

DESCRIPTION

Title of Invention

ADSORPTION INHIBITOR FOR INORGANIC FINE PARTICLES TO BE USED
IN SOFT CONTACT LENSES

Technical Field

[0001]

The present invention relates to an inorganic fine-particle adsorption inhibitor for soft contact lenses, containing a copolymer having a particular structure.

Background Art

[0002]

Pollen particles, such as cedar pollen or cypress pollen, and house dust are considered as a main cause of allergic conjunctivitis in the field of ophthalmology. Further, it has been reported that particulate inorganic matter such as yellow sand, PM10 or PM2.5, which generates recent global air pollution, also causes allergic conjunctivitis (non-patent documents 1 and 2). Allergic conjunctivitis is developed on attachment or adsorption of such an air pollutant to the conjunctiva or cornea, producing allergic symptoms such as bloodshot eyes, eye mucus, and teary eyes. Various technological developments have been made to cure, relieve, or prevent such allergic symptoms. Known treatment methods include a pharmaceutical/chemical method which cures or relieves the symptoms with a medicine or eyedrops containing an anti-allergic agent (patent document 1), and a physical method which involves wearing glasses or a mask to inhibit contact of an air pollutant with the conjunctiva or cornea (patent documents 2 and 3). While the pharmaceutical/chemical method is a highly effective method, it is known to cause a side effect such as drowsiness. While the physical method is effective before attachment or adsorption of an air pollutant to the conjunctiva or cornea, its effectiveness is lost upon attachment or adsorption of an air pollutant to the conjunctiva or cornea.

When an air pollutant is attached or adsorbed to the surface of a soft contact lens worn by a person, it is difficult to remove the pollutant with tears or artificial tears. Thus, the person wearing may suffer from allergic symptoms

over a long period of time.

Therefore, there has been a demand for the development of a technology which can inhibit attachment or adsorption of an air pollutant to the conjunctiva or cornea, and to the surface of a soft contact lens, thereby relieving allergic symptoms and relieving or reducing discomfort. However, such a technological development has not yet been made satisfactorily; there is no known effective method.

Citation List

Patent Literature

[0003]

Patent document 1: Japanese Patent Laid-Open Publication No. 2018-203791

Patent document 2: Japanese Patent Laid-Open Publication No. 2017-134100

Patent document 3: Japanese Patent Laid-Open Publication No. 2014-111147

Non-Patent Literature

[0004]

Non-Patent document 1: Tatsuya Mimura, Topic 1. Allergy and environmental factors in the field of ophthalmology, Allergy, 63(7), 901-906, 2014

Non-Patent document 2: Tatsuya Mimura et al., Airborne particulate matter (PM_{2.5}) and the prevalence of allergic conjunctivitis in Japan, Science of the Total Environment, 493-499, 2014

Summary of Invention

Technical Problem

[0005]

It is an object of the present invention to provide an inorganic fine-particle adsorption inhibitor for soft contact lenses, which inhibits adsorption of inorganic fine particles, such as PM₁₀, PM₅ or PM_{2.5}, to the surface of a soft contact lens, thereby relieving or reducing the symptoms of allergic conjunctivitis and improving discomfort.

Solution to Problem

[0006]

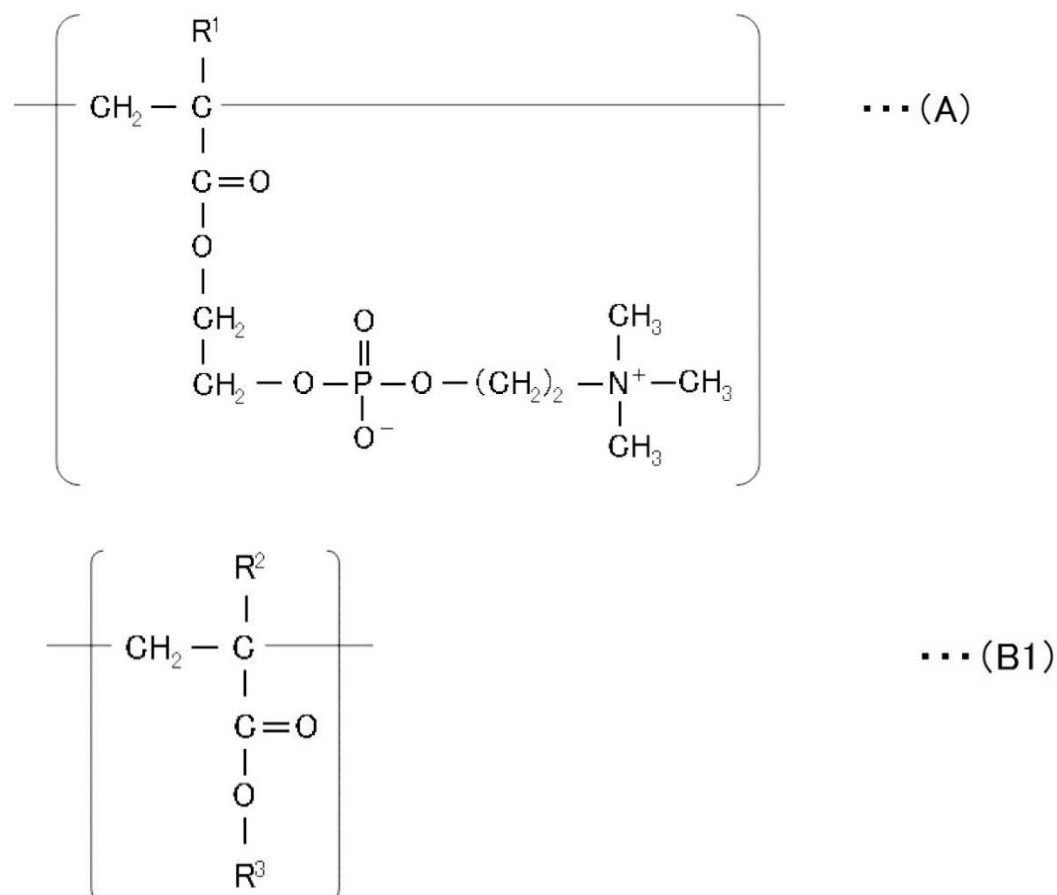
The present inventors, through their intensive studies to achieve the object, have found that the use of a material, containing a copolymer having a particular weight-average molecular weight and a particular structure, for a soft contact lens can inhibit adsorption of harmful inorganic fine particles, such as PM₁₀, PM₅ or

