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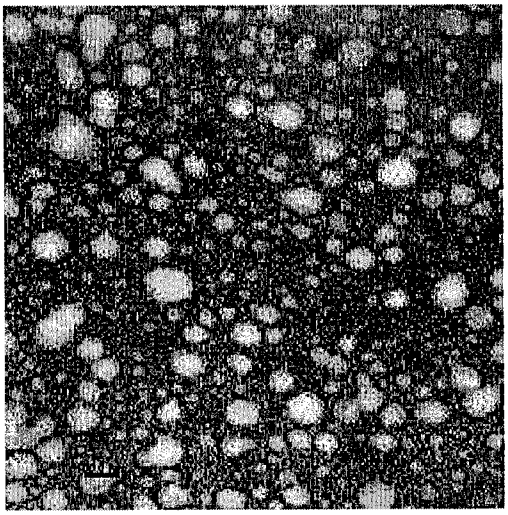
(54) **Title:** POLYMER NANOCAPSULES AND THE PROCESS FOR PREPARING THE SAME, AND THE SKIN EXTERNAL COMPOSITION CONTAINING THE NANOCAPSULES



(57) **Abstract:** The present invention relates to aqueous polymer nanocapsules stabilizing a compound of a molecular weight of 100-1,000 having both a disulfide bond and a carboxyl group, a method of preparing the same, and an external skin composition containing the same. More particularly, the aqueous polymer nanocapsules of the present invention comprise a compound of a molecular weight of 100-1,000, having both a disulfide bond and a carboxyl group, encapsulated in a hydrophobic polymer, wherein the hydrophobic polymer contains a moiety of cationic functional groups capable of absorbing the said compound, and a moiety of functional groups capable of inducing a dipole bond with the said compound.

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【DESCRIPTION】

【Invention Title】

POLYMER NANOCAPSULES AND THE PROCESS FOR PREPARING THE SAME, AND THE SKIN EXTERNAL COMPOSITION CONTAINING THE NANOCAPSULES

【Technical Field】

The present invention relates to aqueous polymer nanocapsules stabilizing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, a method of preparing the same, and an external skin composition containing the same. More particularly, the aqueous polymer nanocapsules of the present invention comprise a compound of a molecular weight of 100~1,000, having both a disulfide bond and a carboxyl group, encapsulated in a hydrophobic polymer. Said hydrophobic polymer contains a moiety of cationic functional groups capable of absorbing the said compound, and a moiety of functional groups capable of inducing a dipole bond with the said compound. The method of preparing the aqueous polymer nanocapsules of the present invention comprises the steps of: (1) polymerizing a hydrophobic polymer having a moiety of cationic functional groups that are capable of absorbing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, and a moiety of functional groups that are capable of inducing a dipole bond with the said compound; and (2) encapsulating the said compound in the hydrophobic polymer of step (1).

【Background Art】

Generally, methods for using polymer particles to stabilize oil-soluble

active ingredients are being widely studied. However, encapsulating an oil-soluble active ingredient within a polymer particle is not enough to stabilize an active ingredient completely. Especially, when such particles are used in a cosmetic formulation, the polymer swells through contact with water, surfactant and oil, thereby unstable active ingredients can leak and denature to the outer slowly over a long period of time.

Alpha-lipoic acid is an essential material of metabolism, as it functions as a coenzyme(CoA), which is related to thiamine, in a complete oxidative decarboxylation system such as pyruvic acid or alpha-ketoglutaric acid. Recently, it has been proved that alpha-lipoic acid has an effect on diet and on diabetic treatment, thus it is widely used as a physiological active ingredient. Moreover, the demand for applying to cosmetic is raised due to excellent effects such as skin wrinkle improvement and whitening. However, there are problems in that the alpha-lipoic acid is easily discolored and degraded by contact with external factors such as water, light, and surfactant, and show a decrease in titer, leading to a reduction in effect, and thus the use thereof is extremely limited.

