

PHARMACEUTICAL COMPOSITION FOR SOFT CONTACT LENS

TECHNICAL FIELD

[0001]

5 The present invention relates to a pharmaceutical composition for a soft contact lens, wherein the composition comprises an alkyldiaminoethylglycine and adsorption of the alkyldiaminoethylglycine on a soft contact lens is suppressed.

10 BACKGROUND ART

[0002]

Various pharmaceutical compositions for a soft contact lens which compositions have the component composition similar to tears have been developed in order to relieve discomfort in

15 wearing a soft contact lens or a hard contact lens. Tears mean a mixture of a lacrimal gland secretion secreted by a main lacrimal gland and four or more substances secreted by an accessory lacrimal gland, and contain inorganic components such as Na, K, Ca and Cl and organic components such as

20 glucose, ascorbic acid, citric acid, urea, ammonia, an amino acid and a protein. Although there are individual differences of the concentration of glucose in tears, the concentration is approximately 0.001 to 0.01 w/v%. On the one hand, glucose may be mixed in an ophthalmic aqueous liquid composition as a

25 nutritional component in a higher concentration than that in tears in some cases. For example, the glucose concentrations in the ophthalmic aqueous liquid compositions described in Patent documents 1 to 4 are approximately 0.1 w/v%. Glucose, however, may promote growth of the bacteria that can

30 metabolize glucose into pyruvic acid to produce energy. In

general, glucose is therefore mixed in a lower concentration than that of tears particularly in the ophthalmic aqueous liquid composition of which content amounts of a preservative agent and an antiseptic agent are reduced.

5 [0003]

Even if the concentration of glucose is reduced, an antiseptic agent is mixed in a pharmaceutical composition for preservation. An antiseptic agent may be possibly associated with an adverse effect, since an ophthalmic solution is
10 directly administered to an eye. For example, it is described in Non-patent documents 1 to 5 that an antiseptic agent such as benzalkonium chloride impairs a cell and causes irritation to the skin, povidone-iodine has the lowest toxicity, and the toxicity of an alkyldiaminoethylglycine is medium. Patent
15 documents 1 to 4 disclose ophthalmic compositions containing an alkyldiaminoethylglycine hydrochloride.

PRIOR ART DOCUMENT

PATENT DOCUMENT

20 [0004]

Patent document 1: JP 2001-302518 A

Patent document 2: JP 2001-302545 A

Patent document 3: JP 2009-46480 A

Patent document 4: JP 2005-336153 A

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NON-PATENT DOCUMENT

[0005]

Non-patent document 1: TAKAHASHI Nobuo et al., The Journal of the Japan Ophthalmologists Association, 58: 10, pp. 945-950

30 (1987)

Non-patent document 2: TSUJI Akiyoshi et al., Japanese Journal of Environmental Infections, Vol. 11, No. 3, pp. 207-220 (1996)

Non-patent document 3: AJISAI, Vol. 12, No. 4, pp. 67-73 (2003)

Non-patent document 4: NAKASHIMA Keiji et al., Journal of
5 Japanese Society of Hospital Pharmacists, Vol. 40, No. 12, pp.
1559-1562 (2004)

Non-patent document 5: SHIRAISHI Tadashi, The Journal of the Japanese Society of Internal Medicine, Vol. 99, No. 8, pp. 166-172 (2010)

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SUMMARY

PROBLEMS TO BE SOLVED BY THE DISCLOSURE

[0006]

The objective of the present disclosure is to provide a
15 pharmaceutical composition for a soft contact lens, wherein the composition comprises an alkyldiaminoethylglycine and adsorption of the alkyldiaminoethylglycine on a soft contact lens is suppressed.

20 MEANS FOR SOLVING THE PROBLEMS

[0007]

The inventor of the present disclosure made extensive studies to solve the above-described problem. As a result, the inventor completed the present disclosure by finding that when an
25 alkyldiaminoethylglycine hydrochloride is mixed in a pharmaceutical composition for a soft contact lens in a low concentration, the alkyldiaminoethylglycine tends to adsorb particularly on a soft contact lens but such adsorption can be

suppressed by further mixing a metal chloride.

Hereinafter, the examples of the present disclosure is described.

[0007a]

5 In one aspect, the present disclosure refers to a pharmaceutical composition for a soft contact lens, comprising 0.001 w/v% or more and 0.008 w/v% or less of an alkyldiaminoethylglycine hydrochloride and 0.3 w/v% or more and 0.8 w/v% or less of a metal chloride, wherein the metal chloride is one or more salts
10 selected from the group consisting of an alkali metal chloride and a group 2 metal chloride.

[0008]

[1] A pharmaceutical composition for a soft contact lens, comprising 0.001 w/v% or more and 0.008 w/v% or less of an
15 alkyldiaminoethylglycine hydrochloride and a metal chloride.

[2] The pharmaceutical composition for a soft contact lens according to the above [1], comprising 0.001 w/v% or more and 0.0075 w/v% or less of the alkyldiaminoethylglycine hydrochloride.

20 [3] The pharmaceutical composition for a soft contact lens according to the above [1], comprising 0.001 w/v% or more and 0.005 w/v% or less of the alkyldiaminoethylglycine hydrochloride.

[4] The pharmaceutical composition for a soft contact lens
25 according to any one of the above [1] to [3], wherein the metal chloride is one or more salts selected from the group consisting of an alkali metal chloride and a group 2 metal chloride.

[5] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [3], wherein the metal
30 chloride is sodium chloride and/or potassium chloride.

[6] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [5], comprising 0.05 w/v% or more and 5.0 w/v% or less of the metal chloride.

5 [7] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [5], comprising 0.1 w/v% or more and 2.0 w/v% or less of the metal chloride.

[8] The pharmaceutical composition for a soft contact lens

according to any one of the above [1] to [7], further comprising glucose.

[9] The pharmaceutical composition for a soft contact lens according to the above [8], comprising 0.001 w/v% or more and
5 0.01 w/v% or less of the glucose.

[10] The pharmaceutical composition for a soft contact lens according to the above [8], comprising 0.002 w/v% or more and 0.008 w/v% or less of the glucose.

[11] The pharmaceutical composition for a soft contact lens
10 according to any one of the above [1] to [10], comprising 0.001 w/v% or more and 0.005 w/v% or less of the alkyldiaminoethylglycine hydrochloride and 0.5 w/v% or more and 1 w/v% or less of the metal chloride.

[12] The pharmaceutical composition for a soft contact lens
15 according to any one of the above [1] to [11], comprising:

0.001 w/v% or more and 0.005 w/v% or less of the alkyldiaminoethylglycine hydrochloride,
0.5 w/v% or more and 1 w/v% or less of the metal chloride,
and

20 0.002 w/v% or more and 0.008 w/v% or less of the glucose.

[13] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [12], further comprising a non-ionic surfactant.

[14] The pharmaceutical composition for a soft contact lens
25 according to the above [13], wherein the non-ionic surfactant is one or more non-ionic surfactants selected from the group consisting of polyoxyethylene hydrogenated castor oil, polyoxyethylene sorbitan long-chain fatty acid monoester, polyethylene glycol long-chain fatty acid monoester and
30 polyoxyethylene-polyoxypropylene block copolymer.

[15] The pharmaceutical composition for a soft contact lens according to the above [14], wherein the polyoxyethylene hydrogenated castor oil is polyoxyethylene hydrogenated castor oil 60.

5 [16] The pharmaceutical composition for a soft contact lens according to any one of the above [13] to [15], comprising 0.001 w/v% or more and 0.5 w/v% or less of the non-ionic surfactant.

10 [17] The pharmaceutical composition for a soft contact lens according to any one of the above [13] to [15], comprising 0.001 w/v% or more and 0.1 w/v% or less of the non-ionic surfactant.

[18] The pharmaceutical composition for a soft contact lens according to any one of the above [13] to [15], comprising
15 0.005 w/v% or more and 0.05 w/v% or less of the non-ionic surfactant.

[19] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [18], further comprising a buffering agent.