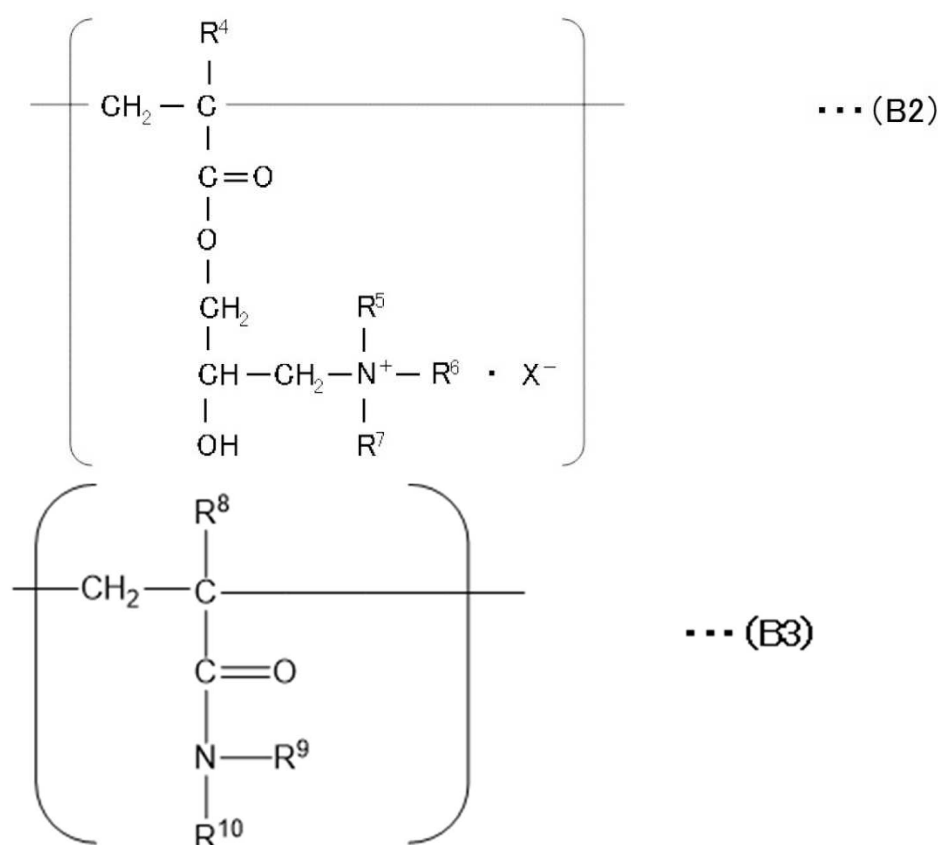
PM2.5, to the soft contact lens. Thus, it has been found that the material can serve as an inorganic fine-particle adsorption inhibitor for soft contact lenses, which can relieve or reduce the symptoms of allergic conjunctivitis and can improve discomfort. The present invention has been accomplished based on this finding.

Thus, the present invention provides the following inorganic fine-particle adsorption inhibitor for soft contact lenses.

[0007]

[1] An inorganic fine-particle adsorption inhibitor for soft contact lenses, containing a copolymer (P) having a weight-average molecular weight of 10,000 to 5,000,000 and comprising 10 to 90 mol % of the following structural units (A) based on 2-(meth)acryloyloxyethyl phosphorylcholine and 90 to 10 mol % of at least one type of structural units selected from the group consisting of the following structural units (B1) based on a (meth)acrylic monomer having an alkyl group, the following structural units (B2) based on a (meth)acrylic monomer having a quaternary ammonium group, and the following structural units (B3) based on a (meth)acrylamide monomer:





where R¹ represents a hydrogen atom or a methyl group, R² represents a hydrogen atom or a methyl group, R³ represents an alkyl group having 4 to 18 carbon atoms, R⁴ represents a hydrogen atom or a methyl group, R⁵, R⁶ and R⁷ each independently represent a hydrogen atom or an alkyl group having 1 to 8 carbon atoms, X⁻ represents a halogen ion or an acid residue, R⁸ represents a hydrogen atom or a methyl group, and R⁹ and R¹⁰ each independently represent a hydrogen atom or an alkyl group having 1 to 6 carbon atoms.

Advantageous Effects of Invention

[0008]

The use of the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention can inhibit adsorption of inorganic fine particles, such as such as PM₁₀, PM₅ or PM_{2.5}, to a soft contact lens after it is worn. Therefore, the agent makes it possible to relieve or reduce the symptoms of allergic conjunctivitis, thus improving discomfort.

Description of Embodiments

[0009]

The inorganic fine-particle adsorption inhibitor for soft contact lenses of

the present invention contains a copolymer (P).

The present invention will now be described in detail.

Lower limit values and upper limit values, which are set forth herein in a stepwise manner in a preferable numerical range (e.g. a content range or a weight-average molecular weight range), can be combined independently. For example, from the phrase “preferably 10 or more, more preferably 20 or more, and preferably 100 or less, more preferably 90 or less”, the “preferable lower limit value 10” and the “more preferable upper limit value 90” can be combined into the range of “10 or more and 90 or less”. Similarly, the range of “10 to 90” can be drawn from the phrase “preferably 10 to 100, more preferably 20 to 90”.

As used herein, “(meth)acrylic” refers to acrylic or methacrylic, (meth)acryloyl refers to acryloyl or methacryloyl, and “(meth)acrylate” refers to acrylate or methacrylate.

[0010]

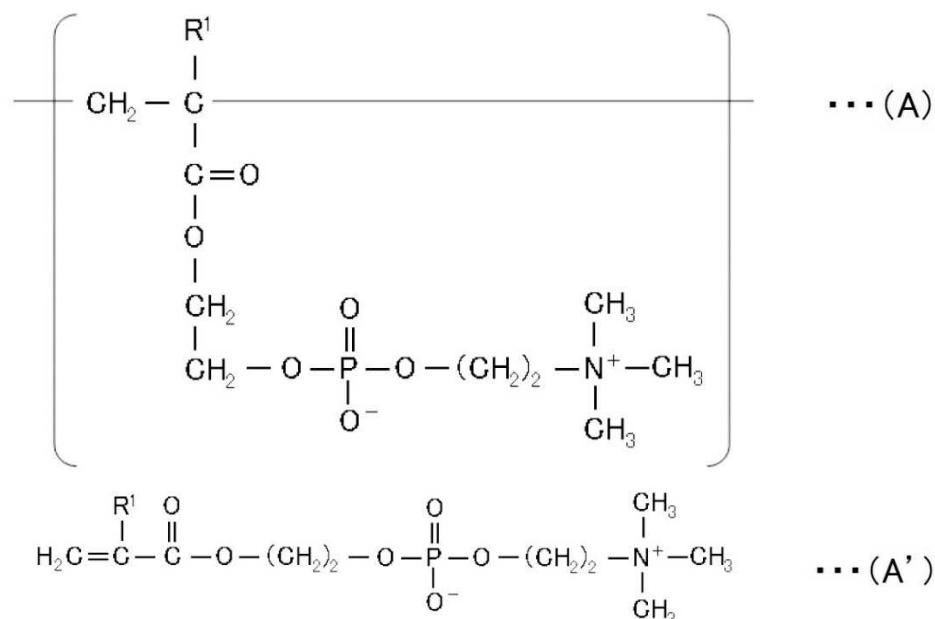
<Inorganic Fine-Particle Adsorption Inhibitor for Soft Contact Lenses>

The inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention contains the copolymer (P) comprising structural units (A) based on 2-(meth)acryloyloxyethyl phosphorylcholine and at least one type of structural units selected from the group consisting of structural units (B1) based on a (meth)acrylic monomer having an alkyl group, structural units (B2) based on a (meth)acrylic monomer having a quaternary ammonium group, and structural units (B3) based on a (meth)acrylamide monomer.

