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PATENT REQUEST: STANDARD PATENT

I/We, the Applicant(s)/Nominated Person(s) specified below, request I/We be granted a patent for the invention disclosed in the accompanying standard complete specification.

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[54] Invention Title:

Method and Composition for Cleaning and Disinfecting Contact Lenses

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Divisional Application Details

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Person by whom made :Bausch & Lomb Incorporated

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Bausch & Lomb Incorporated

By:

Registered Patent Attorney

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AUSTRALIAN PATENT OFFICE

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Notice Of Entitlement

I, John David O'Connor, of 31 Market Street, Sydney, New South Wales, 2000, Australia, being the Patent Attorney for the Applicant/Nominated Person in respect of Application No. 30439/92, state the following:-

The Applicant/Nominated Person has entitlement from the actual inventors as follows:

The Applicant/Nominated Person is the assignee of the actual inventors.

The Applicant/Nominated Person is the applicant of the original application.

DATED this Twenty-eighth Day of February 1996

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METHOD AND COMPOSITION FOR CLEANING AND DISINFECTING CONTACT LENSES

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(56) Prior Art Documents
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(57) Claim

1. A method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is poly((dimethyliminio)-2-butene-1,4-diyl chloride), α-(4-(tris(2-hydroxyethyl)ammonio)2-butenyl)-ω-(tris(2-hydroxyethyl)ammonio)-dichloride and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 400 mOsm./kg. water.

5. A method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is hexamethylene biguanide and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 600 mOms./kg. water.

10. A composition for simultaneously cleaning and disinfecting contact lenses said composition comprising water, a disinfecting amount of an antimicrobial agent which is polymeric quaternary ammonium salt used in ophthalmic applications, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 400 mOms./kg. water.

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16. An aqueous composition for simultaneously cleaning and disinfecting contact lenses, said composition having a pH of about 6.5 to about 8.5 and comprising about 0.00003 to about 0.05 percent by weight/volume of a hexamethylene biguanide polymer, and effective amount of a proteolytic enzyme, and wherein the final osmotic value of said composition is less than about 600 mOsm./kg. water.

21. A composition for simultaneously cleaning and disinfecting contact lenses said composition comprising water, a disinfecting amount of an antimicrobial agent which is a biguanide, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 600 mOms./kg. water.

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COMPLETE SPECIFICATION

SUBSTITUTE FOR A STANDARD PATENT SUBSTITUTE

ORIGINAL

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Invention Title: Method and Composition for Cleaning and Disinfecting Contact Lenses

The following statement is a full description of this invention, including the best method of performing it known to me/us:-

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METHOD AND COMPOSITION FOR CLEANING AND DISINFECTING CONTACT LENSES

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to a method for cleaning and disinfecting contact lenses and a composition for the same. More specifically, the present invention is directed to a method for simultaneously cleaning and disinfecting contact lenses by contacting the lenses with an aqueous system containing an antimicrobial agent and a proteolytic enzyme. A composition for simultaneously cleaning and disinfecting the lenses is also provided.

Description of Art

In the normal course of wearing contact lenses, tear film and debris consisting of proteinaceous, oily, sebaceous, and related organic matter have a tendency to deposit and build up on lens surfaces. As part of the routine care regimen, contact lenses must be cleaned to remove these tear film deposits and debris. If these deposits are not properly removed, both the wettability and optical clarity of the lenses is substantially reduced causing discomfort for the wearer.

Further, contact lenses, especially those made from hydrophilic materials, must be continuously disinfected to kill any harmful microorganisms that may be present or grow on the lenses. A number of methods for disinfecting contact lenses have been used such as the use of high temperatures, the use of oxidative chemicals, and the use of antimicrobial agents. However, current disinfecting solutions do not exhibit significant cleaning ability for the removal of proteinaceous material.

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Conventionally, the cleaning of contact lenses is accomplished with one or both of two general classes of cleaners. Surfactant cleaners, generally known as "daily cleaners" because of their recommended daily use, are effective for the removal of most carbohydrate and lipid derived matter. However, they are not as effective for the removal of proteinaceous matter such as lysozyme. Typically, proteolytic enzymes derived from plant, animal, and microbial sources are used to remove the proteinaceous deposits. These "enzyme" cleaners are recommended for weekly use and are conventionally employed by dissolving enzyme tablets in suitable aqueous solutions.