As methods for stabilizing alpha-lipoic acid in formulations to overcome such limitations, PCT/EP02/13346 discloses techniques for stabilizing alpha-lipoic acid in a sodium hydroxide solution, US Patent No. 5,089,269 discloses techniques for stabilizing alpha-lipoic acid using micro particles of 0.1~2000㎛ that are applied in a gelatin film, US Patent No. 2005-068052 discloses techniques for applying alpha-lipoic acid to an external skin composition containing collagen, and Korean Patent Application No. 2003-0075004 discloses techniques for stabilizing alpha-lipoic acid using cyclodextrin.

However, all of the above methods have limitations in their

application to external skin compositions, especially with regard to a peculiar smell due to denaturation of alpha-lipoic acid and stimulation of alpha-lipoic acid itself.

【Disclosure】

【Technical Problem】

Accordingly, the present inventors have conducted studies on a method of stabilizing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, especially alpha-lipoic acid, in polymer particles. It has thereby been determined that, by preparing a random copolymer by polymerizing a monomer having a moiety of cationic functional groups capable of inducing an ion-ion bond and a moiety of functional groups capable of inducing a dipole bond, and a monomer capable of a barrier function, then preparing an aqueous polymer nanocapsule by encapsulating a compound of a molecular weight of 100~1,000, having both a disulfide bond and a carboxyl group, in said random copolymer, the said compound of a molecular weight of 100~1,000 hiving both a disulfide bond and a carboxyl group can be perfectly stabilized, thereby completing the present invention.

Therefore, an object of the present invention is to provide aqueous polymer nanocapsules that are capable of stabilizing perfectly a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group.

Another object of the present invention is to provide a method of preparing said polymer nanocapsules.

Another object of the present invention is to provide an external skin composition containing said polymer nanocapsules.

【Description of Drawings】

FIG. 1 is a transmission electron microscope image of polymer nanocapsules containing alpha lipoic acid prepared in Example 1.

【Best Mode】

To achieve the above objects, in an aspect of the present invention, provided are aqueous polymer nanocapsules, comprising a compound of a molecular weight of 100~1,000, having both a disulfide bond and a carboxyl group, encapsulated in a hydrophobic polymer, wherein the hydrophobic polymer contains a moiety of cationic functional groups capable of absorbing the said compound, and a moiety of functional groups capable of inducing a dipole bond with the said compound.

In another aspect of the present invention, provided is a method of preparing said polymer nanocapsules, comprising the steps of: (1) polymerizing a hydrophobic polymer having a moiety of cationic functional groups that are capable of absorbing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, and a moiety of functional groups that are capable of inducing a dipole bond with the said compound; and (2) encapsulating the said compound in the hydrophobic polymer of step (1).

Hereinafter, the present invention is described in more detail.

The aqueous polymer nanocapsules according to the present invention are a double stabilization system that stabilizes a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, in which an encapsulating capacity is maximized by an ion-ion bond between the carboxyl group inside the said compound and cationic functional groups, and

in which the chemical structure is stabilized by functional groups capable of inducing a dipole bond with a disulfide bond inside said compound to block a molecular denaturation, so as to stabilize effectively the compound in the capsules, thereby preventing leakage of the capsules and molecular denaturation, and that further stabilizes the compound in the particles using the outer polymer walls.

Hereinafter, the steps of the inventive preparation method are described in more detail.

Step (1) is a step of polymerizing a hydrophobic polymer having a moiety of cationic functional groups that are capable of absorbing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, and a moiety of functional groups that are capable of inducing a dipole bond with the said compound.

The said compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group contains specifically alpha-lipoic acid.

In the present invention, the polymerization of a polymer is conducted using an emulsifier-free emulsion polymerization process.