20 [20] The pharmaceutical composition for a soft contact lens according to the above [19], wherein the buffering agent is one or more buffering agents selected from the group consisting of a borate buffering agent, a phosphate buffering agent, a carbonate buffering agent, a citrate buffering agent,
25 an acetate buffering agent, a HEPES buffering agent and a MOPS buffering agent.

[21] The pharmaceutical composition for a soft contact lens according to the above [19], wherein the buffering agent is boric acid and/or borax.

30 [22] The pharmaceutical composition for a soft contact lens

according to any one of the above [19] to [21], comprising 0.05 w/v% or more and 5.0 w/v% or less of the buffering agent.

[23] The pharmaceutical composition for a soft contact lens according to any one of the above [19] to [21], comprising 0.1

5 w/v% or more and 1.0 w/v% or less of the buffering agent.

[24] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [23], further comprising a thickening agent.

[25] The pharmaceutical composition for a soft contact lens
10 according to the above [24], wherein the thickening agent is hydroxypropyl methylcellulose.

[26] The pharmaceutical composition for a soft contact lens according to the above [24] or [25], comprising 0.01 w/v% or more and 1 w/v% or less of the thickening agent.

15 [27] The pharmaceutical composition for a soft contact lens according to the above [24] or [25], comprising 0.05 w/v% or more and 0.5 w/v% or less of the thickening agent.

[28] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [27], further
20 comprising an amino acid.

[29] The pharmaceutical composition for a soft contact lens according to the above [28], wherein the amino acid is one or more amino acids selected from the group consisting of taurine, glutamic acid, aspartic acid, glycine, alanine,
25 arginine, lysine, γ -aminobutyric acid, γ -aminovaleric acid and salts thereof.

[30] The pharmaceutical composition for a soft contact lens according to the above [28], wherein the amino acid is taurine.

30 [31] The pharmaceutical composition for a soft contact lens

according to any one of the above [28] to [30], comprising
0.01 w/v% or more and 1.0 w/v% or less of the amino acid.

[32] The pharmaceutical composition for a soft contact lens
according to any one of the above [28] to [30], comprising

5 0.05 w/v% or more and 0.5 w/v% or less of the amino acid.

[33] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [31], comprising:

0.001 w/v% or more and 0.005 w/v% or less of the
alkyldiaminoethylglycine hydrochloride,

10 0.1 w/v% or more and 2.0 w/v% or less of the metal
chloride,

0.002 w/v% or more and 0.008 w/v% or less of the glucose,

0.005 w/v% or more and 0.05 w/v% or less of the
polyoxyethylene hydrogenated castor oil,

15 0.1 w/v% or more and 2.0 w/v% or less of the buffering
agent,

0.05 w/v% or more and 0.5 w/v% or less of the thickening
agent, and

0.05 w/v% or more and 0.5 w/v% or less of the amino acid.

20 [34] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [33], further
comprising a pH adjuster.

[35] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [34], wherein pH is

25 5.0 or more and 8.5 or less.

[36] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [34], wherein pH is
5.5 or more and 8.0 or less.

[37] The pharmaceutical composition for a soft contact lens
30 according to any one of the above [1] to [34], wherein pH is

6.5 or more and 7.5 or less.

[38] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [37], further comprising a monoterpene.

5 [39] The pharmaceutical composition for a soft contact lens according to the above [38], wherein the monoterpene is one or more monoterpenes selected from the group consisting of menthol, camphor and borneol.

10 [40] The pharmaceutical composition for a soft contact lens according to the above [38], wherein the monoterpene is l-menthol.

[41] The pharmaceutical composition for a soft contact lens according to any one of the above [38] to [40], comprising 0.0005 w/v% or more and 0.1 w/v% or less of the monoterpene.

15 [42] The pharmaceutical composition for a soft contact lens according to any one of the above [38] to [40], comprising 0.001 w/v% or more and 0.035 w/v% or less of the monoterpene.

[43] The pharmaceutical composition for a soft contact lens according to any one of the above [1] to [42], further
20 comprising a chelating agent.

[44] The pharmaceutical composition for a soft contact lens according to the above [43], wherein the chelating agent is ethylenediaminetetraacetic acid or a salt thereof.

25 [45] The pharmaceutical composition for a soft contact lens according to the above [43] or [44], comprising 0.001 w/v% or more and 0.1 w/v% or less of the chelating agent.

[46] The pharmaceutical composition for a soft contact lens according to the above [43] or [44], comprising 0.005 w/v% or more and 0.05 w/v% or less of the chelating agent.

30 [47] The pharmaceutical composition for a soft contact lens

according to any one of the above [1] to [46], comprising:

0.001 w/v% or more and 0.005 w/v% or less of the
alkyldiaminoethylglycine hydrochloride,

0.5 w/v% or more and 1.0 w/v% or less of the metal

5 chloride,

0.002 w/v% or more and 0.008 w/v% or less of the glucose,

0.005 w/v% or more and 0.05 w/v% or less of the non-ionic
surfactant,

0.1 w/v% or more and 2.0 w/v% or less of the buffering

10 agent,

0.05 w/v% or more and 0.5 w/v% or less of the thickening
agent,

0.05 w/v% or more and 0.5 w/v% or less of the amino acid,

0.001 w/v% or more and 0.035 w/v% or less of the

15 monoterpene, and

0.005 w/v% or more and 0.05 w/v% or less of the chelating
agent.

[48] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [46], comprising:

20 0.001 w/v% or more and 0.005 w/v% or less of the

alkyldiaminoethylglycine hydrochloride,

0.5 w/v% or more and 1.0 w/v% or less of the metal

chloride,

0.002 w/v% or more and 0.008 w/v% or less of the glucose,

25 0.005 w/v% or more and 0.05 w/v% or less of the non-ionic
surfactant,

0.1 w/v% or more and 2.0 w/v% or less of the buffering

agent,

0.05 w/v% or more and 0.5 w/v% or less of the thickening

30 agent,

0.05 w/v% or more and 0.5 w/v% or less of the amino acid,
0.001 w/v% or more and 0.035 w/v% or less of the
monoterpene, and

0.005 w/v% or more and 0.05 w/v% or less of the chelating
5 agent,

wherein pH is 6.5 or more and 7.5 or less.

[49] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [48], wherein the
pharmaceutical composition is ophthalmic.

10 [50] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [48], wherein the
pharmaceutical composition is an aqueous liquid composition.

[51] The pharmaceutical composition for a soft contact lens
according to any one of the above [1] to [48], wherein the
15 pharmaceutical composition is an ophthalmic solution.

[52] Use of a metal chloride for suppressing adsorption of an
alkyldiaminoethylglycine on a soft contact lens in a
pharmaceutical composition comprising 0.001 w/v% or more and
0.008 w/v% or less of an alkyldiaminoethylglycine
20 hydrochloride.

[53] Use of a metal chloride for producing a pharmaceutical
composition, wherein the pharmaceutical composition comprises
0.001 w/v% or more and 0.008 w/v% or less of an
alkyldiaminoethylglycine hydrochloride, and adsorption of the
25 alkyldiaminoethylglycine on a soft contact lens is suppressed
in the pharmaceutical composition.

[54] A method for suppressing adsorption of an
alkyldiaminoethylglycine on a soft contact lens,

wherein a pharmaceutical composition for a soft contact
30 lens comprises 0.001 w/v% or more and 0.008 w/v% or less of an

alkyldiaminoethylglycine hydrochloride,

the method comprising the step of mixing a metal chloride in the pharmaceutical composition for a soft contact lens.

[55] The method according to the above [54], wherein the
5 pharmaceutical composition for a soft contact lens further comprises glucose.

The matters specified in the above [1] to [51] can be applied to the above-described use and method.

10 EFFECT OF THE DISCLOSURE

[0009]

The pharmaceutical composition for a soft contact lens of the present disclosure comprises an alkyldiaminoethylglycine hydrochloride, and the adsorption of the
15 alkyldiaminoethylglycine on a soft contact lens is suppressed.