[0011]

<Structural Units (A) Based on 2-(Meth)acryloyloxyethyl Phosphorylcholine>

The structural units (A) based on 2-(meth)acryloyloxyethyl phosphorylcholine are represented by the following formula (A) and, in particular, are obtained by polymerization of a monomer represented by the following formula (A').



In the formulae (A) and (A'), R¹ may be either a hydrogen atom or a methyl group, and is preferably a methyl group.

[0012]

Owing to the inclusion of the structural units (A) in the molecular chain, the copolymer (P) for use in the present invention can produce the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.

The content of the structural units (A) in the copolymer (P) for use in the present invention is 10 to 90 mol %. If the content is less than 10 mol %, the copolymer (P) cannot produce the intended inorganic fine-particle adsorption inhibiting effect. If the content is more than 90 mol %, the copolymer (P) exhibits poor adsorption onto a soft contact lens due to the ultra-hydrophilicity of the (meth)acryloyloxyethyl phosphorylcholine segment. Accordingly, the intended effect of inhibiting adsorption of inorganic fine particles cannot be imparted to a soft contact lens.

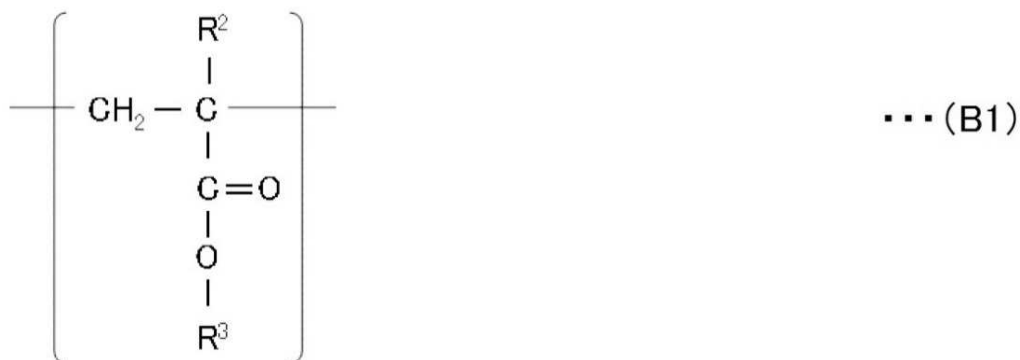
The content of the structural units (A) in the copolymer (P) is preferably 20 to 90 mol %, more preferably 30 to 90 mol %.

[0013]

<Structural Units (B1) Based on a (Meth)acrylic Monomer Having an Alkyl Group>

The structural units (B1) based on a (meth)acrylic monomer having an alkyl group are represented by the following formula (B1) and, in particular, are obtained by polymerization of a monomer represented by the following formula (B1'). The inclusion of the structural units (B1) in the molecular chain of the

copolymer (P) for use in the present invention can enhance the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.



In the formulae (B1) and (B1'), R² may be either a hydrogen atom or a methyl group, and is preferably a methyl group. R³ is an alkyl group having 4 to 18 carbon atoms, and may be either linear or branched.

[0014]

Specific examples of the linear alkyl group having 4 to 18 carbon atoms include an n-butyl group, an n-pentyl group, an n-hexyl group, an n-heptyl group, an n-octyl group, an n-nonyl group, an n-decyl group, an n-undecyl group, an n-dodecyl group, an n-tridecyl group, an n-tetradecyl group, an n-pentadecyl group, an n-hexadecyl group, an n-heptadecyl group, and an n-octadecyl group. Specific examples of the branched alkyl group having 4 to 18 carbon atoms include a t-butyl group, an isobutyl group, an isopentyl group, a t-pentyl group, a neopentyl group, an isohexyl group, an isoheptyl group, an isooctyl group, an isononyl group, an isodecyl group, an isoundecyl group, an isododecyl group, an isotridecyl group, an isotetradecyl group, an isopentadecyl group, an isohexadecyl group, an isoheptadecyl group, and an isoctadecyl group.

An n-butyl group, an n-dodecyl group, and an n-octadecyl group are preferred from the viewpoint of the effect of the copolymer (P) of inhibiting adsorption of inorganic fine particles to a soft contact lens.

[0015]

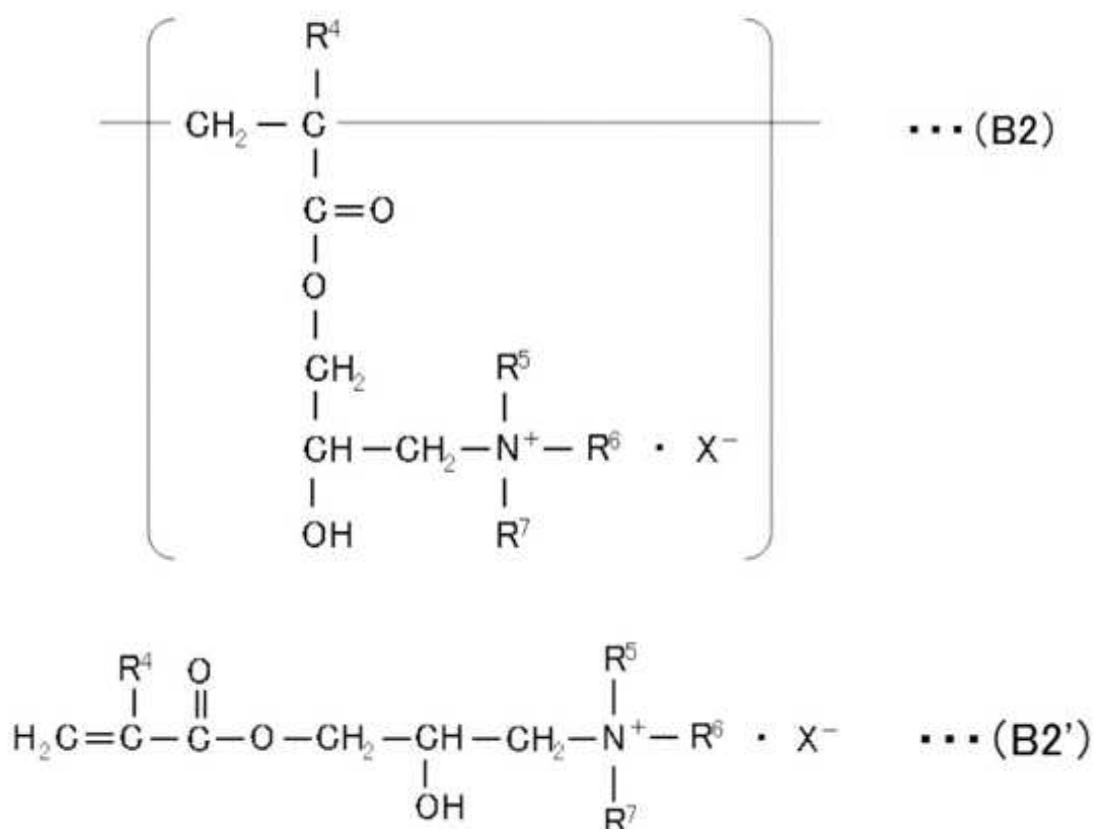
Any (meth)acrylic monomer having an alkyl group can be used as long as it provides the copolymer (P) with the structural units (B1) because the structural units ensure sufficient adsorption of the copolymer (P) to a soft contact lens.

