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(54) Title: COMPOSITION, BACTERIAL REPELLING COATING AND METHOD FOR FORMING THE SAME, AND ARTICLE HAVING BACTERIAL REPELLING COATING

(57) Abstract: To provide a material that can impart excellent bacterial repelling property to a variety of surfaces. A bacterial repelling composition comprising a structure of a self-organized lipid-peptide compound, wherein the lipid-peptide compound comprises a lipid portion consisting of an aliphatic group having 9 to 23 carbon atoms, and a peptide moiety comprising an amino acid sequence of 2 to 4 amino acids

COMPOSITION, BACTERIAL REPELLING COATING AND METHOD FOR FORMING THE SAME, AND ARTICLE HAVING BACTERIAL REPELLING COATING

TECHNICAL FIELD

The present disclosure relates to a composition comprising a lipid-peptide compound which has bacterial repelling property, a bacterial repelling coating and a method for forming the same, and an article having a bacterial repelling coating comprising a lipid-peptide compound.

BACKGROUND

It is known that incorporation of a material that prevents or suppresses attachment of bacteria onto a surface imparts bacterial repelling property or antibacterial property to those surfaces. Examples of surfaces which can be treated with material that prevents or suppresses attachment of bacteria include the external part and the internal part of a living body, for example, the skin, the interior of the oral cavity etc., or into the surfaces of articles such as medical instruments, medical facilities, tableware, sanitary goods, and nursing care equipment, by coating, kneading or the like

Patent Document 1 (JP-A-2011-153101) describes "an oral agent for preventing attachment of microorganisms, comprising a phosphorylcholine group-containing polymer (PC polymer) as a microorganism attachment preventing ingredient, a water-soluble polysaccharide as a binder ingredient, and a poly(meth)acrylic acid derivative as a compatibilizing ingredient".

Patent Document 2 (JP-A-2016-175956) describes "a bacterial repelling material comprising a polyacetal resin (A) containing an ester-terminal group, represented by the following formula, wherein the ester-terminal group is contained at a ratio of 20 μmol or

less per 1 g of the polyacetal resin (A). RCOO- (wherein R represents a hydrogen atom or an alkyl group)".

Patent Document 3 (JT-A-2009-523890) describes "a curable antibacterial film-forming composition, comprising a polymer matrix, a carrier solvent, and at least one long-chain compound comprising a functional group capable of forming a chemical bond with the matrix when the carrier solvent is vaporized, and the composition is dried or cured, wherein the functional group is selected from the group consisting of amine, thiol, carboxyl, aldehyde, hydroxyl and a combination thereof, the at least one long-chain compound is non-leachable when the composition is dried or cured, has a sufficient length for protruding into an organic sediment that was deposited on the surface of the curable composition with time, and over the sediment, permeates a cellular wall of a microorganism, and can inhibit microorganism colony formation on the surface of the curable composition".

SUMMARY

The present disclosure provides a material that can impart excellent bacterial repelling property to a variety of surfaces.

The present inventors found out that a structure of a self-organized lipid-peptide compound has the function of imparting bacterial repelling property to the surface to which the structure was applied. In the present disclosure, "antibacterial repelling property" means physical property of a material that suppresses or prevents a microorganism from being attached to the surface.

According to one embodiment of the present disclosure, there is provided a bacterial repelling composition comprising a structure of a self-organized lipid-peptide compound wherein the lipid-peptide compound is represented by the formula (1):

RCOP (1)

wherein R represents an aliphatic group having 9 to 23 carbon atoms, and P represents a peptide moiety comprising an amino acid sequence of 2 to 4 amino acids. The composition also comprises not less than 30% water.

According to another embodiment the bacterial repelling composition comprises an amino acid sequence of 2 to 4 amino acids, wherein the 2 to 4 amino acids are selected from the group of amino acids consisting of alanine (Ala), glutamic acid (Glu), glycine (Gly), histidine (His), Asparagine (Asn), glutamine (Gln), tryptophan (Trp), Tyrosine (Tyr).

According to another embodiment the bacterial repelling composition comprises a fatty acid residue portion RCO, which is composed of R and an adjacent carbonyl group, comprises a lauroyl group, a dodecylcarbonyl group, myristoyl group, a tetradecylcarbonyl group, a palmitoyl group, a margaroyl group, an oleoyl group, an elaidoyl group, a linoleoyl group, a stearoyl group, a vaccenoyl group, an octadecylcarbonyl group, an arachidoyl group, an eicosylcarbonyl group, a behenoyl group, an erucanoyl group, a docosylcarbonyl group, a lignoceroyl group, or a nervonoyl.

According to another embodiment of the present disclosure, there is provided a method for forming a bacterial repelling coating, comprising applying the bacterial repelling composition to the surface.

According to still another embodiment of the present disclosure, there is provided a bacterial repelling coating comprising a structure of a self-organized lipid-peptide compound.