The process of cleaning and disinfecting contact lenses with enzyme cleaners (as well as daily cleaners) involves two steps. The first step consists of the cleaning phase whereby lenses are conventionally soaked in an enzyme cleaning solution at ambient temperature conditions, i.e, cold soaking for a period of up to 12 hours, to achieve effective removal of proteinaceous deposits. At the conclusion of the cleaning step, the lenses are separately disinfected. Disinfection involves contacting the lenses with a solution containing either an oxidative chemical or an antimicrobial agent at ambient temperatures or exposing the lenses to elevated temperatures for specified periods of time. The latter disinfection technique requires specific electrical disinfecting apparatus.

New methods have been developed which can remove proteinaceous material from contact lenses while disinfecting the lenses. For example, U.S. Patent 4,614,549 discloses a single-step method of cleaning and disinfecting contact lenses in aqueous solutions of proteolytic enzymes at temperatures of between 60°C and 100°C. This method requires the use of electrical disinfecting apparatus and elevated temperatures.

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U.S. Patent Re. 32,672 discloses a method which immerses the lenses in a solution containing peroxide and a peroxide-active enzyme. However, this method requires an additional step for the neutralization of the residual peroxide prior to inserting the lens into the eye.

In order to develop an improved simultaneous cleaning and disinfecting method that does not require neutralization of any oxidative chemical, proteolytic enzymes in tablet form were tested in combination with a disinfecting solution containing hexamethylene biguanide polymers as the antimicrobial agent at ambient conditions. However, subsequent microbicidal efficacy studies revealed that the antimicrobial agent was rendered less effective for killing certain microorganisms during these initial studies.

However, it has now been discovered that the disinfecting ability of antimicrobial agents, particularly at ambient temperatures, is most effective under conditions of suitable osmolality for the agent employed. When the osmotic level of the solution is too high, the antimicrobial agents are rendered less effective for killing certain microorganisms.

Thus, according to this invention, proteolytic enzymes can be used in combination with antimicrobial agents to simultaneously clean and disinfect contact lenses. Under ambient temperatures, the disinfection has been found to be most effective at suitable osmotic conditions. The present invention provides a less complex and more convenient regimen for cleaning and disinfecting contact lenses without the need for a separate neutralizing step or electrical disinfecting apparatus.

Summary of the Invention

According to this invention, a method for simultaneously cleaning and disinfecting contact lenses is provided comprising contacting the lenses with an aqueous system containing an antimicrobial agent and a proteolytic enzyme for a time sufficient to clean and disinfect the lenses. Preferably, the aqueous system will have an osmotic value which does not substantially inhibit the activity of the antimicrobial agent.

Also provided is a composition for simultaneously cleaning and disinfecting contact lenses containing an antimicrobial agent and a proteolytic enzyme and an osmotic value of less than about 800 mOsm./kg. water.

According to a first embodiment of this invention there is provided a method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is poly((dimethyliminio)-2-butene-1,4-diyl chloride), α-(4-(tris(2-hydroxyethyl)ammonio)-2-butenyl)-ω-(tris(2-hydroxyethyl)ammonio)-dichloride and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 400 mOsm./kg. water.

According to a second embodiment of this invention there is provided a method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is hexamethylene biguanide and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 600 mOms./kg. water.

According to a third embodiment of this invention there is provided a composition for simultaneously cleaning and disinfecting contact lenses said composition comprising water, a disinfecting amount of an antimicrobial agent which is polymeric quaternary ammonium salt used in ophthalmic applications, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 400 mOms./kg. water.

According to a fourth embodiment of this invention there is provided an aqueous composition for simultaneously cleaning and disinfecting contact lenses, said composition having a pH of about 6.5 to about 8.5 and comprising about 0.00003 to about 0.05 percent by weight/volume of a hexamethylene biguanide polymer, and effective amount of a proteolytic enzyme, and wherein the final osmotic value of said composition is less than about 600 mOsm./kg. water.

According to a fifth embodiment of this invention there is provided a composition for simultaneously cleaning and disinfecting contact lenses said composition comprising

water, a disinfecting amount of an antimicrobial agent which is a biguanide, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 600 mOms./kg. water.

Detailed Description of the Invention

The present invention can be used with all contact lenses such as conventional hard, soft, rigid gas permeable, and silicone lenses but is preferably employed with soft lenses such as those commonly referred to as hydrogel lenses prepared from monomers such as hydroxyethylmethacrylate, hydroxyethylmethyl methacrylate, vinylpyrrolidone, glycerolmethacrylate, methacrylic acid or acid esters and the like. Hydrogel lenses typically absorb significant amounts of water such as from 4 to 80 percent by weight.

The compositions employed herein for the cleaning and disinfecting of contact lenses are composed of at least water, one or more proteolytic enzymes, and one or more antimicrobial agents. Generally, these cleaning and disinfecting systems are prepared by mixing two components, the enzyme and a disinfecting solution containing the antimicrobial agents. However, other methods of combining the active components as

well as off the shelf compositions containing all of the active components are contemplated as being within the scope of this invention.