However, from the viewpoint of enhancing adsorption of the copolymer (P) to a soft contact lens, it is preferred to use butyl (meth)acrylate, lauryl (meth)acrylate, or stearyl (meth)acrylate, in particular stearyl (meth)acrylate as the (meth)acrylic monomer having an alkyl group.

[0016]

<Structural Units (B2) Based on a (Meth)acrylic Monomer Having a Quaternary Ammonium Group>

The structural units (b2) based on a (meth)acrylic monomer having a quaternary ammonium group are represented by the following formula (B2) and, in particular, are obtained by polymerization of a monomer represented by the following formula (B2'). The inclusion of the structural units (B2) in the molecular chain of the copolymer (P) for use in the present invention can enhance the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.



[0017]

In the formulae (B2) and (B2'), R⁴ may be either a hydrogen atom or a methyl group, and is preferably a methyl group. R⁵, R⁶ and R⁷ each independently represent a hydrogen atom or an alkyl group having 1 to 8 carbon atoms. The alkyl group may be linear, branched or cyclic.

[0018]

Specific examples of R^5 , R^6 and R^7 include a methyl group, an ethyl group, a propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-pentyl group, an isopentyl group, an n-hexyl group, an isohexyl group, an n-heptyl group, an isoheptyl group, an n-octyl group, an isooctyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, and a cyclohexyl group.

R^5 , R^6 and R^7 are each preferably a methyl group, an ethyl group, a propyl group, or an isopropyl group, and more preferably a methyl group.

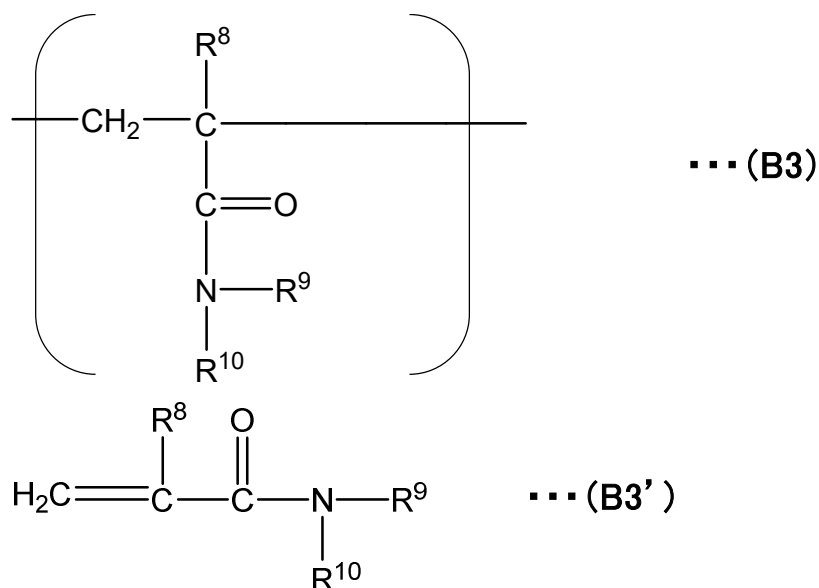
X is a halogen ion such as a chloride ion, or an acid residue such as a sulfate ion or a methylsulfate ion, and is preferably a halogen ion.

From the viewpoint of enhancing the effect of the copolymer (P) of inhibiting adsorption of inorganic fine particles to a soft contact lens, it is preferred to use, for example, 2-hydroxy-3-(meth)acryloyloxypropyl trimethyl ammonium chloride as the (meth)acrylic monomer having a quaternary ammonium group.

[0019]

<Structural Units (B3) Based on a (Meth)acrylamide Monomer>

The structural units (B3) based on a (meth)acrylamide monomer are represented by the following formula (B3) and, in particular, are obtained by polymerization of a monomer represented by the following formula (B3'). The inclusion of the structural units (B3) in the molecular chain of the copolymer (P) for use in the present invention can increase the molecular weight of the copolymer and can enhance the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.



[0020]

In the formulae (B3) and (B3'), R^8 may be either a hydrogen atom or a methyl group, and is preferably a hydrogen atom. R^9 and R^{10} each independently represent a hydrogen atom or an alkyl group having 1 to 6 carbon atoms. The alkyl group may be linear, branched or cyclic. Specific examples of the alkyl group include a methyl group, an ethyl group, a propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, an n-pentyl group, an isopentyl group, an n-hexyl group, an isohexyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, and a cyclohexyl group. R^9 and R^{10} are each preferably a hydrogen atom, a methyl group, an ethyl group, a propyl group, or an isopropyl group, and more preferably a methyl group.

From the viewpoint of increasing the molecular weight of the copolymer (P) and enhancing the effect of the copolymer (P) of inhibiting adsorption of inorganic fine particles to a soft contact lens, it is preferred to use, for example, N,N-dimethylacrylamide as the (meth)acrylamide monomer.

[0021]

The copolymer (P) for use in the present invention has, in the molecular chain, at least one type of structural units selected from the group consisting of the structural units (B1), (B2) and (B3). The copolymer (P) for use in the present invention may have only one type of structural units selected from the group consisting of the structural units (B1), (B2) and (B3), two types of structural units (e.g., a combination of (B1) and (B2), a combination of (B2) and (B3) or a combination of (B3) and (B1)) selected from the group consisting of the structural units (B1), (B2) and (B3), or all the structural units (B1), (B2) and (B3).

[0022]

Owing to the inclusion of the structural units (A) in addition to the structural units (B1) to (B3) in the polymer chain, the copolymer (P) for use in the present invention can serve as an inorganic fine-particle adsorption inhibitor for soft contact lenses which exerts the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.

[0023]

The content of the structural units (B1) to (B3) in the copolymer (P) for use in the present invention (the content of the structural units (B1), (B2) or (B3) when the copolymer (P) has only that one type of structural units, or the total content of two or more types of structural units when the copolymer (P) has two or more types

of structural units) is preferably 10 to 90 mol %, more preferably 10 to 80 mol %, and even more preferably 10 to 70 mol %. If the content is less than 10 mol %, the copolymer (P) has high hydrophilicity, and therefore exhibits poor adsorption or adhesion to a soft contact lens. Accordingly, the copolymer (P) may not exert the intended inorganic fine-particle adsorption inhibiting effect. If the content is more than 90 mol %, the solubility of the copolymer (P) in water is low. Therefore, it can be difficult to produce the inorganic fine-particle adsorption inhibitor for soft contact lenses.

[0024]

The copolymer (P) for use in the present invention preferably has the structural units (A) and the structural units (B1) to (B3) in the molecular chain based on one of the following combinations of monomers from the viewpoint of producing the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens:

[0025]

2-(meth)acryloyloxyethyl phosphorylcholine and butyl (meth)acrylate;

2-(meth)acryloyloxyethyl phosphorylcholine and stearyl (meth)acrylate;

2-(meth)acryloyloxyethyl phosphorylcholine and 2-hydroxy-3-(meth)acryloyloxypropyl trimethyl ammonium chloride; and

2-(meth)acryloyloxyethyl phosphorylcholine, N,N-dimethylacrylamide, and stearyl (meth)acrylate.

