hours to prepare a compound represented by Chemical Formula 7; and
 reacting the resulting compound represented by Chemical Formula 7 with a compound represented by Chemical Formula 5 at 10 to 200 °C for 1 to 48 hours:

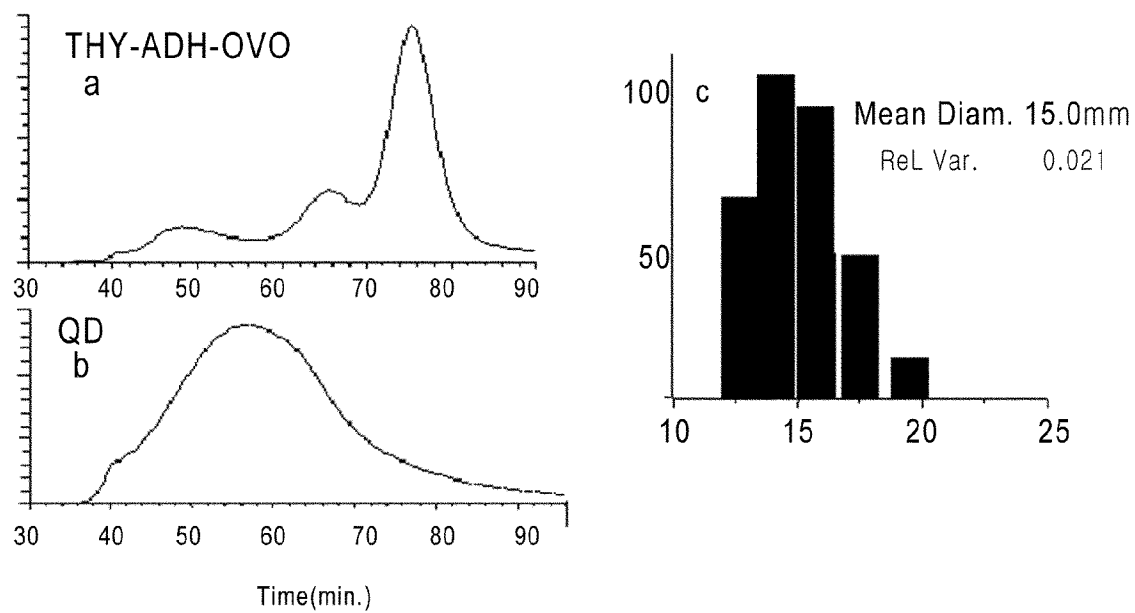


wherein n is from 1 to 500; R₁ is C₁-C₃₀ alkyl; R₂ is hydrogen or C₁-C₃₀ alkyl; R₃ is hydrogen or C₁-C₃₀ alkyl; and X is F, Cl, Br or I.