MODE FOR CARRYING OUT THE INVENTION

[0010]

Various pharmaceutical compositions have been developed as
20 described above, and an antiseptic agent is mixed in an ophthalmic solution for the storage stability. The cytotoxicity of an alkyldiaminoethylglycine hydrochloride among antiseptic agents for a pharmaceutical composition is relatively lower than that of benzalkonium chloride or the like.

25 [0011]

The inventor of the present invention found that when an alkyldiaminoethylglycine hydrochloride is mixed in a pharmaceutical composition for a soft contact lens in a relatively low concentration, the alkyldiaminoethylglycine

tends to adsorb on a soft contact lens. The inventor searches the component to suppress such adsorption; and as a result, found that a metal chloride is effective.

[0012]

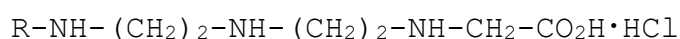
5 The pharmaceutical composition for a soft contact lens of the present invention comprises 0.001 w/v% or more and 0.008 w/v% or less of an alkyldiaminoethylglycine hydrochloride and a metal chloride.

[0013]

10 Hereinafter, an alkyldiaminoethylglycine is abbreviated as "ADG" and a soft contact lens is abbreviated as "SCL" in some cases.

[0014]

15 The "alkyldiaminoethylglycine hydrochloride" has the following chemical structure and has been conventionally used as a component of an antiseptic agent mainly.



wherein R is an alkyl group of C₈H₁₇ to C₁₆H₃₃ and mainly C₁₂H₂₅ and C₁₄H₂₉.

20 [0015]

25 The inventor of the present invention adjusted the content amount of the alkyldiaminoethylglycine hydrochloride in the pharmaceutical composition for a soft contact lens to be relatively low as 0.001 w/v% or more and 0.008 w/v% or less to provide the pharmaceutical composition for a soft contact lens having low cytotoxicity. When the concentration is 0.001 w/v% or more, the antiseptic action can be exerted more surely. When the concentration is 0.008 w/v% or less, the cytotoxicity can be suppressed more surely. In addition, the inventor
30 experimentally found that when the concentration of the

alkyldiaminoethylglycine hydrochloride is lower, the adsorption rate of the alkyldiaminoethylglycine on a soft contact lens becomes higher. The concentration is more preferably 0.002 w/v% or more, and preferably 0.005 w/v% or less, more preferably 0.003 w/v% or less.

[0016]

The "metal chloride" means a salt of a metal cation and a chloride ion (Cl^-) and is mixed as a component to inhibit the adsorption of the alkyldiaminoethylglycine on a soft contact lens in the present invention. An example of the metal chloride includes an alkali metal chloride such as sodium chloride and potassium chloride; and a group 2 metal chloride such as calcium chloride and magnesium chloride. The metal chloride is preferably an alkaline earth metal chloride such as calcium chloride and is preferably soluble in water. The phrase "soluble in water" means that a material to be tested is powderized so that the material can pass Sieve No. 100 having a mesh size of 150 μm , 1 g of the powderized material is added in water, the mixture is vigorously shaken at 20°C for 30 seconds every 5 minutes, and an amount of water required for dissolution of the material within 30 minutes is less than 10 mL.

[0017]

The concentration of the metal chloride in the pharmaceutical composition for a soft contact lens may be appropriately adjusted as long as the above-described adsorption effect can be efficiently exerted and may be adjusted to, for example, 0.05 w/v% or more and 5.0 w/v% or less. When the concentration is included in the range, the adsorption effect is exerted more surely. The concentration is

preferably 0.1 w/v% or more, more preferably 0.5 w/v% or more, and preferably 2.0 w/v% or less, more preferably 1.0 w/v% or less.

[0018]

5 Only one metal chloride may be used alone, or two or more metal chlorides may be used in combination. When two or more metal chlorides are used, the above concentration means a total concentrations.

[0019]

10 The "glucose" is represented by the formula of $C_6H_{12}O_6$ and is one of aldohexoses. Natural glucose is D-glucose and is conjugated to an electron transport system to produce a large amount of ATP in an animal having a respiratory system. There is approximately 0.001 w/v% or more and 0.01 w/v% or less of
15 glucose in tears.

[0020]

Glucose is preferably mixed in the present invention in order to further improve the effect of the metal chloride to suppress the adsorption of the alkyldiaminoethylglycine on a
20 soft contact lens. The pharmaceutical composition for a soft contact lens of the present invention preferably comprises 0.001 w/v% or more and 0.01 w/v% or less of glucose. When the concentration is 0.001 w/v% or more, the adsorption suppression effect can be exerted more surely. When the
25 concentration is 0.01 w/v% or less, the ophthalmic solution can be stabilized more surely. The concentration is more preferably 0.002 w/v% or more, even more preferably 0.004 w/v% or more, and more preferably 0.008 w/v% or less, even more preferably 0.006 w/v% or less.

30 [0021]

The "non-ionic surfactant" means a surfactant that does not dissociate into an ion even when the surfactant is dissolved in water. In general, the polyoxyethylene chain and the hydroxy group thereof act as a hydrophilic group, and the

5 long-chain alkyl group thereof acts as a hydrophobic group.

The non-ionic surfactant contributes to the stability of the ophthalmic solution. An example of the non-ionic surfactant includes one or more non-ionic surfactants selected from the group consisting of polyoxyethylene hydrogenated castor oil, polyoxyethylene sorbitan long-chain fatty acid monoester, 10 polyethylene glycol long-chain fatty acid monoester and polyoxyethylene-polyoxypropylene block copolymer.

[0022]

The polyoxyethylene hydrogenated castor oil means a 15 compound obtained by etherifying hydrogenated castor oil with a polyoxyethylene chain. The addition mole number of the ethylene oxide of the polyoxyethylene chain in the polyoxyethylene hydrogenated castor oil may be adjusted to, for example, 5 or more and 100 or less. The addition mole 20 number is preferably 10 or more or 20 or more, more preferably 30 or more, even more preferably 40 or more, and preferably 90 or less, more preferably 80 or less, even more preferably 70 or less. An example of the polyoxyethylene hydrogenated castor oil includes polyoxyethylene hydrogenated castor oil 5, 25 polyoxyethylene hydrogenated castor oil 10 and polyoxyethylene hydrogenated castor oil 60. Polyoxyethylene hydrogenated castor oil 60 is preferably used. The number after the polyoxyethylene hydrogenated castor oil represents the addition mole number of the ethylene oxide.

30 [0023]

The polyoxyethylene sorbitan long-chain fatty acid monoester is also called as polysorbate and is a polyoxyethylene ether of a sorbitan fatty acid ester. The polyoxyethylene sorbitan long-chain fatty acid monoester can be obtained by reacting sorbitol with a long-chain fatty acid through the heating in the presence of an alkali catalyst to produce a sorbitan long-chain fatty acid ester and condensing the sorbitan long-chain fatty acid ester with ethylene oxide. In general, totally about 18 molecules or more and about 22 molecules or less of ethylene oxide is bound to one molecule of the polyoxyethylene sorbitan long-chain fatty acid monoester. The carbon number of the long-chain fatty acid is generally about 10 or more and about 20 or less, and an example of the long-chain fatty acid includes lauric acid, palmitic acid, stearic acid and oleic acid. For example, polysorbate 20, polysorbate 60, polysorbate 65 and polysorbate 80 can be used as the polyoxyethylene sorbitan long-chain fatty acid monoester, and polysorbate 80 is preferred.

[0024]

The polyethylene glycol long-chain fatty acid monoester means an ester of a long-chain fatty acid and polyethylene glycol. An example of the long-chain fatty acid includes stearic acid. The polymerization degree of the polyethylene glycol is about 10 or more and about 60 or less. Polyoxyl 40 stearate is preferred as the polyethylene glycol long-chain fatty acid monoester.

[0025]

The polyoxyethylene-polyoxypropylene block copolymer means a copolymer of propylene oxide and ethylene oxide. An example of the polyoxyethylene-polyoxypropylene block copolymer

includes polyoxyethylene (160) polyoxypropylene (30) glycol (Poloxamer 188), polyoxyethylene (196) polyoxypropylene (67) glycol (Poloxamer 407) and Poloxamer 235.