[0026]

While the copolymer (P) for use in the present invention may contain structural units other than the structural units (A) and the structural units (B1) to (B3), it preferably consists of the structural units (A) and one type, two types or three types of structural units selected from the group consisting of the structural units (B1), the structural units (B2) and the structural units (B3). Among them, a combination of (A) and (B1), a combination of (A) and (B2), and a combination of (A), (B1) and (B3) are preferred, a combination of (A) and (B1) and a combination of (A), (B1) and (B3) are more preferred, and a combination of (A) and (B1) is even more preferred.

[0027]

The copolymer (P) for use in the present invention has a weight-average molecular weight of 10,000 to 5,000,000, preferably 20,000 to 2,000,000. If the weight-average molecular weight is less than 10,000, the copolymer (P) will exhibit

poor adsorption or adhesion to a soft contact lens. Accordingly, the copolymer (P) may not exert the intended inorganic fine-particle adsorption inhibiting effect. If the weight-average molecular weight is more than 5,000,000, it can be difficult to produce the inorganic fine-particle adsorption inhibitor for soft contact lenses due to a rapid increase of the viscosity.

[0028]

The weight-average molecular weight of the copolymer (P) can be determined in terms of polyethylene glycol by GPC (gel permeation chromatography).

Either a single copolymer having a particular weight-average molecular weight or a mixture of two or more copolymers having different weight-average molecular weights may be used as the copolymer (P) of the present invention. The use as the copolymer (P) of a mixture of two or more copolymers having different weight-average molecular weights can enhance the effect of the copolymer (P) of inhibiting adsorption of inorganic fine particles to a soft contact lens.

[0029]

When a mixture of two copolymers is used, it is preferred to use a combination of a copolymer (P1) having a weight-average molecular weight of 200,000 to 800,000 and a copolymer (P2) having a weight-average molecular weight of 900,000 to 1,500,000, or a combination of a copolymer (P1') having a weight-average molecular weight of 250,000 to 800,000 and a copolymer (P3) having a weight-average molecular weight of 10,000 to 200,000.

The mixing ratio by weight between the copolymer (P1) and the copolymer (P2) may be 1:9 to 9:1, preferably 3:7 to 7:3, and more preferably 4:6 to 6:4.

The mixing ratio by weight between the copolymer (P1') and the copolymer (P3) may be 1:9 to 9:1, preferably 3:7 to 7:3, and more preferably 4:6 to 6:4.

[0030]

The inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention preferably comprises 0.001 to 5.0 w/v % of the copolymer (P), and water as a solvent. A mixed solvent of water and an alcohol may be used as a solvent. Examples of the alcohol include methanol, ethanol, n-propanol, and isopropanol. The inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention can be obtained by dissolving the copolymer (P) in water or the mixed solvent in such a manner that the concentration of the copolymer (P) falls within the range of 0.001 to 5.0 w/v %. If the concentration of

the copolymer (P) is less than 0.001 w/v %, the inhibitor cannot exert a sufficient inorganic fine-particle adsorption inhibiting effect. If the concentration of the copolymer (P) is more than 5.0 w/v %, the inhibitor may not exert an inorganic fine-particle adsorption inhibiting effect that meets the large amount of the copolymer (P) used.

The concentration of the copolymer (P) is preferably 0.01 to 5.0 w/v %, more preferably 0.01 to 4.0 w/v %, and even more preferably 0.01 to 3.0 w/v %.

[0031]

Any water may be used in the present invention as long as it is water for pharmaceutical manufacturing or water having a comparable quality. For example, it is possible to use water specified in Japanese Pharmacopoeia.

The use of the copolymer (P) of the present invention for a soft contact lens can inhibit adsorption of inorganic fine particles to the soft contact lens which is being worn. This makes it possible to relieve or reduce the symptoms of allergic conjunctivitis, thus improving the discomfort of the user wearing the soft contact lens.

[0032]

The inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention can exert an adsorption inhibiting effect on inorganic particles (such as PM10 [fine particles having a particle size of approximately 10 μm or less, which pass through a sizing device having a trapping efficiency of 50% at a particle size of 10 μm]).

In particular, the inhibitor of the present invention is effective against fine particulate matters which are inorganic fine particles (PM10 [particles having a particle size of approximately 10 μm or less, which pass through a sizing device having a trapping efficiency of 50% at a particle size of 10 μm], PM5 [fine particles having a particle size of approximately 5 μm or less, which pass through a sizing device having a trapping efficiency of 50% at a particle size of 5 μm], PM2.5 [fine particles having a particle size of approximately 2.5 μm or less, which pass through a sizing device having a trapping efficiency of 50% at a particle size of 2.5 μm]), yellow sand, and deposit dust.

[0033]

Besides the copolymer (P) and water, the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention can also optionally contain components generally used in ophthalmic preparations, such as a decongestant

component, an anti-inflammatory and astringent component, a vitamin, an amino acid, a sulfa drug, a saccharide, a freshener, an inorganic salt, an organic acid salt, an acid, a base, an antioxidant, a stabilizer, a preservative, and a mucin secretagogue.

[0034]

Examples of the decongestant component include epinephrine or a salt thereof, ephedrine hydrochloride, tetrahydrozoline hydrochloride, naphazoline or a salt thereof, phenylephrine, and methylephedrine hydrochloride.

[0035]

Examples of the anti-inflammatory and astringent component include epsilon-aminocaproic acid, allantoin, berberine or a salt thereof, sodium azulene sulfonate, glycyrrhizic acid or a salt thereof, zinc lactate, zinc sulfate, and lysozyme chloride.

[0036]

Examples of the vitamin include sodium flavin adenine dinucleotide, cyanocobalamin, retinol acetate, retinol palmitate, pyridoxine hydrochloride, panthenol, sodium pantothenate, and calcium pantothenate.

[0037]

Examples of the amino acid include aspartic acid or a salt thereof, and aminoethylsulfonic acid.

[0038]

Examples of the sulfa drug include sulfamethoxazole or a salt thereof, sulfisoxazole, and sodium sulfisomidine.

[0039]

Examples of the saccharide include glucose, mannitol, sorbitol, xylitol, and trehalose.

Examples of the freshener include menthol and camphor.

[0040]

Examples of the inorganic salt include sodium chloride, potassium chloride, borax, sodium hydrogen carbonate, sodium hydrogen phosphate, and anhydrous sodium dihydrogen phosphate.

[0041]

An example of the organic acid salt is sodium citrate.

Examples of the acid include boric acid, phosphoric acid, citric acid, sulfuric acid, acetic acid, and hydrochloric acid.

Examples of the base include sodium hydroxide, potassium hydroxide, trishydroxymethylaminomethane, and monoethanolamine.

[0042] Examples of the antioxidant include tocopherol acetate and dibutylhydroxytoluene.

Examples of the stabilizer include sodium edetate and glycine.

Examples of the preservative include benzalkonium chloride, chlorhexidine gluconate, potassium sorbate, methylparaben, ethylparaben, propylparaben, isopropylparaben, butylparaben, isobutylparaben, and polyhexanide hydrochloride.