Monomers having the cationic functional groups used in step (1) are cationic monomers capable of radical polymerization, examples of which may include 2-vinylpyridine, 3-vinylpyridine, 4-vinylpyridine, acrylamide, (meth)acrylamide, vinylpyrrolidone, vinyl-N-methylpyridinium chloride, 3-methacryloyl-2-ethyl-tetraalkylammonium chloride, methacryloyl-3-hydroxypropyltrimethylammonium chloride, acryloyl-2-ethyl-tetraalkylammonium chloride, acryloyl-3-propyl-tetraalkylammonium chloride, 3-methacryloyl-2-hydroxypropyltrimethylammonium chloride, methacryloyl-3-propyltetraalkylammonium chloride, and (methacryloyl)ethyl dimethylamine. Said monomers having the cationic groups are used in an

amount of 0.1-30 mole% based on the total weight of the polymer to be prepared. If the monomers having the cationic groups are used in an amount of less than 0.1 mole %, water-dispersible nanoparticles are not formed, and if used in an amount of more than 30 mole %, the monomers are dispersed to an external water phase during polymerization, resulting in a decrease in yield.

An initiator used in step (1) is a cationic initiator, examples of which may include azo compounds, such as 2,2′-azobis(N,N′-dimethyleneisobutylamidine)dihydrochloride, 2,2′-azobis(2-methylpropionamidine)dihydrochloride, 2,2′-azobis(2-amidinepropane)dihydrochloride, 2,2′-azobis-2-methyl-N-[1,1-bis(hydroxymethyl)-2-hydroxymethyl]propanamide, 2,2′-azobis-2-methyl-N-[1,1′-bis-(hydroxymethyl)-ethyl]propanamide, and 2,2′-azobis(isobutylamide)dehydrate. The initiator is preferably used in an amount of about 1 wt% based on the total weight of polymer. If the initiator is used in an amount of less than about 1wt%, it does not show an effective initiation effect, and if the initiator is used in an amount of more than about 1wt%, it excessively increases the polymerization rate, resulting in a decrease in the stability of the polymerization system.

Monomers having the functional groups capable of inducing a dipole bond used in step(1) are radical-polymerizable monomers, examples of which may include 1-vinyl cyclohexanol, 3-buten-1-ol, 3-buten-2-ol, 2-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 1-(2-chloro-phenyl)-3-buten-1-ol, 1-(2-methoxyphenyl)-3-buten-1-ol, 1-(4-methoxy-phenyl)-3-buten-1-ol, 2-hydroxyethyl methacrylate, 3-chloro-2-hydroxypropyl methacrylate, 2-hydroxyethyl acrylate, hydroxypropyl acrylate and 4-hydroxybutyl acrylate. Said monomers having the dipole inductive functional groups are used in an amount of 0.1-30 mole% based on the total weight of the polymer to be

prepared. This is for inducing a dipole bond with a disulfide bond of a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, by encapsulating 1:1 based on the equivalent weight of the cationic functional groups moiety, so as to stabilize the said compound.

Hydrophobic monomers used in step (1) are radical-polymerizable monomers, examples of which may include styrene, p- or m-methylstyrene, p- or m-ethylstyrene, p- or m-chlorostyrene, p- or m-chloromethylstyrene, styrenesulfonic acid, p- or m-t-butoxystyrene, methyl(meth)acrylate, ethyl(meth)acrylate, propyl(meth)acrylate, n-butyl(meth)acrylate, isobutyl(meth)acrylate, t-butyl(meth)acrylate, 2-ethylhexyl(meth)acrylate, n-octyl(meth)acrylate, lauryl(meth)acrylate, stearyl(meth)acrylate, 2-hydroxyethyl(meth)acrylate, polyethyleneglycol(meth)acrylate, methoxypolyethyleneglycol(meth)acrylate, glycidyl(meth)acrylate, dimethylaminoethyl(meth)acrylate, diethylaminoethyl(meth)acrylate, vinyl acetate, vinyl propionate, vinyl butyrate, vinyl ether, allyl butyl ether, allyl glycidyl ether, alkyl(meth)acrylamide and (meth)acrylonitrile. Said hydrophobic monomers are used in an amount of 0.1-50 mole% based on the total weight of the polymer to be prepared.

Step (2) is a step of encapsulating the compound of step (1) in the hydrophobic polymer of step (1).