A wide variety of proteolytic enzymes are useful in the present invention such as those derived from plant, animal, and microbial sources. The separation and purification of these enzymes is well known to those skilled in the art with many of these enzymes being commercially available. Moreover, it is anticipated that many of the enzymes can be prepared from new techniques being developed such as those using recombinant DNA techniques and proteolytic enzymes prepared by these techniques are contemplated to be within the scope of the present invention.

The proteolytic enzymes used herein must have at least a partial capability to hydrolyze peptide-amide bonds which reduces the proteinaceous material to smaller water-soluble subunits. Typically, these enzymes will exhibit some lipolytic, amylolytic or related activities associated with the proteolytic activity and may be neutral, acidic or alkaline. In addition, separate lipases or carbohydrases may be used in combination with the proteolytic enzymes.

Examples of suitable proteolytic enzymes include but are not limited to pancreatin, trypsin, chymotrypsin, collagenase, papain, bromelain, aminopeptidase, Aspergillo peptidase, pronase E (from *S. graseus*) and dispase (from *Bacillus polymyxa*). The preferred group of proteolytic enzymes are the microbial derived enzymes such as those derived from *Bacillus*, *Streptomyces*, and *Aspergillus* microorganisms. Most preferred are the *Bacillus* derived alkaline proteases generically called subtilisin enzymes. The subtilisin enzymes include both sub-classes, subtilisin A and subtilison B. Microbial derived enzymes are disclosed in U.S. Patent 4,690,773 incorporated herein by reference.

The present invention employs an effective amount of enzyme to clean the lenses. An effective amount is that which removes a substantial portion of the proteinaceous deposits which occur during normal wear in a reasonable time. The precise amount of enzyme required to make an effective cleaner will depend on several factors including the activity of the enzyme, the purity of the enzyme, the amount of proteinaceous matter deposited on the lenses, the desired soaking period, the specific type of lenses, as well as other factors.

It should be appreciated to one skilled in the art, that the enzyme concentrations useful herein are adjusted depending upon the time allowed for removing the proteinaceous material, the other components in the solutions and the factors previously mentioned. Typically, when the enzyme is provided in solid form, it will be present in amounts from about 0.01 to about 200 milligrams.

Enzyme activity is generally pH dependent and there will be a particular pH range in which any particular enzyme will function best. However, the determination of an optimum pH range can readily be determined by known techniques by those skilled in the art. It is preferred that the enzyme be selected to have substantial activity at a pH between about 6.5 and about 8.5.

The enzyme may be employed in liquid or solid form usually in combination with additional components. Preferably, the enzymes are provided in solid form such as tablets or powders which are mixed with the aqueous solutions prior to use.

Additional components may be added to or incorporated into the enzyme which do not substantially decrease the activity of the enzyme. For example, components such as effervescing agents, stabilizers, buffering agents, chelating and/or sequestering agents, coloring agents, tonicity adjusting

agents, surfactants and the like can be employed. In addition, binders, lubricants, carriers, and other excipients normally used in producing tablets may be incorporated into the enzyme when tablets are employed.

Examples of suitable buffering agents which may be incorporated into the enzyme include, but are not limited to, alkali metal salts such as potassium or sodium carbonates, acetates, borates, phosphates, citrates and hydroxides, and weak acids such as acetic and boric acids. Preferred buffering agents are alkali metal borates such as sodium or potassium borates. Additionally, other pH adjusting agents may be employed such as inorganic acids. For example, hydrogen chloride may be employed in concentrations suitable for ophthalmic uses. Generally, buffering agents are present in amounts from about 0.01 to about 2.5 percent by weight/volume (w/v).

Effervescing agents are typically employed when the enzyme is provided in solid form. Examples of suitable effervescing agents include, but are not limited to, tartaric or citric acid used in combination with a suitable alkali metal salt such as sodium carbonate.

The disinfecting solutions used with the present invention may contain any of the above-mentioned enzyme components as well as other components but typically will contain water, the antimicrobial agent, one or more of a suitable buffering agent, chelating and/or sequestering agent, tonicity adjusting agent, and surfactant.