[0026]

5 The concentration of the non-ionic surfactant in the pharmaceutical composition may be appropriately adjusted and may be adjusted to, for example, 0.001 w/v% or more and 0.5 w/v% or less. When the concentration is included in the range, the effect to stabilize the pharmaceutical composition is
10 exerted more surely. The concentration is preferably 0.005 w/v% or more, more preferably 0.008 w/v% or more, and preferably 0.1 w/v% or less, more preferably 0.05 w/v% or less, even more preferably 0.02 w/v% or less.

[0027]

15 The "buffering agent" mainly means a compound to ease the change of pH caused by a foreign substance and is exemplified by one or more buffering agents selected from the group consisting of a borate buffering agent, a phosphate buffering agent, a carbonate buffering agent, a citrate buffering agent,
20 an acetate buffering agent, a HEPES buffering agent and a MOPS buffering agent. The buffering agent is preferably a borate buffering agent, and more preferably boric acid and/or borax. Boric acid and borax are also used as an antiseptic agent and have a disinfecting effect on the conjunctival sac.

25 [0028]

 The concentration of the buffering agent in the pharmaceutical composition for a soft contact lens may be appropriately adjusted and may be adjusted to, for example, 0.05 w/v% or more and 5.0 w/v% or less. When the concentration
30 is included in the range, the buffering effect by the

buffering agent can be exerted more surely. The concentration is preferably 0.1 w/v% or more, more preferably 0.5 w/v% or more, and preferably 2.0 w/v% or less, more preferably 1.0 w/v% or less.

5 [0029]

The "thickening agent" means a component to increase the viscosity of the pharmaceutical composition for a soft contact lens and to contribute to the suppression of the rapid evaporation of the pharmaceutical composition for a soft
10 contact lens, the improvement of the dripping performance, the suppression of the variation of the dropping quantity and the improvement of the use feeling. Glucose is also used in a pharmaceutical composition as a tonicity agent and a thickening agent; but glucose is excluded from the category of
15 the thickening agent for the sake of convenience in the present invention, since glucose is mixed to further improve the effect to suppress the adsorption of the alkylldiaminoethylglycine on a soft contact lens by the metal chloride in the present invention.

20 [0030]

The viscosity of the pharmaceutical composition for a soft contact lens according to the present invention may be appropriately adjusted and may be adjusted to, for example, 1.0 mPa·s or more and 200 mPa·s or less. The viscosity is
25 preferably 50 mPa·s or less or 30 mPa·s or less, more preferably 10 mPa·s or less, and even more preferably 3.0 mPa·s or less.

[0031]

An example of the thickening agent includes hydroxypropyl
30 methylcellulose, carboxyvinyl polymer, hydroxyethyl cellulose,

methylcellulose, alginic acid, polyvinyl alcohol and polyvinylpyrrolidone, and hydroxypropyl methylcellulose is preferred.

[0032]

5 The concentration of the thickening agent in the pharmaceutical composition for a soft contact lens may be appropriately adjusted and may be adjusted to, for example, 0.01 w/v% or more and 1.0 w/v% or less. When the concentration is included in the range, the above-described effect by the
10 thickening agent can be exerted more surely. The concentration is preferably 0.05 w/v% or more, more preferably 0.08 w/v% or more, and preferably 0.5 w/v% or less, more preferably 0.2 w/v% or less.

[0033]

15 The "amino acid" means a compound having an acidic group, such as a carboxy group and a sulfonic group ($-\text{SO}_3\text{H}$), and an amino group in one molecule, and is not restricted to 20 kinds of so-called protein-constituting amino acids. The amino acid mainly plays a role of a nutrient component for the eye and
20 contributes to reduction of eye fatigue. An example of the amino acid includes one or more amino acids selected from the group consisting of taurine, glutamic acid, aspartic acid, glycine, alanine, arginine, lysine, γ -aminobutyric acid, γ -aminovaleric acid and salts thereof. An example of the amino
25 acid salt includes an alkali metal salt such as sodium salt and potassium salt. The amino acid is preferably taurine. Taurine is a nutrient component and is also said to have a metabolic promoting effect.

[0034]

30 The concentration of the amino acid in the pharmaceutical

composition for a soft contact lens may be appropriately adjusted and may be adjusted to, for example, 0.01 w/v% or more and 1.0 w/v% or less. When the concentration is included in the range, the effect by the respective amino acid can be exerted more surely. The concentration is preferably 0.05 w/v% or more, more preferably 0.08 w/v% or more, even more preferably 0.1 w/v% or more, and preferably 0.5 w/v% or less, more preferably 0.2 w/v% or less.

[0035]

The pH of the pharmaceutical composition for a soft contact lens according to the present invention is adjusted to the range applicable to a living body, especially the eyes. For example, the pH may be adjusted to 5.0 or more and 8.5 or less. The pH is preferably 5.5 or more, more preferably 6.0 or more, even more preferably 6.5 or more, and preferably 8.0 or less, more preferably 7.5 or less. It has been experimentally demonstrated that the effect to suppress the adsorption of the alkylldiaminoethylglycine on a soft contact lens by the metal chloride is particularly significantly exerted in the pH range of 6.5 or more and 7.5 or less in the present invention. The pH of the pharmaceutical composition for a soft contact lens may be adjusted by the above-described buffering agent or a pH adjuster.

[0036]

The pH adjuster is not particularly restricted as long as the pH adjuster is applicable to a living body, especially the eyes. An example of the pH adjuster includes an inorganic acid such as hydrochloric acid and boric acid; an organic acid such as acetic acid, glutamic acid and aspartic acid; an inorganic base such as sodium hydroxide, sodium carbonate and sodium

hydrogencarbonate; and an organic base such as triethanolamine and monoethanolamine. The kind and the additive amount of the pH adjuster may be adjusted depending on the pH to be adjusted of the pharmaceutical composition for a soft contact lens.

5 [0037]

The "monoterpene" means a compound composed of two isoprene units and having a molecular formula of $C_{10}H_{16}$. A monocyclic monoterpene, which has a cooling action, is mainly used in the present invention. An example of the monoterpene includes one
10 or more monoterpenes selected from the group consisting of menthol, camphor and borneol. Any one of l-menthol and dl-menthol may be used as menthol, and l-menthol is preferred. Any one of d-body and dl-body of camphor and borneol may be used, and d-body is preferred.

15 [0038]

The concentration of the monoterpene in the pharmaceutical composition for a soft contact lens may be appropriately adjusted and may be adjusted to, for example, 0.0005 w/v% or more and 0.1 w/v% or less. When the concentration is included
20 in the range, moderate cooling sensation can be obtained more surely. The concentration is preferably 0.001 w/v% or more, more preferably 0.0015 w/v% or more, and preferably 0.02 w/v% or less, more preferably 0.01 w/v% or less.

[0039]

25 The "chelating agent" means a compound to improve the storage stability of the ophthalmic solution by sequestering a metal ion such as calcium ion to prevent an insoluble metal salt thereof from being produced. The chelating agent is not particularly restricted as long as the chelating agent is
30 applicable to a living body, especially the eyes, and has the

above-described action. An example of the chelating agent includes ethylenediaminetetraacetic acid (edetic acid), ascorbic acid, citric acid and salts thereof. An example of the ethylenediaminetetraacetate salt includes

5 ethylenediaminetetraacetic acid tetrasodium salt and ethylenediaminetetraacetic acid disodium salt.

[0040]

The concentration of the chelating agent in the pharmaceutical composition for a soft contact lens may be
10 appropriately adjusted and may be adjusted to, for example, 0.001 w/v% or more and 0.2 w/v% or less. When the concentration is included in the range, the stabilizing effect by the chelating agent can be exerted more surely. The concentration is preferably 0.002 w/v% or more, more
15 preferably 0.005 w/v% or more, and preferably 0.2 w/v% or less, more preferably 0.05 w/v% or less, even more preferably 0.02 w/v% or less.