A method of preparing the nanocapsules according to the present invention can be performed using a general nano precipitation method and comprises:

Dissolving a compound of a molecular weight of 100~1,000, having both a disulfide bond and a carboxyl group, in an amount of 0.01~90mole% based on the total weight of aqueous polymer nanocapsules, and the hydrophobic polymer prepared in step (1), in a suitable organic solvent, i.e. a

highly volatile solvent (generally, alcohol/acetone) that is miscible with water and nontoxic and has a vapor pressure lower than that of water; mixing the aqueous phase with the organic phase by stirring at a suitable rate to induce the self-association of the phases, thus preparing an emulsion; and evaporating the organic phase to prepare nanocapsules present in the aqueous phase.

Herein, the compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group is used in an amount of 0.01~90mole% based on the total weight of the aqueous polymer nanocapsules.

The aqueous polymer nanocapsules prepared through said steps (1) and (2) can be contained in an external skin composition. Herein, the aqueous polymer nanocapsules are used in an amount of 0.01~50wt% based on the total weight of the composition.

The external skin composition can be formulated into, for example, skin lotion, milk lotion, massage cream, nourishing cream, pack, gel, essence, lipstick, makeup base, foundation, lotion, ointment, cream, patch and spray, but the scope of the present invention is not limited thereto.

【Mode for Invention】

Hereinafter, the present invention is described in further detail with reference to examples. It is to be understood, however, that these examples are for illustrative purposes only and are not to be construed to limit the scope of the present invention.

Example 1

Methylmethacrylate in an amount of 50 mole%, based on the total weight of the polymer, was mixed with (methacryloyl)ethyl diethylamine of

25 mole% and hydroxyethyl methacrylate of 25 mole%. The mixture was added to a 0.5% aqueous solution of 2,2'-azobis(2-methylpropionamidine)dihydrochloride and polymerized at 70℃ for 4 hours in a nitrogen atmosphere with stirring at 250 rpm, thus obtaining a polymer latex. The produced polymer latex was condensed with an Ultrafiltration membrane, heated, and water was removed to obtain a film type. The film was recrystallized with acetone/water to remove unreacted monomers, and condensed again with an Ultrafiltration membrane to obtain a film type, and this process was repeated several times. The resulting material was dried and ground in a vacuum oven, thus obtaining polymer as powder.

To prepare nanocapsules encapsulating alpha-lipoic acid, 10 g of the polymer prepared in the foregoing process and 1 g of alpha-lipoic acid were dissolved in 100 ml of ethanol. While 200 ml of distilled water was stirred in a round bottom flask, the mixture of polymer/alpha-lipoic acid/ethanol was added thereto to obtain a self-associated material. From the produced material, ethanol and a small amount of water were evaporated using a rotary evaporator, thus obtaining 50 ml of a polymer nanocapsule.

Comparative Example 1

Capsules were prepared in the same manner as in Example 1, except that, in the preparation of the polymer, (methacryloyl)ethyl diethylamine as the cationic functional groups was not introduced.

Comparative Example 2

Capsules were prepared in the same manner as in Example 1, except that hydroxyethyl methacrylate as the functional groups capable of inducing dipole bonds was not introduced.

Test Example 1

The morphology of the structural polymer nanoparticles prepared in Example 1 was observed with a transmission electron microscope (TEM), and the observation results are shown in FIG. 1.

As shown in FIG 1, it can be seen that the polymer prepared through the preparation method of Example 1 was a spherical polymer.

Formulation 1 and Comparative Formulations 1 and 2

Formulation 1 and Comparative Formulations 1 and 2 containing said Example 1 and Comparative Examples 1 and 2 were prepared in the compositions of Table 1 below as a clear gel-type soluble formulation. The formulations had a viscosity of about 4,000 cps, as measured using Brookfield (LVDVII+) at 30℃ and 12 rpm.

