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(54) Title: ANTIMICROBIAL COMPOSITIONS CONTAINING ETHANOLAMINE BUFFER AND BIGUANIDE DISINFECTANT

(57) Abstract: The use of a composition of one or more aminoalcohol buffers in combination with one or more antimicrobial agents to disinfect contact lenses and preserve ophthalmic lens compositions is described. Ophthalmic lens solutions containing compositions of one or more aminoalcohol buffers in combination with one or more antimicrobial agents and methods of making and using the same are also described.

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ANTIMICROBIAL COMPOSITIONS CONTAINING ETHANOLAMINE BUFFER AND BIGUANIDE DISINFECTANT

Field of the Invention:

The present invention is directed toward the use of a combination of one or more aminoalcohol buffers and one or more antimicrobial agents for disinfection and preservation. More particularly, the present invention is directed toward the use of one or more ethanolamine buffers in combination with one or more biguanides to enhance disinfection and preservation of ophthalmic solutions and devices.

Background of the Invention:

Contact lenses in wide use today fall into two general categories, hard and soft. The hard or rigid corneal type lenses are formed from materials prepared by the polymerization of acrylic esters, such as poly(methyl methacrylate) (PMMA). The gel, hydrogel or soft type lenses are made by polymerizing such monomers as 2-hydroxyethyl methacrylate (HEMA) or, in the case of extended wear lenses, by polymerizing silicon-containing monomers or macromonomers. Both the hard and soft types of contact lenses are exposed to a broad spectrum of microbes during normal wear and become soiled relatively quickly. Contact lenses whether hard or soft therefore require routine cleaning and disinfecting. Failure to routinely clean and disinfect contact lenses properly

can lead to a variety of problems ranging from mere discomfort when being worn to serious ocular infections. Ocular infections caused by virulent microbes such as *Pseudomonas aeruginosa* can lead to loss of the infected eye(s) if left untreated or if allowed to reach an advanced stage before initiating treatment.

U.S. Patent Number 4,758,595 discloses a contact lens disinfectant and preservative containing a biguanide or a water-soluble salt thereof in combination with a buffer, preferably a borate buffer, e.g., boric acid, sodium borate, potassium tetraborate, potassium metaborate or mixtures of the same.

U.S. Patent Number 4,361,548 discloses a contact lens disinfectant and preservative containing dilute aqueous solutions of a polymer; namely, dimethyldiallylammonium chloride (DMDAAC) having molecular weights ranging from about 10,000 to 1,000,000. Amounts of DMDAAC homopolymer as low as 0.00001 percent by weight may be employed when an enhancer, such as thimerosal, sorbic acid or phenylmercuric salt is used therewith. Although lens binding and concomitant eye tissue irritation with DMDAAC were reduced, it was found in some users to be above desirable clinical levels.

Despite the availability of various commercially available contact lens disinfecting systems such as heat, hydrogen peroxide, biguanides, polymeric biguanides, quaternary ammonium polyesters, amidoamines and other chemical agents, there continues to be a need for improved disinfecting

systems. Such improved disinfecting systems include systems that are simple to use, are effective against a broad spectrum of microbes, are non-toxic and do not cause ocular irritation as the result of binding to the contact lens material. There is a particular need in the field of contact lens disinfection and ophthalmic composition preservation for safe and effective chemical agents with antimicrobial activity.

Summary of the Invention:

The present invention relates to improved antimicrobial compositions for disinfecting medical devices, such as, for example, but not limited to contact lenses. More particularly, the present invention relates to the use of an aminoalcohol buffer such as ethanolamine in ophthalmic solutions. It has been found that compositions including an ethanolamine buffer exhibit excellent disinfecting and/or preservative effect, surprisingly without the aid of a borate buffer. The antimicrobial compositions of the present invention likewise stabilize proteins already deposited on worn contact lenses to improve the wearing comfort for contact lens wearers. The antimicrobial compositions of the present invention are also useful for preservation of ophthalmic compositions such as pharmaceuticals, artificial tears and comfort drops against microbial contamination.

The subject antimicrobial compositions are effective in the manufacture of disinfecting systems that are non-toxic, simple to use and do not cause ocular irritation.

Accordingly, it is an object of the present invention to provide compositions useful as antimicrobial agents in the manufacture of ophthalmic disinfecting systems.

Another object of the present invention is to provide a method for using antimicrobial compositions in the disinfection of medical devices.

Another object of the present invention is to provide antimicrobial compositions useful in ophthalmic systems for disinfecting contact lenses.

Another object of the present invention is to provide antimicrobial compositions useful in preserving ophthalmic systems from microbial contamination.

Another object of the present invention is to provide antimicrobial compositions useful in ophthalmic systems for disinfecting contact lenses with reduced or eliminated eye irritation.

Another object of the present invention is to provide a method of making antimicrobial compositions useful in ophthalmic systems.