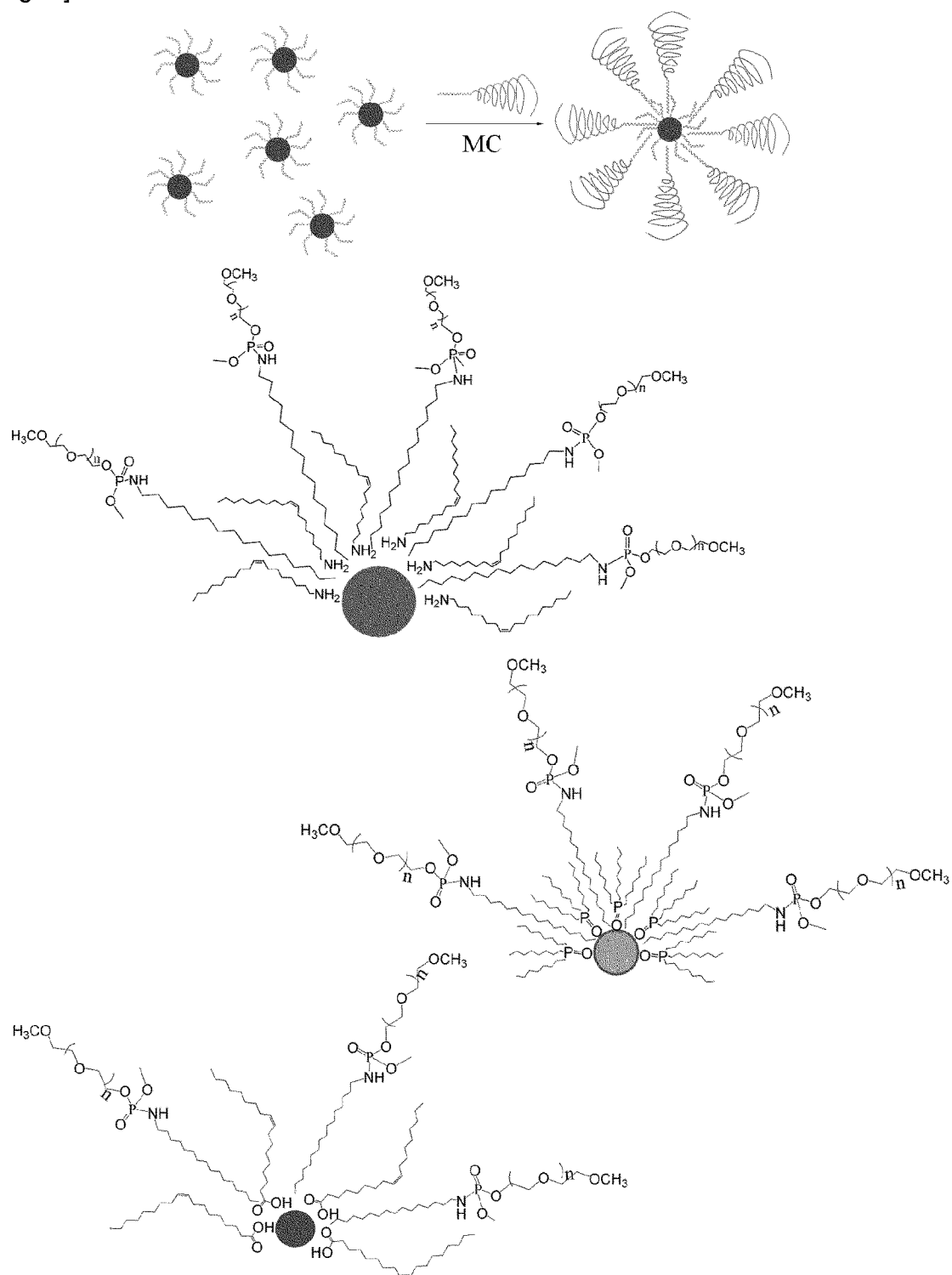
[Claim 5]

The surfactant for dispersing nanoparticles in water represented by Chemical Formula 1 according to claim 4, wherein, in Chemical Formula 1, n is from 10 to 200; R₁ is C₁-C₅ alkyl; R₂ is C₁-C₂₀ alkyl; and R₃ is C₁-C₅ alkyl.