According to still another embodiment of the present disclosure, there is provided a bacterial repelling article comprising a base material, and a bacterial repelling coating comprising a structure of a self-organized lipid-peptide compound, the bacterial repelling coating being attached to the surface of the base material.

By using the bacterial repelling composition of the present disclosure, a bacterial repelling coating having excellent bacterial repelling property can be formed on the surface.

In addition, the above description should not be regarded as having disclosed all embodiments of the present invention and all advantages concerning the present invention.

The present invention will be illustrated in more detail for the purpose of exemplifying representative embodiments of the present invention below, but the present invention is not limited to these embodiments.

DETAILED DESCRIPTION

A bacterial repelling composition in accordance with one embodiment comprises a structure of a self-organized lipid-peptide compound. In the present disclosure, the lipid-peptide compound has a hydrophobic part composed of a fatty acid residue and a hydrophilic part composed of a peptide moiety. While not wishing to be bound by theory, it is believed that a self-organized structure is formed by association of a plurality of lipid-peptide compounds. The self-organized structure may have a variety of shapes, and examples thereof include a spherical shape, a plate shape, a layer shape, a pillar shape, a fibrous shape and the like. In one embodiment, the structure of a self-organized lipid-peptide compound is fibrous, for example, a nano-fiber having a full length of an order of magnitude of nanometers.

As the lipid-peptide compound forming the self-organized structure, a compound represented by the following formula (1) or a pharmaceutically acceptable salt thereof can be used.

RCOP (1)

In the formula (1), R represents an aliphatic group having 9 to 23 carbon atoms. It is desirable that R is a straight aliphatic group having 11 to 23 carbon atoms, optionally having 0 to 2 unsaturated bonds.

Examples of the fatty acid residue RCO, which is composed of R and an adjacent carbonyl group, include a lauroyl group, a dodecylcarbonyl group, myristoyl group, a tetradecylcarbonyl group, a palmitoyl group, a margaroyl group, an oleoyl group, an elaidoyl group, a linoleoyl group, a stearoyl group, a vaccenoyl group, an octadecylcarbonyl group, an arachidoyl group, an eicosylcarbonyl group, a behenoyl group, an erucanoyl group, a docosylcarbonyl group, a lignoceroyl group, or a nervonoyl group. In another embodiment the fatty acid residue portion RCO, which is composed of R and an adjacent carbonyl group, particularly includes a lauroyl group, a myristoyl group, a palmitoyl group, a margaroyl group, an oleoyl group, an elaidoyl group, a stearoyl group, or a behenoyl group.

In the formula (1), P represents a peptide moiety composed of a sequence of 2 to 4 amino acids. As an amino acid constituting the peptide moiety P, an α-amino acid can be used. When the α-amino acid has the optical activity, it may be either a D type or an L type, and it is advantageous that all amino acids constituting the peptide moiety are a D type or an L type. Examples of the α-amino acid include aliphatic amino acids such as Gly, Ala, Val, Leu and Ile, hydroxy group-containing amino acids such as Ser and Thr, sulfur-containing amino acids such as Cys and Met, aromatic amino acids such as Phe, Tyr and Trp, amino acids such as Pro, amide group-containing amino acids such as Asn and Gln, acidic amino acids such as Asp and Glu, basic amino acids such as Lys, His and Arg, and the like. In one embodiment, as the α-amino acid constituting the peptide moiety P, basic amino acids can be used.

In some embodiments, the formula (1), P represents a peptide moiety composed of a sequence of 2 to 4 amino acids, wherein the 2 to 4 amino acids are selected from the group of amino acids consisting of alanine (Ala), glutamic acid (Glu), glycine (Gly), histidine (His), Asparagine (Asn), glutamine (Gln), tryptophan (Trp), Tyrosine (Tyr). In some embodiments, no two amino acids in the sequence of 2 to 4 amino acids are the same amino acid. In other words, the amino acids in the sequence of 2 to 4 amino acids are all different amino acids according to the list of alanine (Ala), glutamic acid (Glu), glycine (Gly), histidine (His), Asparagine (Asn), glutamine (Gln), tryptophan (Trp), Tyrosine (Tyr). In some embodiments at least two of the 2 to 4 amino acids in the sequence of amino acids is the same amino acid, selected from the group of alanine (Ala), glutamic acid (Glu), glycine (Gly), histidine (His), Asparagine (Asn), glutamine (Gln), tryptophan (Trp), Tyrosine (Tyr).

In some embodiments, at least one amino acid in the sequence of 2 to 4 amino acids is selected from the group consisting of glycine, histidine, and lysine. In some embodiments, at least two amino acids in the sequence of 2 to 4 amino acids are selected from the group consisting of glycine, histidine, and lysine.