【Table 1】

Components (Content; wt%)	Formulation 1	Comparative Formulation 1	Comparative Formulation 2
Glycerin	5	5	5
Propylene glycol	4	4	4
Nanocapsule of Example 1	10	-	-
Nanocapsule of Comparative Example 1	-	10	-
Nanocapsule of Comparative Example 2	-	-	10
Ethanol	10	10	10
Sodium polyacrylate	0.5	0.5	0.5
Preservative	q.s.	q.s.	q.s.
Purified water	Balance	Balance	Balance

Formulation 2 and Comparative Formulations 3 and 4

Formulation 2 and Comparative Formulations 3 and 4 containing said

Example 1 and Comparative Examples 1 and 2 were prepared in the compositions of Table 2 below as an opaque gel-type lotion formulation. Each of the oil and aqueous phases was completely dissolved at 70 ℃, and emulsified at 7,000 rpm for 5 minutes. The formulation had a viscosity of about 2,500 cps, as measured using Brookfield (LVDVII+) at 30℃ and 12 rpm.

【Table 2】

Components (Content; wt%)		Formulation 2	Comparative Formulation 3	Comparative Formulation 4
Oil phase	Stearic acid	2	2	2
	Cetyl alcohol	2	2	2
	Lanolin alcohol	2	2	2
	Liquid paraffin	7	7	7
	Cyclomethicone	5	5	5
	Polyoxyethylene monooleic acid ester	2	2	2
	Preservative/antioxidant	q.s.	q.s.	q.s.
Aqueous phase	Glycerin	3	3	3
	Propylene glycol	5	5	5
	Triethylamine	1	1	1
	Nanocapsule of Example 1	10	-	-
	Nanocapsule of Comparative Example 1	-	10	-
	Nanocapsule of Comparative Example 2	-	-	10
	Sodium polyacrylate	0.15	0.15	0.15
	Purified water	Balance	Balance	Balance

Formulation 3 and Comparative Formulations 5 and 6

Formulation 3 and Comparative Formulations 5 and 6 containing said Example 1 and Comparative Examples 1 and 2 were prepared in the compositions of Table 3 below as a cream formulation. The preparation process was the same as in Formulation 2.

【Table 3】

Components (Content; wt%)	Formulation 3	Comparative Formulation 5	Comparative Formulation 6
Beeswax	2	2	2
Stearylalcohol	5	5	5
Stearic acid	8	8	8
Squalane	10	10	10
Propyleneglycolmonostearate	3	3	3
Polyoxyethylenecetylether	1	1	1
Preservative/antioxidant	q.s	q.s	q.s
Propylene glycol	8	8	8
Glycerin	4	4	4
Triethylamine	1	1	1
Nanocapsule of Example 1	10	-	-
Nanocapsule of Comparative Example 1	-	10	-
Nanocapsule of Comparative Example 2	-	-	10
Purified water	Balance	Balance	Balance

Test Example 2

To examine the stability within formulation of the prepared Formulations 1~3 and Comparative Formulations 1~6, each of Formulations 1~3 and Comparative Formulations 1~6 were stored in an oven at room temperature and at 40℃. After predetermined periods of time, samples were

taken, and the amount of the remaining active ingredient in each of the samples was measured using liquid chromatography. The measurement results are shown in Tables 4~6.

【Table 4】

Capsules	Storage temperature (℃)	Retention rate (%) of initial concentration			
		After 1 week	After 2 weeks	After 4 weeks	After 8 weeks
Formulation 1	Room temp.	100	100	100	100
	40℃	100	100	100	100
Comparative Formulation 1	Room temp.	99	92	93	86
	40℃	98	89	86	82
Comparative Formulation 2	Room temp.	98	90	92	84
	40℃	99	91	86	79
Soluble formulation containing 0.2% lipoic acid	Room temp.	95	85	80	67
	40℃	88	82	72	53

【Table 5】

Capsules	Storage temperature (℃)	Retention rate (%) of initial concentration			
		After 1 week	After 2 weeks	After 4 weeks	After 8 weeks
Formulation 2	Room temp.	100	100	100	100
	40℃	100	100	100	100
Comparative Formulation 3	Room temp.	98	94	95	86
	40℃	99	84	83	78
Comparative Formulation 4	Room temp.	99	93	91	75
	40℃	99	91	82	76
Soluble formulation containing 0.2% lipoic acid	Room temp.	94	87	78	62
	40℃	89	83	69	48