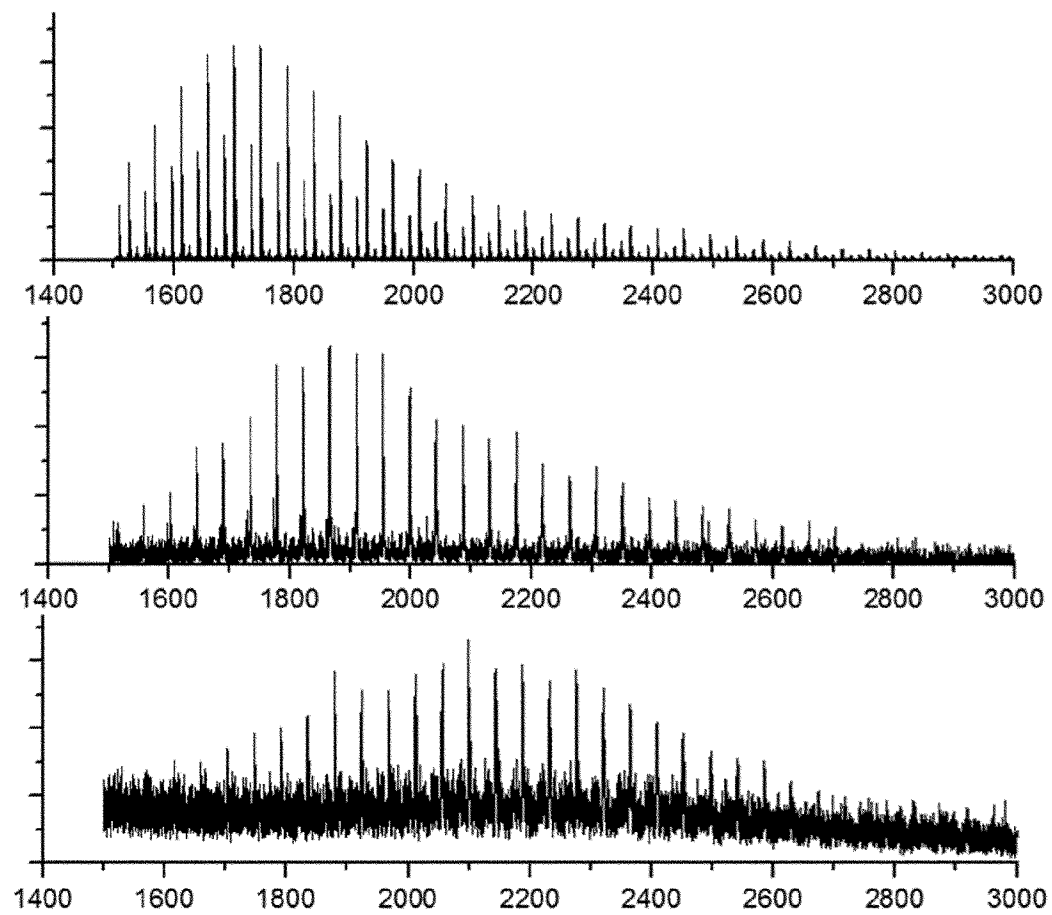
[Fig. 1]



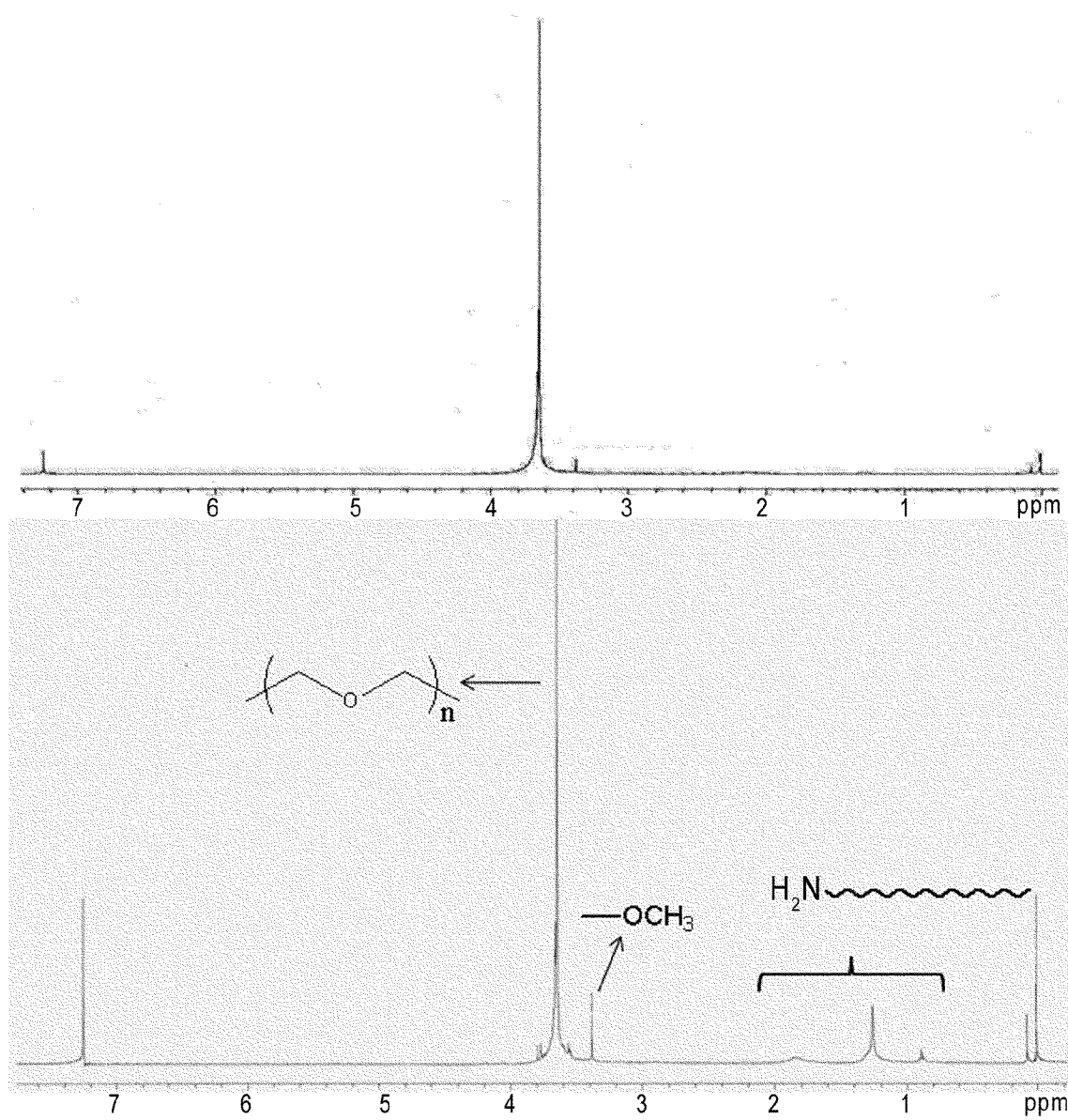
[Fig. 2]