Still another object of the present invention is to provide a method of making antimicrobial compositions useful as disinfecting and preservative agents.

These and other objectives and advantages of the present invention, some of which are specifically described and others that are not, will become apparent from the detailed description and claims that follow.

Detailed Description of the Invention:

The compositions of the present invention can be used with all contact lenses such as conventional hard and soft lenses, as well as rigid and soft gas permeable lenses. Such suitable lenses include both hydrogel and non-hydrogel lenses, as well as silicone and fluorine-containing lenses. Of primary interest are soft lenses fabricated from a material having a proportion of hydrophilic repeat units such that the water content of the lens during use is at least 20 percent by weight. The term "soft contact lens" as used herein generally refers to those contact lenses that readily flex under small amounts of force. Typically, soft contact lenses are formulated from polymers having a certain proportion of repeat units derived from monomers such as 2-hydroxyethyl methacrylate and/or other hydrophilic monomers, typically crosslinked with a crosslinking agent. However, newer soft lenses, especially for extended wear, are being made from high-Dk silicone-containing materials.

Compositions of the present invention comprise one or more antimicrobial agents such as one or more biguanides as a disinfectant or preservative, and one or more aminoalcohols such as mono-, di- or tri-ethanolamine as a buffering agent. It is surprising that the subject antimicrobial compositions exhibit excellent disinfecting and/or preservative effect without the aid of borate, which is contrary to the teachings of U.S. Patent Number 4,758,595.

The antimicrobial compositions of the present invention are useful for disinfecting medical devices, particularly those soiled with proteinaceous matter. The antimicrobial compositions of the present invention are also useful in contact lens care solutions for disinfecting contact lenses. Compositions of the present invention are preferably in solution in sufficient concentration to destroy harmful microorganisms on the surface of a contact lens within the recommended minimum soaking time. The recommended minimum soaking time is included in the package instructions for use of the solution. The term "disinfecting solution" does not exclude the possibility that the solution may also be useful as a preserving solution, or that the disinfecting solution may be useful for other purposes such as daily cleaning, rinsing, and storage of contact lenses, depending on the particular formulation containing the subject compositions. Additionally, compositions of the present invention can be used in conjunction with other known disinfecting or preserving compounds if desired.

Solutions according to the present invention are physiologically compatible. Specifically, the solution must be "ophthalmically safe" for use with a contact lens, meaning that a contact lens treated with the solution is generally suitable and safe for direct placement on the eye without rinsing, that is, the solution is safe and comfortable for daily contact with the eye via a contact lens that has been wetted with the solution. An ophthalmically safe solution has a tonicity and pH that is compatible with the eye and comprises materials, and amounts thereof, that are non-cytotoxic according to ISO (International Standards Organization) standards and U.S. FDA (Food and Drug Administration) regulations. The solution should be sterile in that the absence of microbial contaminants in the product prior to release must be statistically demonstrated to the degree necessary for such products.

Compositions of the present invention include one or more antimicrobial agents, more preferably one or more biguanides, present in a total amount of from approximately 0.000001 to approximately 0.05 percent by weight based on the total weight of the composition. Suitable antimicrobial agents include for example but are not limited to 1,1'-hexamethylene-bis[5-(p-chlorophenyl)biguanide] (Chlorhexidine) or water soluble salts thereof, 1,1'-hexamethylene-bis[5-(2-ethylhexyl)biguanide] (Alexidine) or water soluble salts

thereof, poly(hexamethylene biguanide) or water soluble salts thereof, polyquaternium-1 and quaternary ammonium esters. Biguanides are described in U.S. Patent Numbers: 5,990,174; 4,758,595 and 3,428,576, each incorporated herein in its entirety by reference. The preferred antimicrobial agents due to their ready commercial availability are poly(aminopropyl biguanide) (PAPB), also commonly referred to as poly(hexamethylene biguanide) (PHMB), and 1,1'-hexamethylene-bis[5-(2-ethylhexyl)biguanide] (Alexidine).

Compositions of the present invention likewise include one or more aminoalcohol buffers, such as ethanolamine buffers, present in a total amount of from approximately 0.02 to approximately 3.0 percent by weight based on the total weight of the composition. Suitable aminoalcohol buffers include for example but are not limited to monoethanolamine (MEA), diethanolamine (DEA), triethanolamine (TEA), 2-amino-2-methyl-1,3-propanediol (AMPD), 2-dimethylamino-2-methyl-1-propanediol (DMAMP), 2-amino-2-ethylpropanol (AEP), 2-amino-1-butanol (AB) and 2-amino-2-methyl-1-propanol (AMP), but preferably MEA, DEA or TEA.

