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(54) [TITLE OF INVENTION] AQUEOUS COMPOSITION

(57) [ABSTRACT]

[SUBJECT] To provide a safe aqueous composition that possesses a stable and superior preservative effectiveness.

[SOLUTION] An aqueous composition, characterized in that it contains sorbic acid or its salts and zinc salt, such as zinc sulfate or zinc salt of oxycarboxylic acid, by making an aqueous composition coexist that contains sorbic acid or its salts with zinc salt, such as zinc

sulfate or zinc salt of oxycarboxylic acid, a method to improve the preservative effectiveness of said aqueous composition.

[PATENT CLAIMS]

[Claim 1] An aqueous composition characterized in that it contains sorbic acid or its salts and zinc salt.

[Claim 2] An aqueous composition as described in claim 1, wherein the zinc salts are selected from zinc salt of carboxylic acids and zinc sulfate.

[Claim 3] Moreover, an aqueous composition as described in claim 1 or 2, wherein it further contains monoterpenes.

[Claim 4] One of the aqueous compositions as described in claims 1~3, wherein it is an aqueous composition for mucous application.

[Claim 5] One of the aqueous compositions as described in claims 1~4, wherein it is for ophthalmological use.

[Claim 6] A method to enhance antibacterial activity by adding zinc salt to the aqueous composition, which contains sorbic acid or its salt.

[DETAILED DESCRIPTION OF THE INVENTION]

[0001]

[Field of the Invention]

The present invention relates to an aqueous composition having improved antibacterial activity.

[0002]

[Prior Art]

Preservatives (pasteurization, hydrostatic bacteria agents) are added to aqueous compositions of pharmaceutical products and cosmetics to prevent contamination by microorganisms. The type of preservatives to be used is selected based on suitability, taking into consideration the stimulus level in relation to the type of composition or the level of antibacterial effect. For example, for ophthalmological aqueous compositions such as eye drops, one or two more types of cationic surfactants such as benzalkonium chloride, benzethonium chloride, chlorhexidine gluconate, amphoteric surfactants such as alkyl polyaminoethyl glycine, parabens, chlorobutanol, and sorbic acid, etc. can be combined for use as preservatives. Within these, sorbic acid or its salts, in comparison to other preservatives such as benzalkonium chloride, is used in various fields due to having less potential of damage to corneal epithelial cells, including extensively as ophthalmologic aqueous composition. However, there was a problem of its having low antimicrobial action. Also, the antimicrobial action was low especially at a high pH, and there was a problem of it not being able to achieve a stable preservative effect.

[0003] Hitherto, to solve this kind of problem, a buffer with a high preservative effect such as boric acid was simultaneously combined, or a pharmaceutical device such as combining a flavor as well as ethylenediaminetetraacetic acid or its salts (JP-A-H11-292793) is used, but the effect was insufficient, and a method to stably improve the preservative effectiveness of sorbic acid or its salts was strongly desired. This kind of method gives various uses to sorbic acid or its salts that

function as a preservative for aqueous composition, and is also useful not only to the medicinal but also to the cosmetic field, making it possible to provide an aqueous composition whose preservative effectiveness is stably heightened.

[0004]

[The problem that the invention attempts to solve] The goal of the present invention is to provide an aqueous composition that contains sorbic acid or its salts that presents high preservative effectiveness and high safety.

[0005]

[Means to solve the problem] The inventors, as a result of diligently investigating in order to accomplish the aforementioned goal, came to the completion of this invention by aptly combining an aqueous composition or its salts with zinc sulfate and zinc salt such as that of carboxylic acids, at which point said composition produces an unexpectedly high preservative effectiveness.

[0006] That is to say, this invention is regarding: (1) an aqueous composition characterized in that it contains sorbic acid or its salt and zinc salt, (2) an aqueous composition listed in (1) characterized in that its zinc salt is chosen from zinc salts of carboxylic acids and zinc sulfate, (3) an aqueous composition listed in (1) or (2) characterized in that it contains monoterpenes, (4) one of the aqueous compositions listed in (1)~(3) characterized in that it is a composition for mucous application, (5) one of the aqueous compositions listed in (1)~(4) characterized in that it is an ophthalmological composition, and (6) a method for enhancing antibacterial activity by adding zinc salt to aqueous composition that contains sorbic acid or its salts.

[0007]

[The form of execution of the invention] Within this detailed statement, unless otherwise noted, % means w/v %. Also the phrase contact lens (CL), unless otherwise noted, includes all types of lenses such as hard, oxygen-permeable hard, and soft.

[0008] Sorbic acid, or salts allowed pharmacologically or physiologically, may be used as sorbic acid or its salts. Salts allowed pharmacologically or physiologically may be used as sorbic acid or its salts can be illustrated as, for example, salts with organic base (e.g. methylamine, triethylamine, triethanolamine, morpholine, piperazine, pyrrolidine, amino acid, polypyridine, picoline, and such salts with organic amine), salts with an inorganic base (e.g. alkaline metals such as ammonium salts, sodium, and potassium, alkaline earth metals such as calcium and magnesium, and salts with metal such as aluminum). Specifically, there are sorbic acid, potassium sorbate, sodium sorbate, and triclocarban sorbate. Preferably salts with an inorganic base or sorbic acid that is especially sorbic acid, potassium sorbate, or sodium sorbate is ideal. Sorbic acid or its salts could be used individually or combined with two or more types.