【Table 6】

Capsules	Storage temperature (℃)	Retention rate (%) of initial concentration			
		After 1 week	After 2 weeks	After 4 weeks	After 8 weeks
Formulation 3	Room temp.	100	100	100	100
	40℃	100	100	100	100
Comparative Formulation 5	Room temp.	98	95	96	89
	40℃	99	84	83	79
Comparative Formulation 6	Room temp.	99	94	93	81
	40℃	99	92	86	77
Soluble formulation containing 0.2% lipoic acid	Room temp.	93	88	77	61
	40℃	86	84	71	53

As can be seen in Table 4 above, in the soluble formulation, alpha-lipoic acid present in the polymer capsules had excellent stability. Further, as can be seen in Table 5 above, in the emulsion suspension formulation, alpha-lipoic acid present in the nanocapsules also had excellent stability. This suggests that the polymer nanocapsules according to the present invention are an excellent double-stabilization system, in which alpha-lipoic acid is encapsulated with the cationic functional groups and the dipole bond inductive functional groups to maintain the chemical structure thereof, and alpha-lipoic acid is prevented from leaking out of the capsules, and protected from an external harmful environment by the polymer matrix.

Also, as can be seen in Table 6, in the cream formulation, the cationic functional groups and the dipole bond inductive functional groups greatly contributed to the stabilization of alpha-lipoic acid in the formulation, as in the said case of the lotion formulation.

As described above, the cationic moiety and the dipole bond inductive

moiety stabilize the alpha-lipoic acid effectively, and the alpha-lipoic acid in polymer is effectively being protected against water, oil or surfactants in cosmetic formulations. Also, when the cationic moiety and the dipole bond inductive moiety are introduced together in one structure, the alpha-lipoic acid shows excellent stability in the formulations, compared to the other systems, because the dipole bond inductive moiety stabilizes the chemical structure of alpha-lipoic acid through the hydrogen bond and the cationic moiety has an increased ability to capture alpha-lipoic acid through ion-ion bond so as to prevent alpha-lipoic acid from leaking out of the capsules. Accordingly, in the polymer nanocapsules prepared in Example 1, chemical structure denaturation and desorption of particles to external of alpha-lipoic acid, caused by water or oil in the formulation, was prevented. This is due to the cationic functional groups absorbing alpha-lipoic acid, to the dipole bond inductive functional groups maintaining a chemical bond with a hydrogen bond, and to the polymer matrix walls, and thus an excellent stabilization effect was shown compared to other systems.

【Industrial Applicability】

As described above, the polymer nanocapsules according to the present invention can provide an effective stabilization material that enables initial activity of a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, especially alpha-lipoic acid, to be maintained at the nanometer-sized particle level that can maximize the efficiency of active ingredients. Also, according to the present invention, a process for preparing the polymer nanocapsules for encapsulating a compound a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group can be significantly simplified.

【CLAIMS】

【Claim 1】

Polymer nanocapsules, comprising a compound of a molecular weight of 100~1,000, having both a disulfide bond and a carboxyl group, encapsulated in a hydrophobic polymer;

wherein the hydrophobic polymer contains a moiety of cationic functional groups capable of absorbing the said compound, and a moiety of functional groups capable of inducing a dipole bond with the said compound.

【Claim 2】

The polymer nanocapsules of Claim 1, wherein the compound of molecular weight of 100~1,000 is alpha-lipoic acid.

【Claim 3】

The polymer nanocapsules of Claim 1, wherein a monomer having the cationic functional groups is a radical-polymerizable cationic monomer selected from the group consisting of 2-vinylpyridine, 3-vinylpyridine, 4-vinylpyridine, acrylamide, (meth)acrylamide, vinylpyrrolidone, vinyl-N-methylpyridinium chloride, 3-methacryloyl-2-ethyl-tetraalkylammonium chloride, methacryloyl-3-hydroxypropyltrimethylammonium chloride, acryloyl-2-ethyl-tetraalkylammonium chloride, acryloyl-3-propyl-tetraalkylammonium chloride, 3-methacryloyl-2-hydroxypropyltrimethylammonium chloride, methacryloyl-3-propyltetraalkylammonium chloride, and (methacryloyl)ethyl dimethylamine.