Examples of the peptide moiety composed of two amino acids, which is used in the lipid-peptide compound represented by the formula (1), include -Gly-His, -Gly-Gln, -Gly-Asn, -Gly-Trp, -Gly-Lys, -Gly-Tyr, -Gly-Glu, -Gly-Gly, -Ala-His, -Ala-Gln, -Ala-Asn, -Ala-Trp, -Ala-Lys, -Ala-Tyr, -Ala-Glu, -Ala-Gly, -His-Gly, -Gln-Gly, -Asn-Gly, -Trp-Gly, -Lys-Gly, -Tyr-Gly, -Glu-Gly, -His-Ala, -Gln-Ala, -Asn-Ala, -Trp-Ala, -Lys-Ala, -Tyr-Ala, -Glu-Ala, -Gly-Ala, and the like. These peptide moieties can be appropriately combined with the fatty acid residues to give lipid-peptide compounds.

In some embodiments, the lipid-peptide compound in which the peptide moiety is composed of two amino acids may be: lauroyl-Gly-His, lauroyl-Ala-His, myristoyl-Gly-

His, myristoyl-Ala-His, palmitoyl-Gly-His, palmitoyl-Gly-Tyr, palmitoyl-Gly-Glu, palmitoyl-Gly-Lys, palmitoyl-Gly-Gly, palmitoyl-Ala-His, stearoyl-Gly-His, or stearoyl-Ala-His.

Examples of the peptide moiety composed of three amino acids, which is used in the lipid-peptide compound represented by the formula (1), include -Gly-Gly-His, -Gly-Gly-Gln, -Gly-Gly-Asn, -Gly-Gly-Trp, -Gly-Gly-Lys, -Gly-Gly-Tyr, -Gly-Gly-Glu, -Gly-Gly-Gly, -Gly-Ala-His, -Gly-Ala-Gln, -Gly-Ala-Asn, -Gly-Ala-Trp, -Gly-Ala-Lys, -Ala-Gly-His, -Ala-Gly-Gln, -Ala-Gly-Asn, -Ala-Gly-Trp, -Ala-Gly-Lys, -Ala-Gly-Tyr, -Ala-Gly-Glu, -Ala-Gly-Gly, -Gly-His-Gly, -His-Gly-Gly, -Gln-Gly-Gly, -Asn-Gly-Gly, -Trp-Gly-Gly, -Lys-Gly-Gly, -His-Ala-Gly, -Gln-Ala-Gly, -Asn-Ala-Gly, -Trp-Ala-Gly, -Lys-Ala-Gly, -His-Gly-Ala, -Gln-Gly-Ala, -Asn-Gly-Ala, -Trp-Gly-Ala, -Lys-Gly-Ala, and the like. These peptide moieties can be appropriately combined with the fatty acid residues to give lipid-peptide compounds.

Examples of the peptide moiety composed of four amino acids, which is used in the lipid-peptide compound represented by the formula (1), include -Gly-Gly-Gly-His, -Gly-Gly-His-Gly, -Gly-His-Gly-Gly, -His-Gly-Gly-Gly, -Gly-Gly-Gly-Lys, -Gly-Gly-Lys-Gly, -Gly-Lys-Gly-Gly, -Lys-Gly-Gly-Gly, and the like. These peptide moieties can be appropriately combined with the fatty acid residues to give lipid-peptide compounds.

As the lipid-peptide compound, the compounds represented by the formula (1) or pharmaceutically acceptable salts thereof can be used alone or can be used by combining two or more of them.

In one embodiment, the lipid-peptide compound is a compound represented by the formula (1):

RCOP (1)

wherein R represents an aliphatic group having 9 to 23 carbon atoms, and P is a two amino acid peptide moiety selected from the group consisting of -Gly-His, -Gly-Gly, and -Gly-Lys or a pharmaceutically acceptable salts thereof.

In some embodiments, the amount of the lipid-peptide compound as a percent of the entire composition can be, for example, 0.01% by mass or more, 0.02% by mass or more, 0.1% by mass or more, 0.2% by mass or more, 0.5% by mass or more, 1% by mass or more, 2% by mass or more, 5% by mass or more, 10% by mass or more, or about 15% by mass or more. In some embodiments, the amount of the lipid-peptide compound as a percent of the entire composition can be, for example, 20% by mass or less, 10% by mass or less, 7% by mass or less, 5% by mass or less, 3% by mass or less, 2% by mass or less, or 1% by mass or less.

The bacterial repelling composition may further contain a bactericidal agent. Examples of the bactericidal agent include cationic surfactants such as benzalkonium chloride, benzethonium chloride, and cetylpyridinium chloride; biguanide compounds such as chlorhexidine gluconate, and chlorhexidine hydrochloride; iodine-based compounds such as iodine ion, iodoform, and povidone iodine; inorganic compounds such as a silver compound that generates a silver ion; phenol-based compounds such as cresol and isopropylmethylphenol, parabens such as methylparaben, benzoic acid, and salts thereof. The bactericidal agents can be used alone or can be used by combining two or more of them. The blending amount of the bactericidal agent can be, for example, totally about 0.001% by mass or more, about 0.01% by mass or more, or 0.05% by mass or more, and about 10% by mass or less, about 5% by mass or less, or about 1% by mass or less, based on the total amount of the bactericidal agent.