The tonicity adjusting agent which may be a component of the disinfecting solution and may optionally be incorporated into the enzyme is employed to adjust the osmotic value of the final cleaning and disinfecting solution to more closely

resemble that of human tears and to maintain a suitable level for optimum activity by the antimicrobial agent. Suitable tonicity adjusting agents include, but are not limited to, sodium and potassium chloride, dextrose, calcium and magnesium chloride, the buffering agents listed above and combinations thereof. The tonicity adjusting agents are individually used in amounts ranging from about 0.01 to 2.5% (w/v) and preferably, from about 0.5 to about 1.5% (w/v). Most preferably, the tonicity agent will be employed in an amount to provide a final osmotic value of the cleaning and disinfecting solutions of less than about 800 millosmoles/kilogram water (mOsm./kg. water)

Suitable surfactants can be either cationic, anionic, nonionic or amphoteric. Preferred surfactants are neutral or nonionic surfactants which may be present in amounts up to 5% (w/v). Examples of suitable surfactants include, but are not limited to, polyethylene glycol esters of fatty acids, polyoxypropylene ethers of C_{12}-C_{18} alkanes and polyoxyethylene, polyoxypropylene block copolymers of ethylene diamine (i.e. poloxamine).

Examples of preferred chelating agents include Ethylenediaminetetraacetic acid (EDTA) and its salts (disodium) which are normally employed in amounts from about 0.025 to about 2.0% (w/v). Other known chelating (or sequestering agents) such as certain polyvinyl alcohols can also be employed.

The disinfecting solutions used with this invention will contain a disinfecting amount of one or more antimicrobial agents which are compatible with and do not precipitate in the presence of the enzymes. As used herein, antimicrobial agents are defined as non-oxidative organic chemicals which derive their antimicrobial activity through a chemical or

physiochemical interaction with the organisms. Suitable antimicrobial agents are those generally employed in ophthalmic applications and include, but are not limited to, quaternary ammonium salts used in ophthalmic applications such as poly((dimethyliminio)-2-butene-1,4-diyl chloride), α-(4-(tris(2-hydroxyethyl)ammonio)2-butenyl)-ω-(tris(2-hydroxyethyl)ammonio)-dichloride (chemical registry number 75345-27-6) generally available as polyquaternium 1® from ONYX Corporation and benzalkonium halides, and biguanides such as salts of alexidine, alexidine free base, salts of chlorhexidine, hexamethylene biguanides and their polymers. The salts of alexidine and chlorhexidine can be either organic or inorganic and are typically gluconates, nitrates, acetates, phosphates, sulphates, halides and the like. Preferred antimicrobial agents are the biguanides with hexamethylene biguanides, their polymers and water-soluble salts being most preferred. Generally, the hexamethylene biguanide polymers, also referred to as polyaminopropyl biguanide (PAPB), have molecular weights of up to about 100,000. Such compounds are known and are disclosed in US 4,758,595 which is incorporated herein by reference.

A disinfecting amount of antimicrobial agent is an amount which will at least partially reduce the microorganism population in the formulations employed. Preferably, a disinfecting amount is that which will reduce the microbial burden by two log orders in four hours and more preferably by one log order in one hour. Most preferably, a disinfecting amount is an amount which will eliminate the microbial burden on a contact lens when used in regimen for the recommended soaking time (FDA Chemical Disinfection Efficacy Test-July, 1985 Contact Lens Solution Draft Guidelines). Typically, such agents are present in concentrations ranging from about 0.00001 to about 0.5% (w/v), and more preferably, from about 0.00003 to about 0.05% (w/v).

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As mentioned above, it has been found that the antimicrobial agents at simulated commercial concentrations are rendered less effective in environments having high osmotic values, generally above about 800 mOsm./kg. water at typical commercial concentrations (generally less than about 0.05% (w/v)). This is a particularly important discovery since it is common in the industry to add bulking agents to the active enzyme when used in tablet or powder form. These bulking agents usually increase the osmotic values of the cleaning solutions, often significantly reducing the antimicrobial activity. Further, the various components discussed above, as well as others, may also raise the osmolality of the final formulation.

Moreover, it should also be understood that the particular osmotic value rendering any given antimicrobial agent ineffective will vary from agent to agent. The determination of the suitable osmotic range for any particular antimicrobial agent can be easily determined by routine experimentation by one skilled in the art. However, a preferred range of osmotic values has been found to be less than about 800 mOsm./kg. water and more preferable about 200 to about 600 mOsm./kg. water at antimicrobial agent concentrations of less than about 0.05% (w/v).

During practice of this invention, the enzyme formulation, either in solid or liquid form, is typically dissolved in a predetermined amount of disinfecting solution which may be isotonic or hypotonic, to obtain a cleaning and disinfecting solution having the proper osmotic value. This solution is then contacted with lenses at ambient temperatures for a sufficient time to clean and disinfect.