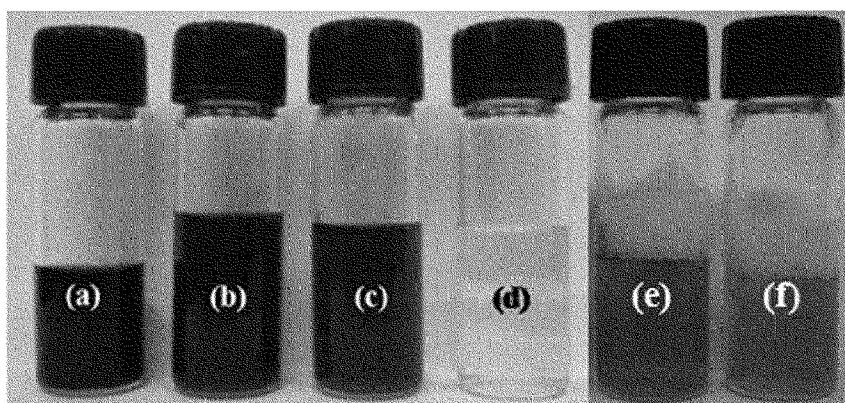
[Fig. 3]



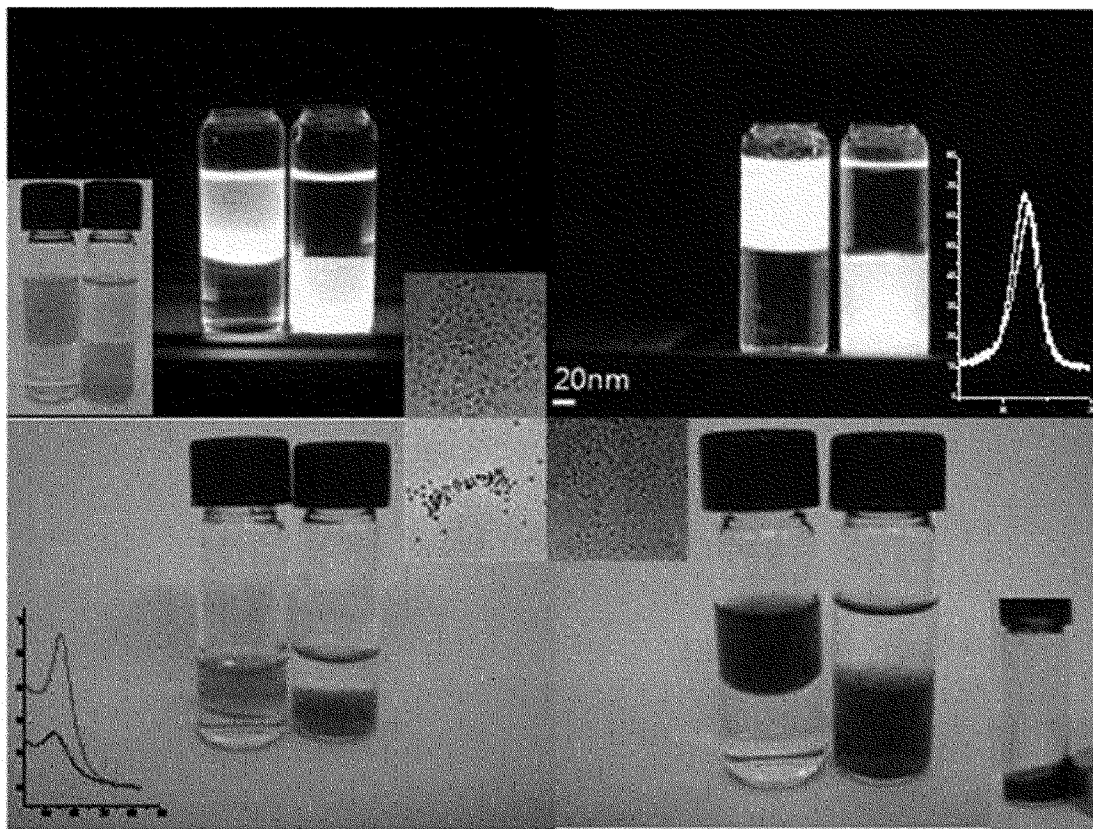
[Fig. 4]