The bacterial repelling composition may further contain an anti-inflammatory agent or an antiphologistic agent. Examples of the anti-inflammatory agent or the

antiphologistic agent include glycyrrhizic acid and a derivative thereof, a glycyrrhetic acid derivative, salicylic acid derivative, hinokitiol, guaiazulene, allantoin, indomethacin, ketoprofen, ibuprofen, diclofenac, loxoprofen, celecoxib, infliximab, etanercept, zinc oxide, hydrocortisone acetate, prednisone, diphedramine hydrochloride, chlorpheniramine maleate, plant extract (e.g. peach leaf extract or sage brush extract) and the like. The anti-inflammatory agents or the antiphologistic agents can be used alone or can be used by combining two or more of them. The blending amount of the anti-inflammatory agent or the antiphologistic agent can be, for example, totally about 0.001% by mass or more, about 0.01% by mass or more, or about 0.05% by mass or more, and about 10% by mass or less, about 5% by mass or less, or about 2% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may further contain a calcium phosphate compound. The calcium phosphate compound functions as a dentin-strengthening agent that promotes remineralization when used in dental use. Calcium phosphate also functions as a polishing agent in some cases. Examples of the calcium phosphate include tricalcium α-phosphate, tricalcium β-phosphate, tetracalcium phosphate, hydroxyapatite and the like. The calcium phosphate compounds can be used alone or can be used by combining two or more of them. The blending amount of the calcium phosphate compound can be, for example, about 0.001% by mass or more, about 0.01% by mass or more, or about 0.05% by mass or more, and about 1% by mass or less, about 0.5% by mass or less, or about 0.1% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may further contain long-chain alkylhydroxycarboxylic acid or a salt thereof. When the calcium phosphate compound is further added to the composition containing the bactericidal agent and/or the anti-inflammatory agent or the antiphologistic agent at the high concentration, addition of long-

chain alkylhydroxycarboxylic acid or a salt thereof promotes self-organization of the lipid-peptide compound, thereby, dispersibility of the calcium phosphate compound can be more enhanced. Examples of the long-chain alkylhydroxycarboxylic acid or a salt thereof include mono-, di-, tri-, or tetra-hydroxycarboxylic acid in which the number of carbon atoms of an alkyl chain is 9 to 23, and salts of an alkali metal such as sodium and potassium thereof. Examples of such long-chain alkylhydroxycarboxylic acid include 12-hydroxystearic acid. The long-chain alkylhydroxycarboxylic acids can be used alone or can be used by combining two or more of them. The blending amount of the long-chain alkylhydroxycarboxylic acid can be, for example, totally about 0.01% by mass or more, about 0.1% by mass or more, or about 1% by mass or more, and about 20% by mass or less, about 10% by mass or less, or about 5% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may further contain a solvent. As the solvent, polar solvents such as water, ethanol and isopropanol can be used. The solvents can be used alone or can be used by combining two or more of them. In one embodiment, the solvent contains water, and the bacterial repelling composition is an aqueous composition. Water may be purified water. The content of the solvent can be, for example, about 30% by mass or more, about 50% by mass or more, or about 70% by mass or more, and about 95% by mass or less, about 90% by mass or less, or about 80% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may contain an abrasive. Examples of the abrasive include calcium hydrogen phosphate, aluminum hydroxide, silicic anhydride, calcium carbonate, and the like. The abrasives can be used alone or can be used by combining two or more of them. The blending amount of the abrasive can be, for example, totally about 1% by mass or more, about 10% by mass or more, or about 20% by mass or

more, about 50% by mass or less, about 40% by mass or less, or about 30% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may contain a binder or a thickener. Examples of the binder or the thickener include, for example, water-soluble polysaccharides such as hydroxypropylmethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, and carboxymethylcellulose, carboxymethylcellulose sodium, a carboxyvinyl polymer, sodium alginate, carrageenan, and the like. The binders or the thickeners can be used alone or can be used by combining two or more of them. The blending amount of the binder or the thickener can be, for example, totally about 0.01% by mass or more, about 0.05% by mass or more, or about 0.1% by mass or more, and about 15% by mass or less, about 10% by mass or less, or about 5% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may contain a wetting agent. Examples of the wetting agent include, for example, polyhydric alcohols such as ethylene glycol, propylene glycol, dipropylene glycol, 1,3-butylene glycol, 1,4-butylene glycol, pentylene glycol, hexylene glycol, isoprene glycol, ethylhexanediol, isopentyldiol, glycerin, diglycerin, polyglycerin, sorbitol, xylitol, maltitol, mannitol, and erythritol. The wetting agents can be used alone or can be used by combining two or more of them. Since when the bacterial repelling composition is used in dental use, it easily fits the oral mucous membrane, and is good in flavor, glycerin, sorbitol, and xylitol are advantageously used. The blending amount of the wetting agent can be, for example, totally about 0.1% by mass or more, about 1% by mass or more, or about 5% by mass or more, and about 40% by mass or less, about 30% by mass or less, or about 20% by mass or less, based on the total mass of the bacterial repelling composition.