Examples of the mucin secretagogue include diquafosol sodium and rebamipide.

[0043]

There is no particular limitation on the product form or type of the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention as long as it is an ophthalmic preparation. Examples may include soft contact lens care products such as eye-drops, a contact lens wetting solution, a contact lens cleaning solution, a contact lens cleaning and storage solution, and a filling solution for contact lenses.

[0044]

From the viewpoint of enhancing the inorganic fine-particle adsorption inhibiting effect, the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention is preferably applied to soft contact lenses (ionic soft contact lenses) belonging to Groups III and IV of the FDA classification. The FDA classification is a classification of soft contact lenses as defined by the United States Food and Drug Administration (FDA): Group I: non-ionic soft contact lenses having a water content of less than 50%, Group II: non-ionic soft contact lenses having a water content of 50% or more, Group III: ionic soft contact lenses having a water content of less than 50%, and Group IV: ionic soft contact lenses having a water content of 50% or more.

[0045]

Specific examples of soft contact lens belonging to Group III or IV include the following (each numerical value in parentheses represents a water content, followed by a main component constituting the soft contact lens).

[0046]

(Soft Contact Lenses of Group III)

balafilcon A (36%. Tris-VC, NVP)

[0047]

(Soft Contact Lenses of Group IV)

etafilcon A (58%, 2-hydroxyethyl methacrylate-methacrylic acid), ocufilcon B (52%, 2-hydroxyethyl methacrylate-methacrylic acid), ocufilcon D (55%, 2-hydroxyethyl methacrylate-methacrylic acid), phemefilcon A (55%, 2-hydroxyethyl methacrylate-ethoxyethyl methacrylate-methacrylic acid), vifilcon A (55%, 2-hydroxyethyl methacrylate-polyvinylpyrrolidone-methacrylic acid), methafilcon A (55%, 2-hydroxyethyl methacrylate-methacrylic acid), bufilcon A (55%, 2-hydroxyethyl methacrylate-diacetone acrylamide-methacrylic acid), perfilcon A (71%, 2-hydroxyethyl methacrylate-N-vinylpyrrolidone-methacrylic acid), and SEED 1dayPure moisture (58%, 2-hydroxyethyl methacrylate-a methacrylate compound having a quaternary ammonium group-a methacrylate compound having a carboxy group-methacrylic acid-ethylene glycol dimethacrylate)

[0048]

Among them, soft contact lenses belonging to Group IV are preferred, and soft contact lenses belonging to Group IV and having a water content of 55% or more are more preferred from the viewpoint of the effect of inhibiting adsorption of inorganic fine particles to a soft contact lens.

Examples

[0049]

The following examples illustrate the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention in greater detail and are not intended to limit the scope of the invention. The following copolymers are used in Examples and Comparative Examples.

[0050]

Copolymer (P1): 2-methacryloyloxyethyl phosphorylcholine-butyl methacrylate copolymer [structural units (A) 80 mol %, structural units (B1) 20 mol %, weight-average molecular weight 600,000]

Copolymer (P2): 2-methacryloyloxyethyl phosphorylcholine-butyl methacrylate copolymer [structural units (A) 80 mol %, structural units (B1) 20 mol %, weight-average molecular weight 1,100,000]

Copolymer (P3): 2-methacryloyloxyethyl phosphorylcholine-butyl methacrylate copolymer [structural units (A) 80 mol %, structural units (B1) 20 mol %, weight-average molecular weight 150,000]

Copolymer (P4): 2-methacryloyloxyethyl phosphorylcholine-butyl methacrylate copolymer [structural units (A) 30 mol %, structural units (B1) 70 mol %, weight-average molecular weight 142,000]

Copolymer (P5): 2-methacryloyloxyethyl phosphorylcholine-stearyl methacrylate copolymer [structural units (A) 80 mol %, structural units (B1) 20 mol %, weight-average molecular weight 60,000]

Copolymer (P6): 2-methacryloyloxyethyl phosphorylcholine-2-hydroxy-3-methacryloyloxypropyl trimethyl ammonium copolymer [structural units (A) 70 mol %, structural units (B2) 30 mol %, weight-average molecular weight 450,000]

Copolymer (P7): 2-methacryloyloxyethyl phosphorylcholine-N,N-dimethylacrylamide-stearyl methacrylate copolymer [structural units (A) 50 mol %, structural units (B3) 45 mol %, structural units (B1) 5 mol %, weight-average molecular weight 200,000]

[0051]

Comparative polymer (Q1): butyl methacrylate polymer [weight-average molecular weight 180,000], purchased from FUJIFILM Wako Pure Chemical Corporation (product name Poly(n-butyl methacrylate))

Comparative polymer (Q2): 2-hydroxy-3-methacryloyloxypropyl trimethyl ammonium polymer [weight-average molecular weight 300,000], obtained by polymerization carried out by a method described in the working examples of Japanese Patent Laid-Open Publication No. H8-258403

Comparative polymer (Q3): N,N-dimethylacrylamide polymer [number-average molecular weight 10,000], purchased from Sigma-Aldrich Japan (product name Poly(N,N-dimethylacrylamide), DDMAT terminated)

[0052]

The weight-average molecular weight of each of the above copolymers was measured by GPC (gel permeation chromatography) under the following conditions. GPC System: High-Performance Liquid Chromatography System CCP & 8020 Series (manufactured by Tosoh Corporation)

Columns: Shodex OHpak SB-802.5HQ (manufactured by Showa Denko KK) and SB-806HQ (manufactured by Showa Denko KK) were connected in series

Developing solvent: 20 mM sodium phosphate buffer solution (pH 7.4)

Detector: differential refractive index detector, UV detector (wavelength 210 nm)

Molecular weight standard: EasiVial PEG/PEO (manufactured by Agilent Technologies Corporation)

Flow rate: 0.5 mL/min

Column temperature: 45°C

Sample: each copolymer was diluted with the developing solvent to a final concentration of 0.1% by weight

[0053]

<phosphate buffer solution>

A phosphate buffer solution (hereinafter referred to as “PBS”) was used in the below-described inorganic fine-particle adsorption test. The PBS (composition: potassium chloride 0.02 w/v %, potassium dihydrogen phosphate 0.02 w/v %, sodium chloride 0.8 w/v %, disodium hydrogen phosphate 0.115 w/v %) was a product of Sigma-Aldrich.

[0054]

<Inorganic Fine-Particle Adsorption Test>

A test of adsorption of inorganic fine particles to a soft contact lens was performed according to the following procedure.

(1) One soft contact lens was taken from a blister pack, and cleaned with the PBS. The cleansed soft contact lens was placed in one well of a 24-well plate, and 2 mL of a solution of an example or a comparative example was placed into the well.

(2) Thereafter, the 24-well plate was shaken for one hour.

(3) Using urban dust (PM2.5, obtained from National Institute for Environmental Studies), the PBS and an ultrasonic homogenizer (one-minute treatment with the homogenizer), a solution having an urban dust concentration of 1mg/mL was prepared (hereinafter referred to as “the dust solution”).

(4) A new 24-well plate was provided, and 1.5 mL of the dust solution was placed into one well of the 24-well plate. Thereafter, the soft contact lens after the above step (2) was immersed in the dust solution for one hour.