In a preferred embodiment of the invention, an enzyme tablet is dissolved in an aqueous disinfecting solution containing a biguanide as the antimicrobial agent in order to

prepare the cleaning and disinfecting solution. The lenses are then contacted with the cleaning and disinfecting solution, preferably by being immersed therein, and remain in contact with the solution for a sufficient period of time to disinfect the lenses. An effective amount of enzyme agent is used such that the time sufficient to disinfect will also be sufficient to substantially remove the proteinaceous deposits. Typically, the cleaning and disinfecting will take less than about eight hours with about 1 to about 4 hours being preferred. Advantageously, the lenses can be removed from the solution and placed directly into the eye without the need for a separate neutralising step. Preferably, the lenses are rinsed with a suitable isotonic aqueous solution prior to insertion into the eye.

The following detailed examples are presented to illustrate the present invention.

Example 1-36

In order to study the antimicrobial efficacy of the compositions of the present invention, several aqueous solutions were prepared and evaluated for the log kill rate of Serratia marcescens.

Aqueous solutions were prepared having compositions which simulate commercial disinfecting solutions. All percentages indicate throughout these examples are in weight/volume. Each composition had 0.85% boric acid, 0.09% sodium borate, 1.0% Tetronic® 1107 (a poloxamine surfactant purchased from BASF Corporation), simulated commercial concentrations of alexidine dihydrochloride, chlorhexidine gluconate, PAPB, polyquaternium® (purchased from ONYX Corporation), and benzalkonium chloride as the antimicrobial agent respectively and 0.005% of a proteolytic enzyme (subtilising-A

enzyme purchased from NOVO Laboratories, Inc.). The osmolality was varied using sodium chloride as the tonicity adjusting agent. Two separate solutions were tested for each composition. The compositions are shown in Table I.

The microbicidal activity of the above solutions were tested in duplicate by exposing Serratia marcescens at about 1.0×10^6 to about 1.0×10^7 colony forming units per millilitre (CFU/mL.) to 10mL of each solution at room temperature for 1 hour and 4 hour time intervals. An aliquot of each inoculated sample was removed at 1 and 4 hours and diluted in a neutralising broth (Dey-Engley) and plated with neutralising agar. The agar plates were incubated for two days and plate counts were determined to calculate reduction in CFU/mL. for the organism. The calculated log order reductions are shown in Table I.

As can be seen from Table I the log order reductions of the various antimicrobial agents tested were significantly reduced at high osmotic levels.

TABLE I
DISINFECTING

EXAMPLE	DISINFECTING AGENT	SODIUM CHLORIDE % (w/v)	MEASURED OSMOLALITY (mOsm/kg water)	LOG REDUCTION S. MARCESCENS 1 Hour	4 Hours
1A	Alexidine 1.0 ppm	0.20	200	2.6	>4.5
B	Alexidine 1.0 ppm	0.20	200	2.6	>4.5
2A	Alexidine 1.0 ppm	0.53	302	1.2	>4.5
B	Alexidine 1.0 ppm	0.53	302	1.2	>4.5
3A	Alexidine 1.0 ppm	0.85	404	0.5	>4.5
B	Alexidine 1.0 ppm	0.85	404	0.6	>4.5
4A	Alexidine 1.0 ppm	1.15	500	0.2	3.4
B	Alexidine 1.0 ppm	1.15	500	0.0	3.4
5A	Alexidine 1.0 ppm	1.47	602	0.0	1.5
B	Alexidine 1.0 ppm	1.47	602	0.0	1.6
6A	Alexidine 1.0 ppm	2.09	800	0.0	1.1
B	Alexidine 1.0 ppm	2.09	800	0.0	1.1
7A	Chlorhex 100 ppm	0.20	202	>4.5	>4.5
B	Chlorhex 100 ppm	0.20	202	>4.5	>4.5
8A	Chlorhex 100 ppm	0.53	306	>4.5	>4.5
B	Chlorhex 100 ppm	0.53	306	>4.5	>4.5
9A	Chlorhex 100 ppm	0.85	402	2.0	>4.5
B	Chlorhex 100 ppm	0.85	402	2.0	>4.5
10A	Chlorhex 100 ppm	1.15	501	1.0	>4.5
B	Chlorhex 100 ppm	1.15	501	1.4	>4.5

TABLE I

DISINFECTING (Continued)