The bacterial repelling composition may contain additives which are used in the known external agents, in addition to the above-mentioned ingredients. Examples of the additive include, for example, foaming agents, aerosol agents, organic acids, antioxidants, ultraviolet absorbing agents, stabilizers, antiseptics, metal ion sequestering agents, pH adjusting agents, corrigents, flavorants (flavor agents), coloring matters, whitening agents, vitamins, and the like.

The bacterial repelling composition can be prepared, for example, by the following procedure, being not limiting.

1. Purified water at 80°C is prepared. To purified water are appropriately added a wetting agent such as glycerin, a pH adjusting agent such as sodium hydroxide, a bactericidal agent such as cetylpyridinium chloride, an anti-inflammatory agent such as dicalcium glycyrrhizinate, and the like, and the materials are dissolved.

2. To purified water prepared at 1 is added purified water in which a lipid-peptide compound has been dissolved, to obtain a mixture, which is heated at 80°C. Additives such as stearic acid, sodium hydroxide, and 1,3-butanediol are appropriately added to the mixture, and the materials are dissolved.

3. The lipid-peptide compound can also be used by preparing it in the form of a lipid-peptide compound-containing premix (solid matter containing a lipid-peptide compound, and additives such as stearic acid, sodium hydroxide, and 1,3-butanediol). In this case, the lipid-peptide compound-containing premix is heated to 80°C or higher and dissolved, the solution is added to purified water prepared at 1, and the resulting mixture is heated at 80°C.

4. To an aqueous solution containing a binder or a thickener such as a carboxyvinyl polymer is appropriately added a suitable amount of water, this is added to

the above-mentioned mixture in which the lipid-peptide compound has been dissolved, and the materials are further mixed while heating to 80°C or higher.

5. The mixture obtained at 4 is cooled while stirring with a Homo Disper emulsifying device (400 to 600 rpm), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition is prepared.

By applying the bacterial repelling composition to a variety of surfaces, a bacterial repelling coating can be formed on those surfaces. Examples of a method of applying the bacterial repelling composition include coating, immersion, and spraying using a finger, a roller, a brush, a sponge or the like. After application of the bacterial repelling composition, the solvent may be removed by heating.

The bacterial repelling composition can be used in a variety of intended uses. In one embodiment, the bacterial repelling composition is used in dental use in the form of dentrifice, liquid dentrifice, varnish or mouthwash. Dental plaque that is the community of a microorganism, for example, Streptococcus mutans, which is seen in the oral cavity, is widely known as the main cause for dental caries and other oral infection. By applying the bacterial repelling composition to the surface of teeth with a tooth brush, or by gargling, microorganisms can be prevented from being attached to the surface of teeth.

EXAMPLES

In the following Examples, specific embodiments of the present disclosure will be exemplified, but the present invention is not limited to them. Part and percentage are all by mass, unless explicitly described.

Bacterial repelling property assessment

Bacterial repelling property was assessed by the following procedure: A hybrid ceramic resin base material (3M Company, US, Minnesota, Saint Paul) was immersed in a

bacterial repelling composition and allowed to stand for 60 seconds. Using Kimwipes (registered trademark), the moisture attached to the base material surface was wiped out. 100 μL of a test liquid containing Streptococcus mutans which had been aerobically cultured in the BHI medium for 24 hours (OD660 nm=1.0) was applied to the base material surface using a micropipetter. Anaerobic culturing was performed for 5 hours under the environment of 37°C and 80RH%. The base material surface was slightly rinsed with deionized water, and bacteria were stained using a Victoria Blue staining liquid. The base material was placed into and taken out from the liquid until blue was not dissolved out with a decoloring liquid. The stained product was extracted into isopropanol, the absorbance at the wavelength of 595 nm of the extract was measured using the iMark microplate reader (Bio-Rad Laboratories Inc., US California, Hercules), and bacterial repelling property was assessed by the average absorbance from the results of 3 or 5 tests (N=3 or N=5). The magnitude of the absorbance is proportional to an amount of bacteria attached to the base material surface.

Examples 1 to 4, Comparative Example 1

According to formulation shown in Table 1, a bacterial repelling composition was prepared as follows:

1. Purified water at 80°C was prepared.
2. To purified water prepared at 1 was added a lipid-peptide compound-containing premix (product name, NANOFIBERGEL (registered trademark) TW-01W, NISSAN CHEMICAL INDUSTRIES, LTD., Chiyoda-ku, Tokyo, Japan) which had been heated to 80°C or higher and dissolved, and the resulting mixture was heated at 80°C. The lipid-peptide compound-containing premix contains 4% of Palmitoyl Dipeptide-18 (palmitoyl-

Gly-His) which is a lipid-peptide compound, 1% of stearic acid, 0.48% of sodium hydroxide, 40% of 1,3-butanediol, and 54.52% of water.