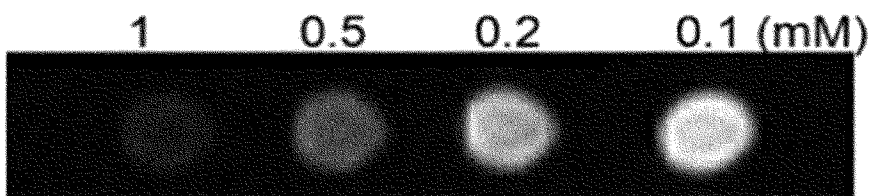
[Fig. 5]



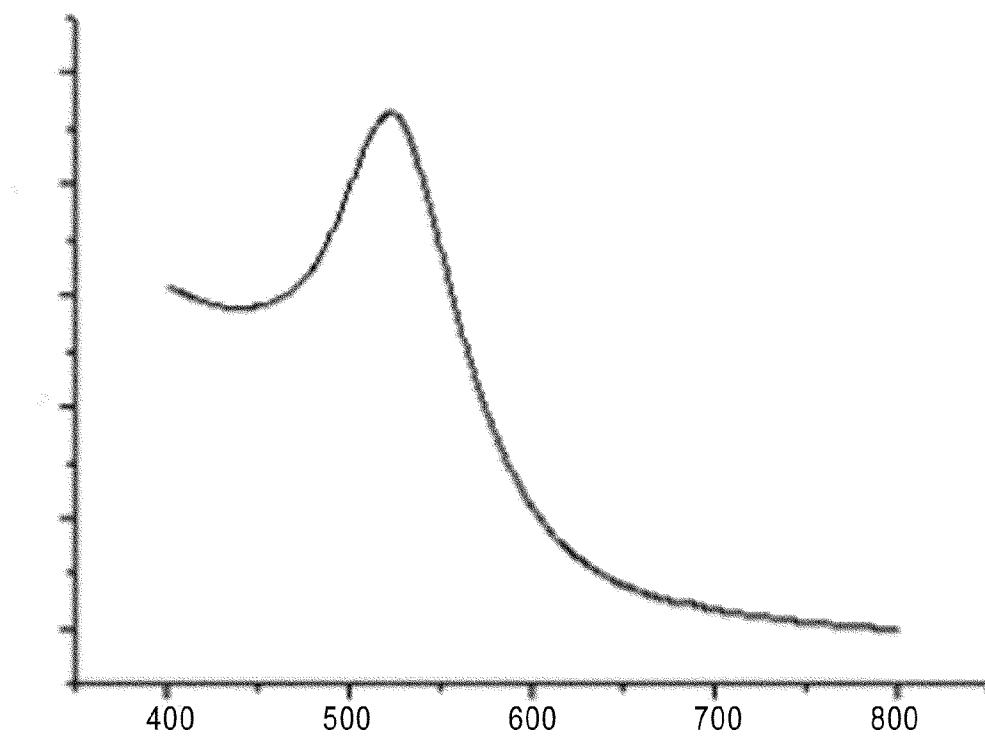
[Fig. 6]