[0041]

A preservative agent or an antiseptic agent may be added in
20 the pharmaceutical composition for a soft contact lens of the present invention in addition to the alkyldiaminoethylglycine hydrochloride without particular restriction as long as the effect of the present invention is not impaired. An example of the preservative agent or antiseptic agent includes
25 benzalkonium chloride, benzalkonium bromide, benzethonium chloride, chlorhexidine hydrochloride, chlorhexidine gluconate, chlorhexidine acetate, chlorobutanol, benzyl alcohol, phenethyl alcohol, sorbic acid or a salt thereof, methyl parahydroxybenzoate, ethyl parahydroxybenzoate, propyl
30 parahydroxybenzoate, dehydroacetic acid or a salt thereof,

zinc chloride, polidronium chloride, thimerosal,
dibutylhydroxytoluene, sodium chlorite, boric acid and borax.

Only one of the preservative agent or antiseptic agent may be
used alone, or two or more of the preservative agents or

5 antiseptic agents may be used in combination.

[0042]

Only one of the above-described each component may be used
alone, or two or more of the above-described components may be
appropriately used in combination.

10 [0043]

A soft contact lens is classified into 4 kinds by FDA: Food
and Drug Administration. Specifically, a soft contact lens is
classified into Group I: water content is less than 50% and
material is nonionic, Group II: water content is 50% or more
15 and material is nonionic, Group III: water content is less
than 50% and material is ionic, Group IV: water content is 50%
or more and material is ionic. The term "ionic" means that the
mol% of the monomer having an anion among the constituent
monomer of the raw material polymer is 1% or more, and the
20 term "nonionic" means that the mol% is less than 1%. The soft
contact lens may be classified into any one of the above-
described soft contact lenses, may be ionic or nonionic, and
may be hydrous or may not be hydrous in this disclosure.

[0044]

25 The "soft contact lens" in this disclosure is exemplified
by a soft contact lens mainly composed of 2-hydroxyethyl
methacrylate (HEMA), EGDMA, SiMAA2, mPDMS 1000, CE-PDMS, TRIS,
EMA, methacryloyloxyethyl phosphorylcholine, Tris VC, MMA, MA,
polyethylene glycol monomethacrylate (PEGMA), glycerol
30 methacrylate (GMA), N,N-dimethylacrylamide (DMA), vinyl

alcohol (VA), N-vinylpyrrolidone (NVP or VP), methacrylic acid (MAA), fluorine-containing methacrylate compound, silicon-containing methacrylate compound, silicone hydrogel or cycloalkyl methacrylate.

5 [0045]

The material of the soft contact lens in this disclosure may be any one of the above-described materials. The soft contact lens mainly composed of 2-hydroxyethyl methacrylate (HEMA) is preferably exemplified, and the soft contact lens
10 mainly composed of 2-hydroxyethyl methacrylate (HEMA) and EGDMA or HEMA and methacryloyloxyethyl phosphorylcholine is more preferably exemplified.

[0046]

The kind of the soft contact lens is not particularly
15 restricted, and the present invention can be applied to any one of a disposable soft contact lens, a periodic replacement soft contact lens, a conventional soft contact lens, a silicone hydrogel soft contact lens and a color contact lens.

[0047]

20 A silicone hydrogel soft contact lens is made of a silicone hydrogel material.

[0048]

The color contact lens is also referred to as a colored contact lens and means a contact lens that is colored for the
25 purpose of beauty such as eye decoration and aesthetics. For example, the colored area of the iris and the cornea can be looked larger by the color contact lens than that in the case where the contact lens is not worn. More specifically, the color contact lens is used for coloring the larger area than
30 the circumference of the iris and the cornea. Such a color

contact lens may be referred to as a circle lens in some cases.

[0049]

Publicly known dye, such as inorganic dye and organic dye,
5 is used as the dye used for coloring a color contact lens. An example of such dye includes azo dye, phthalocyanine dye, diketopyrrolopyrrole dye, anthraquinone dye, tripheno dioxane dye, violanthron dye, isoindoline dye, carbazole dye, quinoline dye, metal oxide dye and carbon black. One dye may
10 be used or a plurality of dyes may be used in combination depending on the color or the design of a color contact lens. Any one of substances referred to as pigment or dye can be used by a publically known means in this disclosure. Even a clear contact lens or a soft contact lens other than a color
15 soft contact lens may be colored lightly to the extent that the color is visually easily recognized in the case where the contact lens is immersed in a solution such as a washing solution.

[0050]

20 The pharmaceutical composition for a soft contact lens of the present invention can be produced by an ordinary method. For example, each component may be dissolved in water as a solvent. Clear water in which the amount of an impurity, a bacterium, a virus, a fungus or the like is less than the
25 detection limit or sufficiently small, such as distilled water, purified water and sterile water, is used as a solvent.

[0051]

The container for the pharmaceutical composition for a soft contact lens of the present invention is not particularly
30 restricted and may be a container that has been conventionally

used as an eyedropper container. The container may be made of glass or plastic. When the container for the pharmaceutical composition for a soft contact lens of the present invention is made of plastic, the material of the plastic container is not particularly restricted and is exemplified by any one kind or two or more kinds mixture of polyethylene naphthalate, polyacrylate, polyethylene terephthalate, polybutylene terephthalate, polypropylene, polyethylene and polyimide. The material of the container main body, in other words, the part in which the pharmaceutical composition for a soft contact lens is contained, is preferably polyethylene terephthalate, polypropylene and polyethylene and more preferably polyethylene terephthalate from the viewpoint to ensure the stability of the pharmaceutical composition for a soft contact lens.

[0052]

Whether the adsorption of an alkyldiaminoethylglycine on a soft contact lens in the pharmaceutical composition for a soft contact lens of the present invention is suppressed or not is evaluated by whether the adsorption rate of the alkyldiaminoethylglycine in the pharmaceutical composition for a soft contact lens after the soft contact lens is immersed in the pharmaceutical composition is lower or not than the adsorption rate of the alkyldiaminoethylglycine in the liquid having a similar composition except that the liquid does not contain a metal chloride after the a soft contact lens is immersed in the liquid. For example, a soft contact lens is immersed in a liquid at 25°C with shaking the liquid for 24 hours. The amount of an alkyldiaminoethylglycine can be measured by high performance liquid chromatography and

absorbance of a light in the reaction liquid of an alkyldiaminoethylglycine and a coloring substance such as eosin.

[0053]

5 The pharmaceutical composition for a soft contact lens of the present invention complements tears and is effective in relieving discomfort, dryness of eyes, eye fatigue and blurred vision in wearing a soft contact lens.

[0054]

10 The pharmaceutical composition of the present invention can be used in either an internal form or an external form depending on the purpose. The composition can be provided as a local administration liquid pharmaceutical agent for various applications. For example, the composition can be provided for
15 pharmaceutical application in an internal form and for ophthalmic, dental, ontological and dermatologic applications in an external form. In particular, the composition can be provided for ophthalmic application.

[0055]

20 The term "ophthalmic pharmaceutical composition" means a pharmaceutical composition for ophthalmic application. An example of the pharmaceutical composition particularly includes an aqueous liquid composition containing water as a solvent. The term "aqueous liquid composition" particularly
25 means a liquid pharmaceutical composition containing water as a solvent. The aqueous liquid composition can be produced by an ordinary method. For example, the aqueous liquid composition can be produced by dissolving or dispersing each component in water as a solvent. The aqueous liquid
30 composition may be a solution, a suspension or an emulsion and

is preferably a solution.

[0056]

An example of the ophthalmic pharmaceutical composition includes an ophthalmic solution, an eye wash, an eye ointment, 5 a soft contact lens fitting liquid and a soft contact lens care liquid. An ophthalmic solution is exemplified by an ophthalmic solution usable with wearing a soft contact lens and is also called as an eye-drop and an ophthalmic agent. An eye wash is exemplified by an eye wash usable with wearing a 10 soft contact lens and is also called as an eye lotion and an eye wash agent. An example of a soft contact lens care liquid includes a cleaning liquid, a preservative solution, a sterilizing liquid and an antiseptic solution such as a multi-purpose solution. The ophthalmic pharmaceutical composition is 15 preferably an ophthalmic solution, a soft contact lens fitting liquid, an eye wash and a soft contact lens care liquid, and particularly preferably an ophthalmic solution.