3. The mixture obtained at 2 was cooled while stirring (400 to 600 rpm) with a Homo Disper (Model 2.5, PRIMIX Corporation, Awaji-shi, Hyogo-ken, Japan), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition was obtained.

Using the resulting bacterial repelling composition, a bacterial repelling property assessment test was performed, and the resulting average absorbance is shown in Table 1. The average absorbance is expressed as a relative value, letting the absorbance of an example as a standard in the table to be 100.

Table 1 (Numerical values of formulation are parts by mass)

	Comparative Example 1	Example 1	Example 2	Example 3	Example 4
Lipid-peptide compound *	-	1.25	2.5	5	10
Purified water	100	98.75	97.5	95	90
Total	100	100	100	100	100
Relative average absorbance at 595 nm (N=5)	100	90.9	89.6	84.1	73.7

* Formulation using palmitoyl-Glycine-Histidine lipid-peptide compound.

Examples 5 to 7, Comparative Example 2

According to formulation shown in Table 2, a bacterial repelling composition was prepared as follows:

1. Purified water at 80°C was prepared, glycerin, a 1N aqueous sodium hydroxide solution, cetylpyridinium chloride (CPC), and dipotassium glycyrrhizinate (GK2) were added, and the materials were dissolved.

2. To purified water prepared at 1 was added a lipid-peptide compound-containing premix (product name, NANOFIBERGEL (registered trademark) TW-01W, NISSAN CHEMICAL INDUSTRIES, LTD., Chiyoda-ku, Tokyo, Japan) which had been heated to 80°C or higher and dissolved, and the resulting mixture was heated at 80°C.

3. To a 2% aqueous carboxyvinyl polymer solution (2% aqueous carbomer solution) was added purified water, this was added to the mixture in which the lipid-peptide compound had been dissolved, and the materials were further mixed while heating to 80°C or higher.

4. To the mixture obtained at 3 was added flavorant, the mixture was cooled while stirring (400 to 600 rpm) with a Homo Disper (Model 2.5, PRIMIX Corporation, Awaji-shi, Hyogo-ken, Japan), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition was obtained.

Using the resulting bacterial repelling composition, a bacterial repelling property assessment test was performed, and the resulting average absorbance is shown in Table 2. The average absorbance is expressed as a relative value, letting the absorbance of an example as a standard in the table to be 100.

Table 2 (Numerical values of formulation are parts by mass)

	Comparative Example 2	Example 5	Example 6	Example 7
Lipid-peptide compound *	-	1.25	2.5	5
CPC	0.05	0.05	0.05	0.05
GK2	0.05	0.05	0.05	0.05
2% aqueous carbomer solution	5	5	5	5
1N NaOH	1	1	1	1
Glycerin	15	15	15	15
Flavorant	0.5	0.5	0.5	0.5
Purified water	78.4	77.15	75.9	73.4
Total	100	100	100	100
Relative average absorbance at 595 nm (N=3)	100	90.0	76.2	66.4

* Formulation using palmitoyl-Glycine-Histidine lipid-peptide compound.

Examples 8 to 9

According to formulation shown in Table 3, a bacterial repelling composition was prepared as follows:

1. Purified water at 80°C was prepared, glycerin, a 1N aqueous sodium hydroxide solution, cetylpyridinium chloride (CPC), and dipotassium glycyrrhizinate (GK2) were added, and the materials were dissolved.

2. To purified water prepared at 1 was added a lipid-peptide compound-containing premix (product name, NANOFIBERGEL (registered trademark) TW-01W, NISSAN CHEMICAL INDUSTRIES, LTD., Chiyoda-ku, Tokyo, Japan) which had been heated to 80°C or higher and dissolved, and the resulting mixture was heated at 80°C.

3. To a 2% aqueous carboxyvinyl polymer solution (2% aqueous carbomer solution) was added purified water, this was added to the mixture in which the lipid-peptide compound had been dissolved, and the materials were further mixed while heating to 80°C or higher.

4. To the mixture obtained at 3 was added flavorant, the materials were cooled while stirring (400 to 600 rpm) with a Homo Disper (Model 2.5, PRIMIX Corporation, Awaji-shi, Hyogo-ken, Japan), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition was obtained.

Example 8 and Example 9 had the same composition, and Example 8 was applied as it was to the base material surface, and Example 9 was shaken vigorously with a hand for 5 seconds immediately before application to the base material surface. In the bacterial repelling composition of Example 8, aggregates existed in the resulting composition (gel) (visual observation). In contrast, in the bacterial repelling composition of Example 9, aggregates in the gel disappeared by shaking.

Using the resulting bacterial repelling composition, a bacterial repelling property assessment test was performed, and the resulting average absorbance is shown in Table 3. The average absorbance is expressed as a relative value, letting the absorbance of an example as a standard in the table to be 100.