(5) After immersion, the soft contact lens was taken out of the solution, and cleaned three times with 10 mL of PBS.

(6) After cleaning, the transmittance of the soft contact lens was measured to determine the amount of dust (amount of inorganic fine particles) adsorbed on the surface of the soft contact lens.

[0055]

The inorganic fine-particle adsorption inhibiting effect of each test solution was evaluated according to the below-described evaluation criteria.

Using Comparative Example 1-4, and Comparative Examples 3-1 to 3-2 as

a reference, the inorganic fine-particle adsorption inhibition rate was calculated according to the following equation to evaluate the inorganic fine-particle adsorption inhibiting effect.

(Inorganic fine-particle adsorption inhibition rate) = $\{1 - ((\text{amount of adsorbed inorganic fine particles in an example or comparative example}) / (\text{amount of adsorbed inorganic fine particles in a comparative example using the corresponding soft contact lens and the corresponding fine particle species}))\} \times 100$
[0056]

(Evaluation Criteria)

Inorganic fine-particle adsorption inhibition rate of 70% or more: very excellent inorganic fine-particle adsorption inhibiting effect

Inorganic fine-particle adsorption inhibition rate of 50% or more and less than 70%: excellent inorganic fine-particle adsorption inhibiting effect

Inorganic fine-particle adsorption inhibition rate of 30% or more and less than 50%: some inorganic fine-particle adsorption inhibiting effect

Inorganic fine-particle adsorption inhibition rate of less than 30%: no inorganic fine-particle adsorption inhibiting effect

[0057]

[Example 1-1]

About 80 g of purified water was weighed, and 1.0 g of the copolymer (P1) was weighed and added to the purified water, followed by stirring of the mixture. Thereafter, purified water was added to the mixture until the total volume reached 100 mL. The mixture was then subjected to aseptic filtration to prepare a solution of Example 1-1. The appearance of the solution is shown in Table 1 below.

[0058]

[Examples 1-2 to 1-9 and Comparative Examples 1-1 to 1-4]

Solutions of Examples 1-2 to 1-9 and Comparative Examples 1-1 to 1-4 were prepared in the same manner as in Example 1-1 but using the components and the amounts shown in Table 1.

[0059]

[Example 2-1]

The above-described inorganic fine-particle adsorption test was performed using the solution of Example 1-1 and SEED 1dayPure moisture (soft contact lens manufactured by SEED). The results are shown in Table 2 below.

[0060]

[Examples 2-2 to 2-9 and Comparative Examples 2-1 to 2-4]

The inorganic fine-particle adsorption test was performed using each of the solutions and soft contact lens of the Examples or Comparative Examples shown in Table 2. The inorganic fine-particle adsorption test was performed in the same manner as in Example 2-1. The results of the inorganic fine-particle adsorption test for Examples 2-2 to 2-9 and Comparative Examples 2-1 to 2-4 are shown in Table 2.

[0061]

[Example 3-1]

The inorganic fine-particle adsorption test was performed in the same manner as in Example 2-1 except for using the solution of Example 1-5 and changing the soft contact lens to Medalist FreshFit (soft contact lens manufactured by Bausch & Lomb Japan). The results are shown in Table 3 below.

[0062]

[Examples 3-2 to 3-6 and Comparative Examples 3-1 and 3-2]

The inorganic fine-particle adsorption test was performed using each of the solutions, soft contact lens and the fine particle species of Examples shown in Table 3. The inorganic fine-particle adsorption test was performed in the same manner as in Example 3-1. The results of the inorganic fine-particle adsorption test for Examples 3-2 to 3-6 and Comparative Examples 3-1 and 3-2 are shown in Table 3.

[0063]

Table 1

	Example 1-1	Example 1-2	Example 1-3	Example 1-4	Example 1-5	Example 1-6	Example 1-7	Example 1-8	Example 1-9	Comp. Ex 1-1	Comp. Ex 1-2	Comp. Ex 1-3	Comp. Ex 1-4
Com- position (g)	Copolymer (P1)	1.0	3.0	0.10	0.5	0.5							
	Copolymer (P2)				0.5								
	Copolymer (P3)					0.5							
	Copolymer (P4)						1.0						
	Copolymer (P5)						1.0						
	Copolymer (P6)							1.0					
	Copolymer (P7)								1.0				
	Copolymer (Q1)									1.0			
	Copolymer (Q2)										1.0		
	Copolymer (Q3)											1.0	
Analytical results	Water	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL	Amount to 100 mL
	Appearance	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid	Colorless trans-parent liquid
										.*		.*	

Water: purified water as specified in Japanese Pharmacopoeia, manufactured by KENEI Pharmaceutical

*: the copolymer was insoluble, and thus a solution could not be prepared

[0064]

Table 2

	Example 2-1	Example 2-2	Example 2-3	Example 2-4	Example 2-5	Example 2-6	Example 2-7	Example 2-8	Example 2-9	Comp. Ex. 2-1	Comp. Ex. 2-2	Comp. Ex. 2-3	Comp. Ex. 2-4
Solution evaluated	Example 1-1	Example 1-2	Example 1-3	Example 1-4	Example 1-5	Example 1-6	Example 1-7	Example 1-8	Example 1-9	Comp. Ex. 1-1	Comp. Ex. 1-2	Comp. Ex. 1-3	Comp. Ex. 1-4
Soft contact lens evaluated	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)	Lens (1)
Fine particles evaluated	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Urban dust
Evaluation results	Transmittance	0.017	0.014	0.015	0.015	0.017	0.001	0.021	0.024	-	0.030	-	0.035
	Inorganic fine-particle adsorption inhibition rate (%)	51.4%	60.0%	37.1%	57.1%	51.4%	97.1%	40.0%	31.4%	Immeasur- able	14.3%	Immeasur- able	-

Lens (1): SEED 1dayPure moisture, manufactured by SEED; power -3.00D; base curve 8.8; diameter 14.2; water content 58%; constituent monomers 2-HEMA-a methacrylate having a quaternary ammonium group-a methacrylate having a carboxy group-MMA-EGDMA; FDA classification Group IV (ionic soft contact lens)

[0065]

The results for Examples 2-1 to 2-9 and Comparative Examples 2-1 to 2-4 indicate that the use of each copolymer (P) inhibits adsorption of inorganic fine particles (urban dust) to a soft contact lens, and that the inorganic fine-particle adsorption inhibiting effect increases with the concentration of the copolymer (P). Further, the results for Examples 2-4 to 2-9 indicate that the use of the various types of copolymers (P) can produce an inorganic fine-particle adsorption inhibiting effect.