[0057]

The pharmaceutical composition of the present invention is 20 exemplified by an ophthalmic solution usable with wearing a soft contact lens. In other words, the pharmaceutical composition of the present invention can be applied to the eye with wearing a soft contact lens. The kind of a soft contact lens is not particularly restricted, and the composition can 25 be used for any one of a disposable soft contact lens, a periodic replacement soft contact lens, a conventional soft contact lens, a silicone hydrogel contact lens and a color contact lens. A silicone hydrogel contact lens is made of a silicone hydrogel material.

30 [0058]

The administration and dosage of the ophthalmic solution according to the present invention is adjusted depending on the symptom, age or the like of a patient, and one drop or more and 3 drops or less of the ophthalmic solution may be
5 generally instilled into an eye one time or more and 6 times or less per one day.

[0059]

The container used for the pharmaceutical composition of the present invention is sterilized by an ordinary method. The
10 sterilization method is not particularly restricted as long as the method is generally used and is exemplified by dry heat sterilization, electron beam sterilization, gamma sterilization and ethylene gas sterilization. Electron beam sterilization is used as a sterilization method in one
15 embodiment.

[0060]

The present invention also relates to a method for suppressing adsorption of an alkyldiaminoethylglycine on a soft contact lens, the method comprising the step of mixing a
20 metal chloride in a pharmaceutical composition for a soft contact lens, wherein a content amount of an alkyldiaminoethylglycine hydrochloride in the pharmaceutical composition for a soft contact lens is 0.001 w/v% or more and 0.008 w/v% or less. The adsorption of the
25 alkyldiaminoethylglycine on a soft contact lens is suppressed further effectively in the method by mixing glucose in the pharmaceutical composition for a soft contact lens in addition to the alkyldiaminoethylglycine hydrochloride and the metal chloride.

[0061]

The reason why the content amount of the alkyldiaminoethylglycine hydrochloride in the pharmaceutical composition for a soft contact lens in the above-described method for suppressing the adsorption is restricted to 0.001 w/v% or more and 0.008 w/v% or less is that the adsorption rate of the alkyldiaminoethylglycine on a soft contact lens is high in such a low concentration range.

[0062]

The above-described kind and the concentration with respect to the alkyldiaminoethylglycine hydrochloride, the metal chloride, glucose and other optional component of the above-described pharmaceutical composition for a soft contact lens may be applied alone or in combination to the kind and the concentration of those in the above-described method for suppressing the adsorption. The pH, container or the like of the pharmaceutical composition can be also similarly applied to the method.

[0063]

The present application claims the benefit of the priority date of Japanese patent application No. 2019-217422 filed on November 29, 2019. All of the contents of the Japanese patent application No. 2019-217422 filed on November 29, 2019, are incorporated by reference herein.

EXAMPLES

[0064]

Hereinafter, the present invention is described in more detail with Examples. The present invention is however not restricted to the following Examples in any way, and it is possible to work the present invention according to the

Examples with an additional appropriate change within the range of the above descriptions and the following descriptions. Such a changed embodiment is also included in the technical scope of the present invention.

5 [0065]

Test example 1: Adsorption test on soft contact lens

Quantitative alkyldiaminoethylglycine hydrochloride liquid ("LEBON LAG-40" manufactured by Sanyo Chemical) was diluted with purified water, and boric acid manufactured by Borax
10 Francais and borax manufactured by KOZAKAI PHARMACEUTICAL were added thereto. The pH was adjusted to 7 using hydrochloric acid to prepare solutions having the compositions shown in Table 1. The unit of the numerical values in the Table is w/v%. A soft contact lens classified into Group I ("SEED 1 day
15 Fine UV plus" manufactured by SEED) was washed using purified water. The above aqueous solution (3 mL) was respectively taken and added into a vial container, and one of the soft contact lens washed using purified water was immersed into a vial container. The vial container was shaken at 25°C for 24
20 hours to obtain SCL immersion liquid. Also, the solution in which a soft contact lens was not immersed was separately shaken at 25°C for 24 hours as control test liquid. Two of the above samples were respectively tested. The "ADG" in the Table represents an alkyldiaminoethylglycine.

25 Separately, the amount of quantitative alkyldiaminoethylglycine hydrochloride liquid (62.5 mg) was accurately measured, and water was added thereto so that the total volume accurately became 100 mL. The solution (2 mL) was accurately measured, and water was added thereto so that the
30 total volume accurately became 20 mL as a standard solution.

The SCL immersion liquid and the standard solution (50 μ L) were accurately measured, and the total areas of alkyldiaminoethylglycine peaks of the liquid chromatography in the following condition was measured.

5 Column: inner diameter 4.6 mm $\times$ length 15 cm
cyanopropylsilylated silica gel ("CN12S05-1546WT" manufactured by YMC)

Detector: ultraviolet absorptiometer

Measured wavelength: 210 nm

10 Mobile phase: water/methanol for liquid chromatography/phosphoric acid mixed liquid = 750/250/1

The ADG content amount in the SCL immersion liquid was calculated from the measured total ADG peak areas by the following formula, and the adsorption rate of ADG on a soft
15 contact lens was further calculated. The result is shown in Table 1.

Content amount of ADG hydrochloride in SCL immersion liquid or control test liquid (μ g/mL) = measured amount of
quantitative ADG hydrochloride liquid (mg) $\times$ content amount of
20 quantitative ADG hydrochloride liquid (w/v%) / 100 / 1.03 / S_s
 $\times S_T$

wherein 1.03 is the density of quantitative ADG hydrochloride liquid (g/cm^3), S_s is total ADG peak area of standard solution, and S_T is total ADG peak area of SCL immersion liquid or
25 standard test liquid.

In addition, the adsorption rate of ADG on a soft contact lens was calculated by the following formula. The result is shown in Table 1.

Adsorption rate of ADG hydrochloride (%) = $100 - [(C_{TAV} / C_{CAV})$
30 $\times 100]$

wherein C_{TAV} is average content amount of ADG in SCL immersion liquid ($\mu\text{g/mL}$), and C_{CAV} is average content amount of ADG in control test liquid ($\mu\text{g/mL}$).

[0066]

Table 1

	Reference example 1	Reference example 2	Reference example 3	Reference example 4	Reference example 5
ADG hydrochloride	0.001%	0.0025%	0.005%	0.0075%	0.01%
Boric acid	0.5%				
Borax	0.04%				
Adsorption rate	39.2%	35.6%	28.9%	25.2%	18.9%

[0067]

It was found as the result shown in Table 1 that when the concentration of ADG is lower, the rate of ADG adsorbed on a soft contact lens tends to be higher.

[0068]

Test example 2: Examination of material of soft contact lens

Reference example 2 of Test example 1 was used as Comparative example 1. The formulation prepared by mixing 0.55 w/v% sodium chloride manufactured by MANAC Incorporated in Reference example 2 was used as Example 1. SCL immersion liquids of each soft contact lens of Groups I to IV shown in Table 2 and control test liquid were prepared in a similar condition to Test example 1. Three of each sample were respectively tested. Groups I to IV are classified by FDA: Food and Drug Administration. Group I has water content of less than 50% and is nonionic, Group II has water content of 50% or more and is nonionic, Group III has water content of less than 50% and is ionic, and Group IV has water content of 50% or more and is ionic.

Separately, the amount of quantitative alkylldiaminoethylglycine hydrochloride liquid ("LEBON LAG-40"

manufactured by Sanyo Chemical) (62.5 mg) was accurately measured, and water was added thereto so that the total volume accurately became 100 mL. Boric acid manufactured by Borax Francais (0.5 g) and borax manufactured by KOZAKAI

5 PHARMACEUTICAL (40 mg) were dissolved in water so that the total volume became 50 mL as an additive solution. The additive solution (25 mL) was added to the above liquid (5 mL), and water was further added thereto so that the total volume accurately became 50 mL as a standard solution. In
10 addition, water was added to the additive solution (10 mL) so that the total volume accurately became 20 mL as a control solution.