Table 3 (Numerical values of formulation are parts by mass)

	Example 8	Example 9
Lipid-peptide compound *	10	10
CPC	0.05	0.05
GK2	0.05	0.05
2% aqueous carbomer solution	5	5
1N NaOH	1	1
Glycerin	15	15
Flavorant	0.5	0.5
Purified water	68.4	68.4
Total	100	100
Relative average absorbance at 595 nm (N=3)	100	54.9

* Formulation using palmitoyl-Glycine-Histidine lipid-peptide compound.

Examples 10 to 13

According to formulation shown in Table 4, a bacterial repelling composition was prepared as follows:

1. Purified water at 80°C was prepared, glycerin, cetylpyridinium chloride (CPC), and dipotassium glycyrrhizinate (GK2) were added, and the materials were dissolved.

2. To purified water prepared at 1 was added a lipid-peptide compound-containing premix (product name, NANOFIBERGEL (registered trademark) TW-01W, NISSAN CHEMICAL INDUSTRIES, LTD., Chiyoda-ku, Tokyo, Japan) which had been heated to 80°C or higher and dissolved, and the resulting mixture was heated at 80°C.

3. 12-Hydroxystearic acid (12-HSA) was added to the mixture in which the lipid-peptide compound had been dissolved, and the materials were further mixed and dissolved while heating to 80°C or higher.

4. To the mixture obtained at 3 were added tripotassium phosphate (TCP) and flavorant, the materials were cooled while stirring (400 to 600 rpm) with a Homo Disper (Model 2.5, PRIMIX Corporation, Awaji-shi, Hyogo-ken, Japan), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition was obtained.

Using the resulting bacterial repelling composition, a bacterial repelling property assessment test was performed, and the resulting average absorbance, dispersibility and the result of observation of the state of the composition are shown in Table 4. The absorbance is expressed as a relative value, letting the absorbance of an example as a standard in the table to be 100. For Examples 10 to 12, since a uniform composition was not obtained, bacterial repelling property assessment was not performed.

Table 4 (Numerical values of formulation are parts by mass)

	Example 10	Example 11	Example 12	Example 13	Comparative Example 1
Lipid-peptide compound *	5	5	5	5	-
CPC	1	1	1	1	-
GK2	1.6	1.6	1.6	1.6	-
TCP	0.25	0.25	0.25	0.25	-

12-HSA	0	0.05	0.1	1	-
Glycerin	15	15	15	15	-
Flavorant	0.5	0.5	0.5	0.5	-
Purified water	76.65	76.6	76.55	75.65	100
Total	100	100	100	100	100
Relative average absorbance at 595 nm (N=5)	N/A	N/A	N/A	73.1	100
Dispersibility	Bad	Bad	Fair	Good	-
State of composition	Liquid	Liquid	Semi-gel	Gel	-

* Formulation using palmitoyl-Glycine-Histidine lipid-peptide compound.

Examples 14 to 18 and Comparative Example 2

According to formulation shown in Table 5, bacterial repelling compositions were prepared as follows:

1. Purified water at 80°C was prepared, glycerin, a 1N aqueous sodium hydroxide solution, cetylpyridinium chloride (CPC), and dipotassium glycyrrhizinate (GK2) were added, and the materials were dissolved.

2. To purified water prepared at 1 was added a lipid-peptide compound-containing premix containing stearic acid, sodium hydroxide, 1,3-butanediol, water, and the lipid-peptide (palmitoyl-Gly-AA), where "AA" designated one of the following amino acids according to Examples 14-18: Tyr=tyrosine, Glu=glutamic acid, His=histidine,

Lys=lysine, Gly=glycine. These lipid amino acids were contract synthesized by GenScript Biotech Corporation. The lipid-peptide compound premix, had been heated to 80°C or higher and dissolved, and the resulting mixture was heated at 80°C.

3. To a 2% aqueous carboxyvinyl polymer solution (2% aqueous carbomer solution) was added purified water, this was added to the mixture in which the lipid-peptide compound had been dissolved, and the materials were further mixed while heating to 80°C or higher.

4. To the mixture obtained at 3 was added flavorant, the materials were cooled while stirring (400 to 600 rpm) with a Homo Disper (Model 2.5, PRIMIX Corporation, Awaji-shi, Hyogo-ken, Japan), to form a structure of a self-organized lipid-peptide compound, thereby, a bacterial repelling composition was obtained.

Using the resulting bacterial repelling composition, a bacterial repelling property assessment test was performed, and the resulting average absorbance, dispersibility and the result of observation of the state of the composition are shown in Table 5.