Example	Disinfecting Agent	Sodium Chloride % (w/v)	Measured Osmolality (mOsm/kg water)	LOG REDUCTION S. MARCESCENS	
				1 Hour	4 Hours
11A	Chlorhex 100 ppm	1.47	602	1.0	>4.5
B	Chlorhex 100 ppm	1.47	602	1.0	>4.5
12A	Chlorhex 100 ppm	2.09	800	0.0	1.6
B	Chlorhex 100 ppm	2.09	800	0.1	1.4
13A	PAPB 1.0 ppm	0.20	199	>4.5	>4.5
B	PAPB 1.0 ppm	0.20	199	4.5	>4.5
14A	PAPB 1.0 ppm	0.53	301	4.2	>4.5
B	PAPB 1.0 ppm	0.53	301	4.3	>4.5
15A	PAPB 1.0 ppm	0.85	402	3.0	>4.5
B	PAPB 1.0 ppm	0.85	402	2.8	>4.5
16A	PAPB 1.0 ppm	1.15	501	2.7	>4.5
B	PAPB 1.0 ppm	1.15	501	2.7	>4.5
17A	PAPB 1.0 ppm	1.47	601	1.9	>4.5
B	PAPB 1.0 ppm	1.47	601	2.1	>4.5
18A	PAPB 1.0 ppm	2.09	801	0.3	>4.5
B	PAPB 1.0 ppm	2.09	801	0.2	>4.5
19A	Polyquaternium 1 100 ppm	0.20	200	3.9	>4.5
B	Polyquaternium 1 100 ppm	0.20	200	4.2	>4.5
20A	Polyquaternium 1 100 ppm	0.53	303	2.4	3.9
B	Polyquaternium 1 100 ppm	0.53	303	2.3	4.2

TABLE I

DISINFECTING (Continued)

Example	Disinfecting Agent	Sodium Chloride % (w/v)	Measured Osmolality (mOsm/kg water)	LOG REDUCTION S. MARCESCENS	
				1 Hour	4 Hours
21A	Polyquaternium 1 100 ppm	0.85	403	0.9	3.1
B	Polyquaternium 1 100 ppm	0.85	403	0.9	3.0
22A	Polyquaternium 1 100 ppm	1.15	502	0.6	2.6
B	Polyquaternium 1 100 ppm	1.15	502	0.5	2.4
23A	Polyquaternium 1 100 ppm	1.47	601	0.4	2.1
B	Polyquaternium 1 100 ppm	1.47	601	0.4	2.1
24A	Polyquaternium 1 100 ppm	2.09	802	0.4	1.4
B	Polyquaternium 1 100 ppm	2.09	802	0.4	1.2
25A	Benzalkonium Chloride 100 ppm	0.20	200	>4.5	>4.5
B	Benzalkonium Chloride 100 ppm	0.20	200	>4.5	>4.5
26A	Benzalkonium Chloride 100 ppm	0.53	304	>4.5	>4.5
B	Benzalkonium Chloride 100 ppm	0.53	304	>4.5	>4.5
27A	Benzalkonium Chloride 100 ppm	0.85	404	>4.5	>4.5
B	Benzalkonium Chloride 100 ppm	0.85	404	>4.5	>4.5
28A	Benzalkonium Chloride 100 ppm	1.15	499	>4.5	>4.5
B	Benzalkonium Chloride 100 ppm	1.15	499	>4.5	>4.5
29A	Benzalkonium Chloride 100 ppm	1.47	598	>4.5	>4.5
B	Benzalkonium Chloride 100 ppm	1.47	598	>4.5	>4.5

TABLE I

DISINFECTING (Continued)

Example	Disinfecting Agent	Sodium Chloride % (w/v)	Measured Osmolality (mOsm/kg water)	LOG REDUCTION S. MARCESCENS	
				1 Hour	4 Hours
30A	Benzalkonium Chloride 100 ppm	2.09	801	2.7	>4.5
B	Benzalkonium Chloride 100 ppm	2.09	801	2.9	>4.5
31A	PAPB 0.5 ppm	0.20	204	0.1	0.2
B	PAPB 0.5 ppm	0.20	204	0.0	0.3
32A	PAPB 0.5 ppm	0.53	309	1.0	2.7
B	PAPB 0.5 ppm	0.53	309	1.1	2.7
33A	PAPB 0.5 ppm	0.85	402	0.1	1.5
B	PAPB 0.5 ppm	0.85	402	0.2	1.5
34A	PAPB 0.5 ppm	1.15	509	-0.1	0.2
B	PAPB 0.5 ppm	1.15	509	-0.1	0.2
35A	PAPB 0.5 ppm	1.47	607	0.0	-0.1
B	PAPB 0.5 ppm	1.47	607	0.0	-0.1
36A	PAPB 0.5 ppm	2.09	806	-0.1	0.0
B	PAPB 0.5 ppm	2.09	806	0.0	0.0

Example 37

In order to study the cleaning efficacy of the present invention, several solutions were prepared and evaluated for removal of lysozyme deposits from contact lenses.