【Claim 4】

The polymer nanocapsules of Claim 3, wherein the cationic monomer is used in an amount of 0.1-30 mole% based on the hydrophobic polymer.

【Claim 5】

The polymer nanocapsules of Claim 1, wherein a monomer having the functional groups capable of inducing a dipole bond is a radical-polymerizable monomer selected from the group consisting of 1-vinyl cyclohexanol, 3-buten-1-ol, 3-buten-2-ol, 2-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 1-(2-chloro-phenyl)-3-buten-1-ol, 1-(2-methoxyphenyl)-3-buten-1-ol, 1-(4-methoxy-phenyl)-3-buten-1-ol, 2-hydroxyethyl methacrylate, 3-chloro-2-hydroxypropyl methacrylate, 2-hydroxyethyl acrylate, hydroxypropyl acrylate, and 4-hydroxybutyl acrylate.

【Claim 6】

The polymer nanocapsules of Claim 5, wherein the monomer having the functional groups capable of inducing a dipole bond is used in an amount of 0.1-30 mole% based on the hydrophobic polymer.

【Claim 7】

The polymer nanocapsules of Claim 1, wherein a hydrophobic polymer monomer is selected from the group consisting of styrene, p- or m-methylstyrene, p- or m-ethylstyrene, p- or m-chlorostyrene, p- or m-chloromethylstyrene, styrenesulfonic acid, lactate, glycolide, caprolactone, p- or m-t-butoxystyrene, methyl(meth)acrylate, ethyl(meth)acrylate, propyl(meth)acrylate, n-butyl(meth)acrylate, isobutyl(meth)acrylate, t-butyl(meth)acrylate, 2-ethylhexyl(meth)acrylate, n-octyl(meth)acrylate, lauryl(meth)acrylate, stearyl(meth)acrylate, 2-hydroxyethyl(meth)acrylate, polyethyleneglycol(meth)acrylate, methoxypolyethyleneglycol(meth)acrylate, glycidyl(meth)acrylate, dimethylaminoethyl(meth)acrylate, diethylaminoethyl(meth)acrylate, vinyl acetate, vinyl propionate, vinyl butyrate, vinyl ether, allyl butyl ether, allyl glycidyl ether, alkyl(meth)acrylamide, and (meth)acrylonitrile.

【Claim 8】

A method of preparing polymer nanocapsules, comprising the steps of:

(1) polymerizing a hydrophobic polymer having a moiety of cationic functional groups that are capable of absorbing a compound of a molecular weight of 100~1,000 having both a disulfide bond and a carboxyl group, and a moiety of functional groups that are capable of inducing a dipole bond with the said compound; and

(2) encapsulating the said compound in the hydrophobic polymer of step (1).

【Claim 9】

The method of Claim 8, wherein a monomer having the cationic functional groups is a radical-polymerizable cationic monomer selected from the group consisting of 2-vinylpyridine, 3-vinylpyridine, 4-vinylpyridine, acrylamide, (meth)acrylamide, vinylpyrrolidone, vinyl-N-methylpyridinium chloride, 3-methacryloyl-2-ethyl-tetraalkylammonium chloride, methacryloyl-3-hydroxypropyltrimethylammonium chloride, acryloyl-2-ethyl-tetraalkylammonium chloride, acryloyl-3-propyl-tetraalkylammonium chloride, 3-methacryloyl-2-hydroxypropyltrimethylammonium chloride, methacryloyl-3-propyltetraalkylammonium chloride, and (methacryloyl)ethyl dimethylamine.

【Claim 10】

The method of Claim 9, wherein the cationic monomer is used in an amount of 0.1-30 mole% based on the hydrophobic polymer.