Potassium dihydrogenphosphate manufactured by FUJIFILM Wako Pure Chemical Corporation (3.4 g) and eosin Y manufactured by
15 FUJIFILM Wako Pure Chemical Corporation (24 mg) were dissolved in water so that the total volume was adjusted to 100 mL to obtain an eosin solution. The eosin solution (4 mL) was respectively mixed in SCL immersion liquid, control test liquid, standard solution and control solution (2 mL), and the
20 mixture was stirred. Absorbance of the light having a wavelength of 545 nm of the liquids was measured, and the amount of ADG in SCL immersion liquid and control test liquid was calculated by the following formula and further the adsorption rate was determined similarly to Reference example
25 1. In addition, adsorption suppression rate was also calculated. The result is shown in Table 2. The "SHCL" is a silicone hydrogel soft contact lens containing silicone in Table 2. When "1-Day ACUVUE MOIST" manufactured by Johnson & Johnson and classified into Group IV was used, SCL was
30 deformed but measurement was similarly carried out.

Amount of ADG hydrochloride in SCL immersion liquid and control test liquid (w/v%) = measured amount of quantitative ADG hydrochloride liquid (mg) / 1.03 × M / 100 × (A_T-A_C) / (A_S-A_C)

5 wherein 1.03 is the density of quantitative ADG hydrochloride liquid (g/cm³), M is the concentration of quantitative ADG hydrochloride liquid (w/v%), A_T is the absorbance of SCL immersion liquid or control test liquid, A_C is the absorbance of control solution, and A_S is the absorbance of standard
10 solution.

Adsorption suppression rate (%) = [(ADG adsorption rate of Comparative example 1 (%) - ADG adsorption rate of Example 1 (%)) / ADG adsorption rate of Comparative example 1 (%)] × 100

Table 2

FDA classification	Product name	Manufacturer or distributor	Material	Adsorption rate			Adsorption suppression rate
				Comparative example 1	Example 1		
I	SEED 1dayFine	SEED	2-HEMA, EGDMA	72.6%	20.8%		71.3%
	1-Day ACUVUE OASYS (SHCL)	Johnson & Johnson	2-HEMA, DMA, SiMAA2, mPDMS1000 and methacrylate cross-linker	71.2%	53.1%		25.4%
	DAILIES TOTAL 1 (SHCL)	Alcon	CE-PDMS, DMA, TRIS	70.3%	59.1%		15.9%
	2WEEK Menicon Premio (SHCL)	Menicon	N,N-dimethylacrylamide, pyrrolidone compound, silicon-containing methacrylate compound, silicon-containing acrylate compound, ethylene glycol dimethacrylate	50.4%	47.4%		6.0%
II	Proclear 1 day	CooperVision	2-hydroxyethyl methacrylate, Methacryloyloxyethyl phosphorylcholine	74.2%	15.4%		79.2%
	DAILIES AquaComfort PLUS	Alcon	improved polyvinyl alcohol	43.3%	0%		100%
	Biotrue ONE day	Bausch & Lomb	2-HEMA, NVP	37.3%	24.0%		35.7%
	2WEEK Menicon DUO	Menicon	N,N-dimethylacrylamide, N-vinylpyrrolidone, alkyl methacrylate compound, ethylene glycol dimethacrylate	24.9%	18.5%		25.7%
III	BAUSCH+LOMB Medalist FreshFit (SHCL)	Bausch & Lomb	TrisVC, NVP	88.9%	84.9%		4.5%
IV	SEED 1 dayPure UP	SEED	2-HEMA, MMA, EGDMA, quaternary ammonium group-containing methacrylate compound, carboxy group-containing methacrylate compound	17.2%	13.0%		24.4%
	1-Day ACUVUE MOIST	Johnson & Johnson	2-HEMA, MAA, and methacrylate cross-linker	79.1%	34.4%		56.5%

[0070]

It was found as the result shown in Table 2 that an alkyldiaminoethylglycine tends to adsorb on a soft contact lens by immersing the soft contact lens in an

5 alkyldiaminoethylglycine hydrochloride solution having a low concentration as 0.0025 w/v%.

It was, however, found that the adsorption of an alkyldiaminoethylglycine is suppressed on the whole by mixing sodium chloride in addition to the low concentration

10 alkyldiaminoethylglycine hydrochloride. It was found that such an adsorption suppression effect is high particularly in the case where the material of a soft contact lens contains hydroxyethyl methacrylate (HEMA).

[0071]

15 Test example 3: Addition effect of glucose

The adsorption rate of an alkyldiaminoethylglycine on a soft contact lens and the adsorption suppression rate relative to the formulation of Comparative example 1 were determined in the same condition as Test example 1 using the formulation of

20 Comparative example 1 containing boric acid and borax in addition to an alkyldiaminoethylglycine hydrochloride and the formulations of Examples 1 to 3 having the compositions shown in Table 3 and further containing sodium chloride or glucose manufactured by San-ei Sucrochemical and sodium chloride. Each
25 of two samples were tested with using "SEED 1dayFine UV plus" as a soft contact lens in this Test example. The result is shown in Table 3.

[0072]

Table 3

	Comparative example 1	Example 1	Example 2	Example 3
ADG hydrochloride	0.0025%			
Sodium chloride	—	0.55%		
Glucose	—	—	0.005%	0.09%
Boric acid	0.5%			
Borax	0.04%			
Adsorption rate	35.6%	25.7%	23.0%	24.1%
Adsorption suppression rate	—	27.8%	34.8%	32.1%

[0073]

It was found as the result shown in Table 3 that the
5 adsorption of an alkyldiaminoethylglycine is suppressed by
sodium chloride and such an adsorption suppression effect is
further improved in combination with glucose.

In addition, the above-described effect by glucose is
particularly enhanced by mixing relatively low concentration
10 of glucose.

[0074]

Test example 4: Addition effect of metal chloride other than
sodium chloride

The adsorption rate of an alkyldiaminoethylglycine on a
15 soft contact lens and the adsorption suppression rate relative
to the formulation of Comparative example 1 containing an
alkyldiaminoethylglycine only were determined in the same
condition as Test example 1 using the formulations having the
compositions shown in Table 4 and containing sodium chloride,
20 or potassium chloride manufactured by AKO KASEI or calcium
chloride manufactured by Tomita Pharmaceutical in place of
sodium chloride. Each of two samples were tested with using

"SEED 1dayFine UV plus" as a soft contact lens in this Test example. The result is shown in Table 4.

[0075]

Table 4

	Comparative example 1	Example 1	Example 4	Example 5	Example 6
ADG hydrochloride	0.0025%				
Sodium chloride	—	0.55%	—	—	—
Potassium chloride	—	—	0.55%	0.15%	—
Calcium chloride	—	—	—	—	0.55%
Boric acid	0.5%				
Borax	0.04%				
Adsorption rate	68.6%	23.8%	22.7%	31.8%	20.0%
Adsorption suppression rate	—	65.3%	66.9%	53.6%	70.8%

5 [0076]

It was found as the result shown in Table 4 that the adsorption of an alkyldiaminoethylglycine on a soft contact lens can be suppressed by metal chlorides such as potassium chloride and calcium chloride other than sodium chloride.

10 [0077]

Test example 5: Experiment of sodium chloride concentration

The adsorption rate of an alkyldiaminoethylglycine on a soft contact lens and the adsorption suppression rate relative to the formulation of Comparative example 1 containing an alkyldiaminoethylglycine only were determined in the same condition as Test example 1 using formulations having the compositions shown in Table 5 and having various sodium chloride concentrations. Each of two samples were tested with using "SEED 1dayFine UV plus" as a soft contact lens in this Test example. The result is shown in Table 5.