The percent light transmission through ten new Bausch & Lomb Softlens® (polymacon) Contact Lenses was read through a uv/vis spectrophotometer at 500 and 280 nanometers (nm). An average transmission value was obtained (Tn) which was used below to calculate percent protein removal. An aqueous solution was prepared containing 0.7% NaCl, 0.22% sodium bicarbonate, 0.17% potassium chloride, 0.0005% calcium chloride and 0.15% lysozyme (3x crystallised from egg white). Five lenses were soaked in the lysozyme solution and heated for about 1 hour at about 90°C. After heating, the lenses were removed, finger rubbed and rinsed with isotonic saline solution to remove any nonbound lysozyme on the lenses. The percent light transmission was taken at 280 and 500 nm (Td).

The lenses were then submerged in 10mL of an aqueous solution containing 0.005% of subtilisin-A proteolytic enzyme (from NOVO Laboratories, Inc.) and alexidine dihydrochloride (1 ppm) at osmotic values adjusted to 300 and 600 mOsm./kg. water. The lenses remained in the solution for 1 hour at ambient temperature. The lenses were removed, rubbed and rinsed in an aqueous isotonic solution and soaked in the aqueous isotonic solution for an additional 15 minutes. The percent light transmission was taken at 280 and 500 nm (Te).

The above transmission readings were placed into the following equation at each reading (280 and 500 nm) to determine the percent of lysozyme removed:

$$\% \text{ protein lysozyme removed} = \frac{(Tn - Td) - (Tn - Te)}{(Tn - Td)}$$

The % protein removed at 500 nm (the visual range of light) and at 280 nm (specific for protein) is shown in Table II.

Examples 38-41

The procedure of Example 37 was repeated except that chlorhexidine gluconate (100 ppm), PAPB (0.5 ppm), polyquaternium 1® (100 ppm), and benzalkonium chloride (100 ppm) were substituted for alexidine dihydrochloride, respectively. The results are shown in Table II.

As can be seen from Table II, the present invention removes proteinaceous deposits from contact lenses. It should be mentioned, that the lysozyme deposition technique used herein results in much more severe protein deposition than occurs during normal wear.

It is to be understood that the subject invention is not limited by the above examples which have been provided merely to demonstrate operability and which do not purport to be wholly definitive of the scope of this invention. The scope of this invention shall include equivalent embodiments, modifications, and variations that fall within the scope of the attached claims.

TABLE II
CLEANING

PRESERVATIVE	OSMOLALITY (mOsm/kg. water)	% PROTEIN REMOVED (500 nm)	% PROTEIN REMOVED (280 nm)
37. alexidine			
1	300	93.4	49.5
2		76.8	35.3
3		75.0	33.3
4		92.5	42.4
5		57.4	35.8
Average		79.0	39.3
1	600	86.8	43.6
2		45.8	11.2
3		16.7	25.0
4		*	33.3
5		70.3	2.9
Average		54.9	23.2
38. chlorhexidine			
1	300	77.1	**
2		25.0	**
3		64.9	**
4		78.9	**
5		64.3	**
Average		62.0	**
1	600	71.0	**
2		53.8	**
3		11.1	**
4		79.3	**
5		40.0	**
Average		51.0	**

* No protein removal observed
** Chlorhexidine interferes with light transmission at 280 nm

TABLE II
CLEANING (Continued)

PRESERVATIVE	OSMOLALITY (mOsm/kg. water)	% PROTEIN REMOVED (500 nm)	% PROTEIN REMOVED (280 nm)
39. PAPB			
1	300	64.8	48.4
2		63.9	45.1
3		54.4	29.1
4		41.0	26.7
5		15.8	7.3
Average		48.0	31.3
1	600	50.0	32.9
2		68.0	27.8
3		31.2	31.1
4		66.7	66.4
5		66.0	45.9
Average		56.4	40.8
40. polyquaternium 10			
1	300	95.9	71.8
2		70.0	42.2
3		85.8	56.7
4		50.9	21.5
5		34.1	26.2
Average		67.3	43.6
1	600	87.5	47.2
2		75.0	45.2
3		89.5	27.1
4		90.2	60.7
5		88.9	30.9
Average		86.2	42.2

TABLE II
CLEANING (Continued)

PRESERVATIVE	OSMOLALITY (mOsm/kg. water)	% PROTEIN REMOVED (500 nm)	% PROTEIN REMOVED (280 nm)
41. benzalkonium chloride			
1	300	17.4	39.5
2		37.5	27.1
3		46.2	37.2
4		44.0	27.2
5		48.0	35.4
Average		38.6	33.3
1	600	50.0	44.1
2		36.4	39.8
3		59.1	21.4
4		8.4	20.6
5		59.4	29.8
Average		42.7	31.1

The claims defining the invention are as follows:-

1. A method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is poly((dimethyliminio)-2-butene-1,4-diyl chloride), α-(4-(tris(2-hydroxyethyl)ammonio)2-butenyl)-ω-(tris(2-hydroxyethyl)ammonio)-dichloride and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 400 mOsm./kg. water.