【Claim 11】

The method of Claim 8, wherein a monomer having functional groups capable of inducing a dipole bond is a radical-polymerizable monomer selected from the group consisting of 1-vinyl cyclohexanol, 3-buten-1-ol, 3-

buten-2-ol, 2-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 1-(2-chlorophenyl)-3-buten-1-ol, 1-(2-methoxyphenyl)-3-buten-1-ol, 1-(4-methoxyphenyl)-3-buten-1-ol, 2-hydroxyethyl methacrylate, 3-chloro-2-hydroxypropyl methacrylate, 2-hydroxyethyl acrylate, hydroxypropyl acrylate, and 4-hydroxybutyl acrylate.

【Claim 12】

The method of Claim 11, wherein the monomer having functional groups capable of inducing a dipole bond is used in an amount of 0.1-30 mole% based on the hydrophobic polymer.

【Claim 13】

The method of Claim 8, wherein a hydrophobic polymer monomer is selected from the group consisting of styrene, p- or m-methylstyrene, p- or m-ethylstyrene, p- or m-chlorostyrene, p- or m-chloromethylstyrene, styrenesulfonic acid, lactate, glycolide, caprolactone, p- or m-t-butoxystyrene, methyl(meth)acrylate, ethyl(meth)acrylate, propyl(meth)acrylate, n-butyl(meth)acrylate, isobutyl(meth)acrylate, t-butyl(meth)acrylate, 2-ethylhexyl(meth)acrylate, n-octyl(meth)acrylate, lauryl(meth)acrylate, stearyl(meth)acrylate, 2-hydroxyethyl(meth)acrylate, polyethyleneglycol(meth)acrylate, methoxypolyethyleneglycol(meth)acrylate, glycidyl(meth)acrylate, dimethylaminoethyl(meth)acrylate, diethylaminoethyl(meth)acrylate, vinyl acetate, vinyl propionate, vinyl butyrate, vinyl ether, allyl butyl ether, allyl glycidyl ether, alkyl(meth)acrylamide, and (meth)acrylonitrile.

【Claim 14】

The method of Claim 8, wherein the compound of a molecular weight of 100~1,000 is alpha-lipoic acid.

【Claim 15】

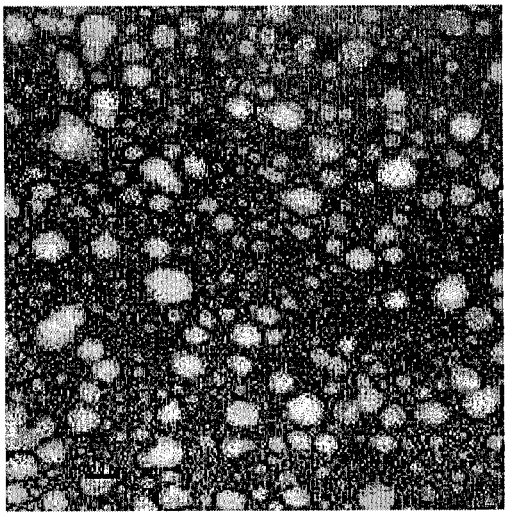
An external skin composition containing the polymer nanocapsules of Claim 1.

【Claim 16】

The external skin composition of Claim 15, formulated as one of the group consisting of skin softener, skin lotion, massage cream, nou rishing cream, pack, gel, essence, lipstick, make-up base, foundation, lotion, ointment, gel, cream, patch, and spray.

FIGURES

FIG. 1



INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2006/005047

A. CLASSIFICATION OF SUBJECT MATTER

A61K 8/11(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)

IPC 8 : as above

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

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

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6432434 B1 (James L. Meyerhoff et al) 13 Aug. 2002 See abstract, column 3 line 25-49, claims 1,2,4,6	1-16
A	US 5089269 A (Akira Noda et al) 18 Feb. 1992) See abstract, column 1 line 33-44, claims 1,2	1-16

☐ 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)
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"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	Date of mailing of the international search report
22 FEBRUARY 2007 (22.02.2007)	**22 FEBRUARY 2007 (22.02.2007)**

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/KR2006/005047

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6432434 B1	13.08.2002	None	
US 5089269 A	18.02.1992	EP 0316054 A1	17.05.1989
		JP 01125313 A	17.05.1989