[0009] The amount of sorbic acid or its salts used in the present invention differs depending on the composition's status, apt method of use, the type of compound, etc.; however, it is generally in the range of 0.0001~10%. More in depth, in the case of aqueous compositions for internal use it is within the range of 0.001~10%, preferably 0.01~5%, and more preferably 0.001~1%, in the case of aqueous compositions for external use it is generally in the range of 0.0001~2%, preferably 0.001~1%, and more preferably 0.005~0.05, and in the case of aqueous compositions for mucous application it is generally in the range of 0.0001~10%, preferably 0.001~5%, and more preferably 0.01~1%.

[0010] As zinc salt, zinc salt of carboxylic acids, such as lactate zinc, zinc glycolate, zinc hydroxyl acid, zinc glycerate, zinc maleate, zinc tartrate, zinc citrate, or zinc sulfate can be used. And ideal salt is zinc lactate, zinc sulfate, and others. Zinc lactate or zinc sulfate also functions as an astringent and the stimulus is low even if given to mucous membrane that is sensitive to ocular membrane stimulus, therefore is ideal for use as aqueous composition for membrane application, such as eye wash or nasal drops, and within these is ideal for use in ophthalmological composition due to its high safety level.

[0011] The amount of zinc salt used in the aqueous composition in the present invention differs depending on the composition's status, apt method of use, the type of compound, etc.; however, it is generally in the range of 0.0001~5%. In more detail, in the case of aqueous composition for internal use, it is in the range of 0.0001~5%, preferably 0.0005~1%, more preferably 0.002~0.5%, and in the case of aqueous composition for external use 0.0005~5%, preferably 0.001~2%, more preferably 0.01~0.5%, in the case of aqueous composition for use for mucous membrane (aqueous liquid medicine) 0.0001~5%, preferably 0.001~2%, and more preferably 0.005~0.5%. The zinc salt can be used alone or by combining two or more kinds.

[0012] The ratio between the sorbic acid or its salts and zinc salt differs depending on the composition's status, apt method of use, the type of compound, etc.; however generally to one part of weight of sorbic acid or its salts, one can employ 0.0001~1000 parts of weight, preferably 0.0005~500 parts of weight, more preferably 0.001~50 parts of weight, and most preferably 0.001~50 parts of weight of zinc salt.

[0013] The present invention is based on the observation that by making sorbic acid or its salts and zinc salt coexist within an aqueous composition, an unpredictably high antibacterial effect is produced for each independently. The composition of the present invention, as long as this antibacterial activity is needed, is appropriate for use in various fields such as medicine, quasi-pharmaceutical products, cosmetics, and food products.

[0014] The form of the aqueous composite of this invention, so long as it is a composite that includes water, is discretionary and can take on various forms

depending on the goal. For example, jelly, liquid, and semisolid (ointments, etc.) are all acceptable forms. Specifically, compositions for oral use such as medicine in jelly form, liquid medicine, soft capsules etc. or compositions for mucous membrane application such as liquid medicine and semisolid preparation (ointments). Because the aqueous composition of the present invention requires a high, stable preservative power and superior safety, it is ideal for internal use, dermatological use, mucous membrane application, and contact lenses. In particular, it is ideal for use as an agent for application for ocular mucous membrane, nasal mucosa, oral mucosa, large intestine mucous membrane, etc., and of them is especially ideal for use for ocular mucous membrane application.

Also, since sorbic acid has almost no adhesiveness to contact lenses, it is effective as all sorts of liquid medicine for contact lenses, including not only a formulation for direct use on ocular mucous membrane while putting on or using contact lenses, but also as liquid medicine for contact lenses for indirect application.

[0015] As specific examples of an aqueous composition of the present invention, beginning with internal medicine and external medicine, we can also list medical products, food products and cosmetics that are aqueous compositions for ophthalmological use or otorhinolaryngological use. As even more specific examples there are eye drops (including eye drops that can be used while wearing contacts), eye wash (medicine) (including eye wash that can be used while wearing contacts), eye ointment (medicine), contact lens wetting solution, medicine for contact lenses (lotion, soaking solution, cleaning/soaking solution, antiseptic solution (multipurpose solution, etc.) etc.), nose drops, solutions used for nasal irrigation, etc. The aqueous composition of the present invention is especially effective for ophthalmological use such as eye drops, eye wash, and medicine for contact lenses.

[0016] The aqueous composition of the present invention can include at least one type of monoterpene to enhance antibacterial activity. Monoterpene to be included in the aqueous composition of the present invention could be menthol, camphor, borneol, geraniol, cineole, anethole, limonene, eugenol, etc. These monoterpenes can be *d* configuration, *l* configuration, or *dl* configuration, but taking into consideration sensual aspects such as a cool sensation and scents and safety, *l*-menthol, *d*-menthol, *dl*-menthol, *d*-camphor, *dl*-camphor, *d*-borneol and *dl*-borneol are preferable. Geraniol, *l*-menthol, *d*-camphor and *d*-borneol are especially preferable. Also the aforementioned monoterpenes can be used in a form containing refined oil, preferable refined oils being eucalyptus oil, bergamot oil, peppermint oil, cool mint oil, spearmint oil, etc. These monoterpenes can be used by choosing one or two or more kinds.

[0017] The density of monoterpenes within the aqueous composition of the present invention differs depending on the composite's status, apt method of use, the type of composition, etc., but ordinarily the range is 0.00001~0.1 weight %, and preferably 0.00001~0.05 weight %.

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