2. The method of claim 1 wherein the osmotic value is from about 200 to about 300 mOsm./kg. water.

3. The method of claim 1, wherein the aqueous system is capable of reducing the microbial burden by at least two log orders in four hours when tested against Serratia marcescens.

4. The method of claim 1, wherein the aqueous system is capable of reducing the microbial burden by at least one log order in one hour when tested against Serratia marcescens.

5. A method for simultaneously cleaning and disinfecting contact lenses comprising contacting the lenses with an aqueous system containing a disinfecting amount of an antimicrobial agent which is hexamethylene biguanide and an effective amount of a proteolytic enzyme for a time sufficient to simultaneously clean and disinfect the lenses and wherein the final osmotic value of said aqueous system is adjusted to a level which is less than about 600 mOsm./kg. water.

6. The method of claim 5, wherein the osmotic value is from about 200 to about 400 mOsm./kg. water.

7. The method of claim 5, wherein the osmotic value is from about 200 to about 300 mOsm./kg. water.

8. The method of claim 5, wherein the aqueous system is capable of reducing the microbial burden by at least two log orders in four hours when tested against Serratia marcescens.

9. The method of claim 5, wherein the aqueous system is capable of reducing the microbial burden by at least one log order in one hour when tested against Serratia marcescens.

10. A composition for simultaneously cleaning and disinfecting contact lenses said composition comprising water, a disinfecting amount of an antimicrobial agent which is polymeric quaternary ammonium salt used in ophthalmic applications, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 400 mOsm./kg. water.

11. The composition of claim 10, wherein said composition is prepared by mixing said proteolytic enzyme in a disinfecting solution containing said antimicrobial agent.

12. The composition of claim 11, wherein said antimicrobial agent is present in an amount ranging from about 0.00001 to about 0.5 percent by weight/volume.

13. The composition of claim 12, wherein said proteolytic enzyme is in tablet or powder form.

14. The composition of claim 13, wherein a tonicity adjusting agent is present.

15. The composition of claim 14, wherein said proteolytic enzyme is a subtilisin enzyme.

16. An aqueous composition for simultaneously cleaning and disinfecting contact lenses, said composition having a pH of about 6.5 to about 8.5 and comprising about 0.00003 to about 0.05 percent by weight/volume of a hexamethylene biguanide polymer, and effective amount of a proteolytic enzyme, and wherein the final osmotic value of said composition is less than about 600 mOsm./kg. water.

17. The composition of claim 10, wherein the osmotic value is from about 200 to about 300 mOsm./kg. water.

18. The composition of claim 10, wherein the composition is capable of reducing the microbial burden by at least two log orders in four hours when tested against Serratia marcescens.

19. The composition of claim 10 is wherein the composition is capable of reducing the microbial burden by at least one log order in one hour when tested against Serratia marcescens.

20. The composition of claims 10, 17, 18 or 19, wherein the antimicrobial agent is poly((dimethyliminio)-2-butene-1,4-diyl chloride), α-(4-tris(2-hydroxyethyl)ammonio)2-buten-yl)-ω-(tris(2-hydroxyethyl)ammonio)-dichloride.

21. A composition for simultaneously cleaning and disinfecting contact lenses said composition comprising water, a disinfecting amount of an antimicrobial agent which is a biguanide, and an effective amount of a proteolytic enzyme, wherein the final osmotic value of the composition is less than about 600 mOsm./kg. water.

22. The composition of claim 21, wherein the osmotic value is from about 200 to about 400 mOsm./kg. water.

23. The composition of claim 21, wherein the osmotic value is from about 200 to about 300 mOsm./kg. water.

24. The composition of claim 21, wherein the composition is capable of reducing the microbial burden by at least two log orders in four hours when tested against Serratia marcescens.

25. The composition of claims 21, wherein the composition is capable of reducing the microbial burden by at least one log order in one hour when tested against Serratia marcescens.

26. The composition of claims 21, 22, 23, 24 or 25, wherein the antimicrobial agent is a polymer of hexamethylene biguanide.

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