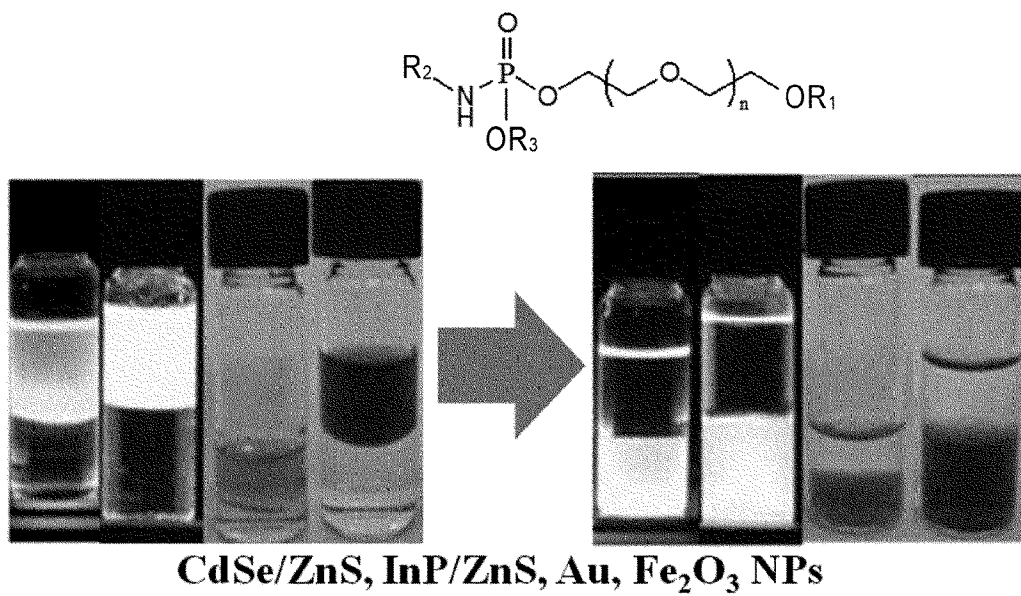
[Fig. 7]



[Fig. 8]



[Fig. 9]



INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2010/008588**A. CLASSIFICATION OF SUBJECT MATTER****C07F 9/24(2006.01)i, B82B 3/00(2006.01)i**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07F 9/24; C07F 9/09

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: N-alkylphosphoramidate, nanoparticle dispersion surfactant, polyoxyalkylene derivatization

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	US 3666844 A (FEARING, R.) 30 May 1972 See abstract, claims.	1-3 4
Y A	NA, H. B. et al. 'Versatile PEG-Derivatized Phosphine Oxide Ligands for Water-dispersible Metal Oxide Nanocrystals.' In: Chem. Commun. 17 October 2007, pp.5167-5169. See page 5167, left column, scheme 1, page 5168, left column.	1-3 4
A	JP 07-228589 A (FUJI PHOTO FILM CO., LTD.) 29 August 1995 See the whole document.	1-4
A	US 2971976 A (BRUST, H. F.) 14 February 1961 See the whole document.	1-4

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

18 AUGUST 2011 (18.08.2011)

Date of mailing of the international search report

18 AUGUST 2011 (18.08.2011)

Name and mailing address of the ISA/KR

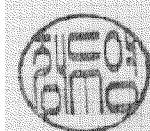
Korean Intellectual Property Office
Government Complex-Daejeon, 189 Cheongsu-ro,
Seo-gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Jung Doo Young

Telephone No. 82-42-481-8699



INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2010/008588**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 5
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

The subject matter of claim 5 is so unclear that no meaningful search could be made: claim 5 is worded in reference to R3 of chemical formula 1 of claim 4, which is not present in claim 4.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2010/008588

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3666844 A	30.05.1972	None	
JP 07-228589 A	29.08.1995	None	
US 2971976 A	14.02.1961	None	