Table 5 (Numerical values of formulation are parts by mass)

	Example 14	Example 15	Example 16	Example 17	Example 18	Comp. Example 2
Lipid-peptide compound	0.2 (Pal-Gly-Tyr)	0.2 (Pal-Gly-Glu)	0.2 (Pal-Gly-His)	0.2 (Pal-Gly-Lys)	0.2 (Pal-Gly-Gly)	-
1,3-butanediol	2.0	2.0	2.0	2.0	2.0	-
Stearic acid	0.05	0.05	0.05	0.05	0.05	-

CPC	0.05	0.05	0.05	0.05	0.05	0.05
GK2	0.05	0.05	0.05	0.05	0.05	0.05
1N NaOH	1.0	1.0	1.0	1.0	1.0	1.0
Glycerin	15	15	15	15	15	15
2% Carbomer	5	5	5	5	5	5
Flavorant	0.5	0.5	0.5	0.5	0.5	0.5
Purified water	76.15	76.15	76.15	76.15	76.15	78.4
Total	100	100	100	100	100	100
Relative average absorbance at 595 nm	0.157	0.129	0.121	0.064	0.111	0.252

What is claimed is:

1. A bacterial repelling composition comprising:

a self-organized lipid-peptide compound, wherein the lipid-peptide compound is represented by the formula (1):

RCOP (1)

wherein R represents an aliphatic group having 9 to 23 carbon atoms, and P represents a peptide moiety comprising an amino acid sequence of 2 to 4 amino acids.

water in an amount not less than 30%,

2 The bacterial repelling composition according to claim 1, wherein the 2 to 4 amino acids are selected from the group of amino acids consisting of alanine (Ala), glutamic acid (Glu), glycine (Gly), histidine (His), Asparagine (Asn), glutamine (Gln), tryptophan (Trp), Tyrosine (Tyr).

3. The bacterial repelling composition according to claim 1, wherein the RCO portion of formula (1), which is composed of R and an adjacent carbonyl group, include a lauroyl group, a dodecylcarbonyl group, myristoyl group, a tetradecylcarbonyl group, a palmitoyl group, a margaroyl group, an oleoyl group, an elaidoyl group, a linoleoyl group, a stearoyl group, a vaccenoyl group, an octadecylcarbonyl group, an arachidoyl group, an eicosylcarbonyl group, a behenoyl group, an erucanoyl group, a docosylcarbonyl group, a lignoceroyl group, or a nervonoyl group.

4. The bacterial repelling composition according to claim 3, wherein the RCO portion of formula (1), is selected from the group consisting of a lauroyl group, a myristoyl group, a palmitoyl group, a margaroyl group, an oleoyl group, an elaidoyl group, a stearoyl group, and a behenoyl group.

5. The bacterial repelling composition according to claim 1, wherein at least one amino acid in the sequence of 2 to 4 amino acids is selected from the group consisting of glycine, histidine, and lysine.

6. The bacterial repelling composition according to claims 1, comprising 0.1% by mass to 20% by mass of said lipid-peptide compound.

7 The bacterial repelling composition according to claims 1, further comprising a bactericidal agent.

8. The bacterial repelling composition according to claim 1, further comprising an anti-inflammatory agent or an antiphologistic agent.

9. The bacterial repelling composition according to claim 1, further comprising a calcium phosphate compound.

10. The bacterial repelling composition according to claim 1, further comprising a thickener selected from the group consisting of hydroxypropylmethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, and carboxymethylcellulose, carboxymethylcellulose sodium, a carboxyvinyl polymer, sodium alginate, and carrageenan.

11. A method for forming a bacterial repelling coating on a surface, comprising applying said bacterial repelling composition as defined in claim 1 to a surface.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/050196

A. CLASSIFICATION OF SUBJECT MATTER
INV. C09D5/14 C07K5/04
ADD.

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)
C09D C07K

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)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/98362 A2 (HERCULES INC [US]) 27 December 2001 (2001-12-27) page 21, para.4-page 22, para.1; page 32, para.5; page 70, last paragraph; claims 16, 30	1-11
X	EP 3 210 613 A1 (ROHTO PHARMA [JP]) 30 August 2017 (2017-08-30) [0054]-[0055], [0169]-[0170]; tables 1-4 and 1-6; claim 1	1-11
X	EP 2 700 691 A1 (NISSAN CHEMICAL IND LTD [JP]) 26 February 2014 (2014-02-26)	1-10
A	[0052]; table 1; claim 1	11

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[X] Further documents are listed in the continuation of Box C.

[X] 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 another 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	Date of mailing of the international search report
7 May 2019	14/05/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Pellegrini, Paolo

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/050196

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MAKOVITZKI ARIK ET AL: "Ultrashort antibacterial and antifungal lipopeptides", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, NATIONAL ACADEMY OF SCIENCES, US, vol. 103, no. 43, 1 October 2006 (2006-10-01), pages 15997-16002, XP009096818, ISSN: 0027-8424, DOI: 10.1073/PNAS.0606129103	1-10
A	abstract; page 15997, col.2, para.3; table 1; page 16001, col.2, para.4-page 16002, col.1, para.1	11

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2019/050196

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2019/050196

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