[0066]

Table 3

		Example 3-1	Example 3-2	Example 3-3	Example 3-4	Example 3-5	Example 3-6	Comp. Ex 3-1	Comp. Ex 3-2
Solution evaluated		Example 1-5	Example 1-6	Example 1-7	Example 1-8	Example 1-9	Example 1-5	Comp. Ex 1-4	Comp. Ex 1-4
Soft contact lens evaluated		Lens (2)	Lens (2)	Lens (2)	Lens (2)	Lens (2)	Lens (1)	Lens (2)	Lens (1)
Fine particles evaluated		Urban dust	Urban dust	Urban dust	Urban dust	Urban dust	Yellow sand	Urban dust	Yellow sand
Evaluation results	Transmittance	0.008	0.010	0.003	0.011	0.011	0.007	0.017	0.015
	Inorganic fine-particle adsorption inhibition rate (%)	52.9%	41.2%	82.4%	35.3%	35.3%	53.3%	-	-

Lens (2): Medalist FreshFit, manufactured by Bausch & Lomb Japan; power - 3.00D; base curve 8.6; diameter 14.0; water content 36%; constituent monomers TrisVC-NVP; FDA classification Group III (ionic soft contact lens)

Yellow sand: Gobi yellow sand (obtained from National Institute for Environmental Studies)

[0067]

The results for Examples 3-1 to 3-6 indicate that each copolymer (P) produces an inorganic fine-particle adsorption inhibiting effect not only on urban dust but also on other air pollutants such as yellow sand.

Industrial Applicability

[0068]

The use of the inorganic fine-particle adsorption inhibitor for soft contact lenses of the present invention can produce soft contact lens care products which can inhibit adsorption of inorganic fine particles to a soft contact lens, thereby

relieving or reducing the symptoms of allergic conjunctivitis and improving discomfort.

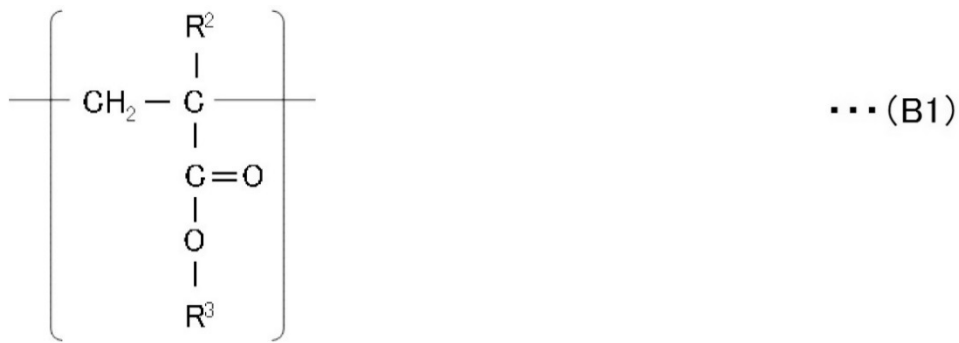
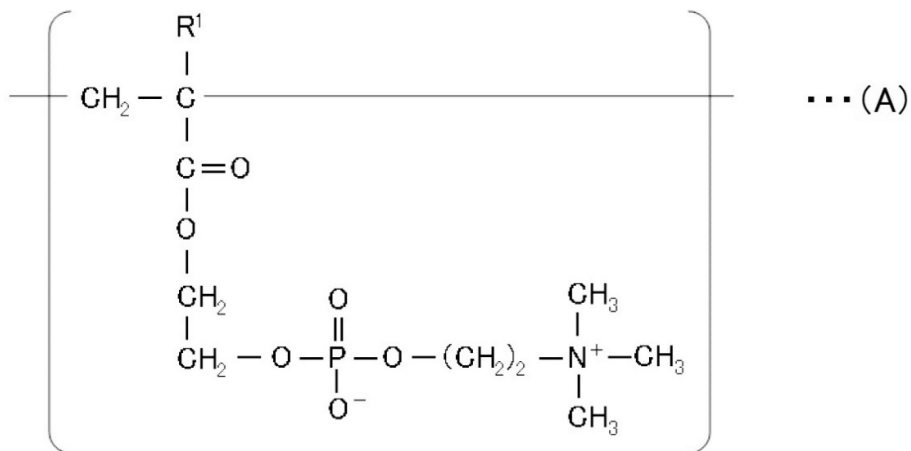
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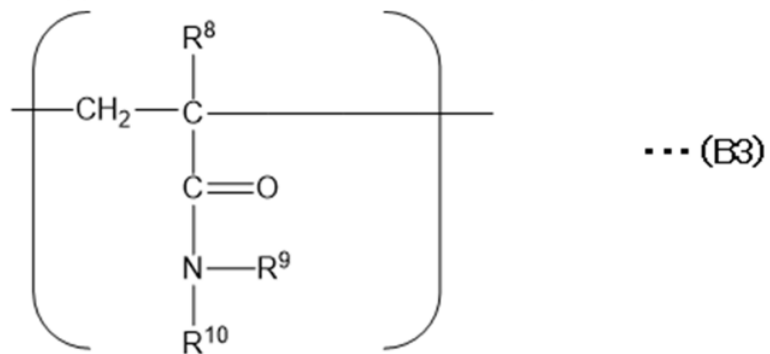
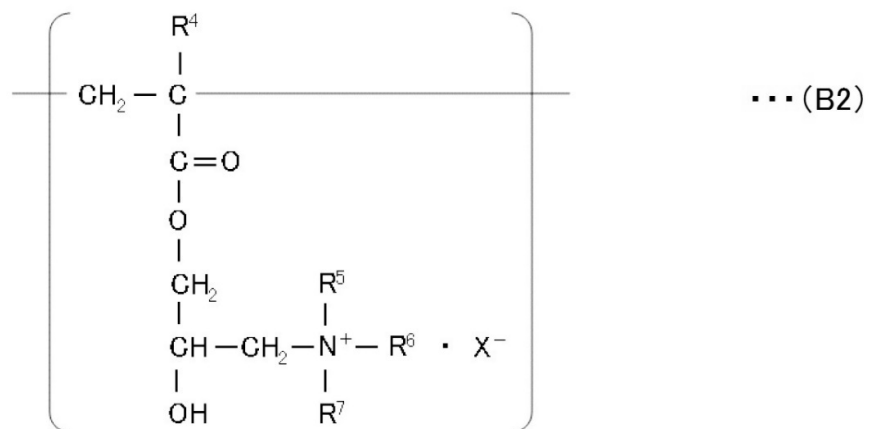
[Claim 1]

An inorganic fine-particle adsorption inhibitor for soft contact lenses, comprising a copolymer (P) having a weight-average molecular weight of 10,000 to 5,000,000 and comprising 10 to 90 mol % of the following structural units (A) based on 2-(meth)acryloyloxyethyl phosphorylcholine and 90 to 10 mol % of the following structural units (B1) based on a (meth)acrylic monomer having an alkyl group,

wherein the copolymer (P) comprises a combination of a copolymer (P1) having a weight-average molecular weight of 200,000 to 800,000 and a copolymer (P2) having a weight-average molecular weight of 900,000 to 1,500,000, or a combination of a copolymer (P1') having a weight-average molecular weight of 250,000 to 800,000 and a copolymer (P3) having a weight-average molecular weight of 10,000 to 200,000,

wherein the definition of copolymer(P1), copolymer (P2), copolymer(P1') and copolymer(P3) are the same as for copolymer (P),





wherein R^1 represents a hydrogen atom or a methyl group in the formula (A), R^2 represents a hydrogen atom or a methyl group, and R^3 represents an alkyl group having 4 to 18 carbon atoms in the formula (B1).