[0078]

Table 5

	Comparative example 1	Example 7	Example 1	Example 8	Example 9
ADG hydrochloride	0.0025%				
Sodium chloride	—	0.8%	0.55%	0.3%	0.1%
Boric acid	0.5%				
Borax	0.04%				
Adsorption rate	68.6%	20.9%	23.8%	25.4%	39.8%
Adsorption suppression rate	—	69.5%	65.3%	63.0%	42.0%

[0079]

It was found as the result shown in Table 5 that the
5 adsorption of an alkyldiaminoethylglycine on a soft contact
lens is suppressed by 0.1 w/v% or more and 0.8 w/v% or less of
sodium chloride, such an adsorption suppression effect is
slightly decreased in the case of 0.1 w/v%, but the adsorption
suppression effect is approximately the same in the range of
10 0.3 w/v% or more and 0.8 w/v% or less.

[0080]

Test example 6: Experiment of alkyldiaminoethylglycine
hydrochloride concentration

The adsorption rate of an alkyldiaminoethylglycine on a
15 soft contact lens and the adsorption suppression rate relative
to the formulation which did not contain sodium chloride and
contained an alkyldiaminoethylglycine in the same
concentration were determined in the same condition as Test
example 1 using formulations having the compositions shown in
20 Table 6 and having various alkyldiaminoethylglycine
hydrochloride concentrations. Each of three samples were
tested with using "SEED 1dayFine UV plus" as a soft contact
lens in this Test example. The result is shown in Table 6.

Table 6

	Comparative example 2	Example 10	Example 11	Comparative example 3	Example 12	Example 13	Comparative example 4	Example 14	Example 15	Comparative example 5	Example 16	Example 17
ADG		0.05%		0.01%				0.005%			0.001%	
hydrochloride	—	0.55%		—	0.55%		—	0.55%		—	0.55%	
Sodium chloride	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%
Glucose												
Boric acid												
Borax												
Adsorption rate	11.6%	13.5%	13.7%	24.7%	23.2%	23.3%	30.1%	23.4%	23.3%	40.3%	23.3%	22.8%
Adsorption suppression rate	—	-16.4%	-18.1%	—	6.1%	5.7%	—	22.3%	22.6%	—	42.2%	43.4%

[0082]

It was found as the result shown in Table 6 that the adsorption of an alkyldiaminoethylglycine on a soft contact lens can be suppressed more effectively in a lower

5 concentration of an alkyldiaminoethylglycine hydrochloride and can be particularly effectively suppressed in the case where the concentration of an alkyldiaminoethylglycine hydrochloride is 0.005 w/v% or less.

[0083]

10 Test example 7: Confirmation of efficiency on color soft contact lens

The adsorption rate of an alkyldiaminoethylglycine on "SEED 1dayFine UV plus" manufactured by SEED, "1DAY-Refrear BIJOU" manufactured by From-eyes and "Trompe-L'oeil 1DAY"

15 manufactured by BeauFrontier and the adsorption suppression rate relative to the formulation of Comparative example 4 which did not contain sodium chloride and contained an alkyldiaminoethylglycine in the same concentration were determined in the same condition as Test example 1 using

20 formulations having the compositions shown in Table 7. The above "1DAY-Refrear BIJOU" and "Trompe-L'oeil 1DAY" are color soft contact lenses and the materials are the same as that of "SEED 1dayFine UV plus". Each of three samples were tested in this Test example. The result is shown in Table 7.

[0084]

Table 7

	SEED 1dayFine UV plus			1DAY-Refrear BIJOU			Trompe-L'oeil 1DAY		
	Comparative example 4	Example 14	Example 15	Comparative example 4	Example 14	Example 15	Comparative example 4	Example 14	Example 15
ADG hydrochloride	0.005%			0.005%			0.005%		
Sodium chloride	—	0.55%		—	0.55%		—	0.55%	
Glucose	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%
Boric acid	0.5%								
Borax	0.04%								
Adsorption rate	29.9%	22.8%	22.8%	46.3%	26.2%	26.2%	21.9%	17.8%	17.7%
Adsorption suppression rate	—	23.7%	23.7%	—	43.4%	43.4%	—	18.7%	19.2%

[0085]

It was found as the result shown in Table 7 that the adsorption suppression effect of an alkyldiaminoethylglycine on a soft contact lens by sodium chloride can be also exerted on a color soft contact lens.

[0086]

Test example 8: Experiment of pH

The adsorption rate of an alkyldiaminoethylglycine on a soft contact lens and the adsorption suppression rate relative to the formulation which did not contain sodium chloride and contained an alkyldiaminoethylglycine in the same concentration were determined in the same condition as Test example 1 using formulations having the compositions shown in Table 8 and having pH values adjusted by hydrochloric acid or a sodium hydroxide aqueous solution. Each of three samples were tested with using "SEED 1dayFine UV plus" as a soft contact lens in this Test example. The result is shown in Table 8.

Table 8

	Comparative example 6	Example 18	Example 19	Comparative example 7	Example 20	Example 21	Comparative example 8	Example 22	Example 23	Comparative example 9	Example 24	Example 25
ADG	0.005%											
hydrochloride	—	0.55%	—	—	0.55%	—	—	0.55%	—	—	0.55%	—
Sodium chloride	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%
Glucose	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%	—	—	0.0075%
Boric acid	0.5%											
Borax	0.04%											
pH	8.5											
Adsorption rate	23.3%	20.4%	19.9%	27.9%	23.0%	20.0%	27.7%	22.1%	21.6%	24.5%	24.2%	22.7%
Adsorption suppression rate	—	12.4%	14.6%	—	17.6%	28.3%	—	20.2%	22.0%	—	1.2%	7.3%

[0088]

It was found as the result shown in Table 8 that the adsorption suppression effect of an alkyldiaminoethylglycine on a soft contact lens by sodium chloride is particularly
5 remarkably exerted in the pH range of 6.5 or more and 7.5 or less.

CLAIMS

1. A pharmaceutical composition for a soft contact lens,
comprising 0.001 w/v% or more and 0.008 w/v% or less of an
5 alkyldiaminoethylglycine hydrochloride and 0.3 w/v% or more
and 0.8 w/v% or less of a metal chloride, wherein the metal
chloride is one or more salts selected from the group
consisting of an alkali metal chloride and a group 2 metal
chloride.
10
2. The pharmaceutical composition for a soft contact lens
according to claim 1, wherein the metal chloride is sodium
chloride and/or potassium chloride.
- 15 3. The pharmaceutical composition for a soft contact lens
according to claim 1 or 2, further comprising glucose.
4. The pharmaceutical composition for a soft contact lens
according to claim 3, comprising 0.001 w/v% or more and 0.01
20 w/v% or less of the glucose.
5. The pharmaceutical composition for a soft contact lens
according to any one of claims 1 to 4, comprising 0.001 w/v%
or more and 0.005 w/v% or less of the alkyldiaminoethylglycine
25 hydrochloride.
6. The pharmaceutical composition for a soft contact lens
according to any one of claims 1 to 4, comprising:
0.001 w/v% or more and 0.005 w/v% or less of the
30 alkyldiaminoethylglycine hydrochloride,

0.3 w/v% or more and 0.8 w/v% or less of the metal
chloride, and

0.002 w/v% or more and 0.008 w/v% or less of the glucose.

5 7. The pharmaceutical composition for a soft contact lens
according to any one of claims 1 to 6, further comprising a
buffering agent.

8. The pharmaceutical composition for a soft contact lens
10 according to claim 7, comprising 0.1 w/v% or more and 2.0 w/v%
or less of the buffering agent.

9. The pharmaceutical composition for a soft contact lens
according to any one of claims 1 to 8, wherein pH is 5.5 or
15 more and 8.0 or less.

10. The pharmaceutical composition for a soft contact lens
according to any one of claims 1 to 9, wherein pH is 6.5 or
more and 7.5 or less.

20

PHARMACEUTICAL COMPOSITION FOR SOFT CONTACT LENS

Abstract

The objective of the present invention is to provide a
5 pharmaceutical composition for a soft contact lens, wherein
the composition comprises an alkyldiaminoethylglycine and
adsorption of the alkyldiaminoethylglycine on a soft contact
lens is suppressed. The pharmaceutical composition for a soft
contact lens according to the present invention comprises
10 0.001 w/v% or more and 0.008 w/v% or less of an
alkyldiaminoethylglycine hydrochloride and a metal chloride.

[No Available Figure]