Compositions of the present invention may likewise include at least one surfactant that has known advantages in terms of cleaning efficacy and comfort. Suitable surfactants include for example but are not limited to polyethers based upon poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene

oxide), i.e., (PEO-PPO-PEO), or poly(propylene oxide)-poly(ethylene oxide)-poly(propylene oxide), i.e., (PPO-PEO-PPO),or a combination thereof. PEO-PPO-PEO and PPO-PEO-PPO are commercially available under the trade names Pluronics™, R-Pluronics™, Tetronics™ and R-Tetronics™ (BASF Wyandotte Corp., Wyandotte, Michigan) and are further described in U.S. Patent Number 4,820,352 incorporated herein in its entirety by reference. Suitable surfactants for use in the present composition should be soluble in the lens care solution, not become turbid, and should be non-irritating to eye tissues.

Likewise, it may be desirable to include one or more water-soluble viscosity agents in the subject composition. Because of the demulcent effect of viscosity agents, the same have a tendency to enhance the lens wearer's comfort by means of a film on the lens surface cushioning impact against the eye. Suitable viscosity agents include for example but are not limited to cellulose polymers like hydroxyethyl or hydroxypropyl cellulose, carboxymethyl cellulose, povidone, polyvinyl alcohol and the like. Viscosity agents may be employed in amounts ranging from about 0.01 to about 4.0 weight percent or less.

Compositions of the present invention when in solution may likewise include one or more buffers, or a buffering system in addition to the aminoalcohol buffer, to adjust the final pH of the solution. Suitable buffers include for example but are not limited to phosphate buffers, borate buffers,

tris(hydroxymethyl)aminomethane (Tris) buffers, bis(2-hydroxyethyl)-imino-tris(hydroxymethyl)methane (bis-Tris) buffers, sodium bicarbonate, and combinations thereof. A suitable buffering system for example may include at least one phosphate buffer and at least one borate buffer, which buffering system has a buffering capacity of 0.01 to 0.5 mM, preferably 0.03 to 0.45, of 0.01 N of HCl and 0.01 to 0.3, preferably 0.025 to 0.25, of 0.01 N of NaOH to change the pH one unit. Buffering capacity is measured by a solution of the buffers only. The pH of lens care solutions of the present invention is preferably maintained within the range of 5.0 to 8.0, more preferably about 6.0 to 8.0, most preferably about 6.5 to 7.8.

Compositions of the present invention may likewise include one or more tonicity agents to approximate the osmotic pressure of normal lachrymal fluids which is equivalent to a 0.9 percent solution of sodium chloride or 2.5 percent glycerin solution. Examples of suitable tonicity agents include but are not limited to sodium and potassium chloride, dextrose, mannose, glycerin, calcium and magnesium chloride. These agents are typically used individually in amounts ranging from about 0.01 to 2.5 percent w/v and preferably, from about 0.2 to about 1.5 percent w/v. Preferably, the tonicity agent is employed in an amount to provide a final osmotic value of 200 to 450 mOsm/kg and more preferably between about 220 to about 350 mOsm/kg, and most preferably between about 220 to about 320 mOsm/kg.

Compositions of the present invention may likewise include one or more sequestering agents to bind metal ions, which in the case of ophthalmic solutions, might otherwise react with protein deposits and collect on contact lenses. Suitable sequestering agents include for example but are not limited to ethylenediaminetetraacetic acid (EDTA) and its salts. Sequestering agents are preferably used in amounts ranging from about 0.01 to about 0.2 weight percent.

The biguanide-based compositions of the present invention are described in still greater detail in the examples that follow.

Example 1 - Preparation and Testing of Biguanide-Based Compositions With and Without Triethanolamine (TEA):

A test was conducted to study the microbiocidal efficacy of solutions prepared according to the present invention with TEA as compared to the same solutions prepared without TEA . The test solutions are identified below in Table 1. The antimicrobial efficacy of each of the solutions for the chemical disinfection of contact lenses was evaluated. Microbial challenge inoculums were prepared using *Pseudomonas aeruginosa* (ATCC 9027), *Staphylococcus aureus* (ATCC 6538), *Serratia marcescens* (ATCC 13880), *Candida albicans* (ATCC 10231) and *Fusarium solani* (ATCC 36031). The test

organisms were cultured on appropriate agar and the cultures were harvested using sterile Dulbecco's Phosphate Buffered Saline plus 0.05 percent weight/volume polysorbate 80 (DPBST) or a suitable diluent and transferred to a suitable vessel. Spore suspensions were filtered through sterile glass wool to remove hyphal fragments. *Serratia marcescens,* as appropriate, was filtered through a 1.2 mu filter to clarify the suspension. After harvesting, the suspension was centrifuged at no more than 5000 x g for a maximum of 30 minutes at 20 to 25 degrees Celsius. The supernatent was poured off and resuspended in DPBST or other suitable diluent. The suspension was centrifuged a second time, and resuspended in DPBST or other suitable diluent. All challenge bacterial and fungal cell suspensions were adjusted with DPBST or other suitable diluent to 1 x 10^7 to 1 x 10^8 cfu/mL. The appropriate cell concentration may be estimated by measuring the turbidity of the suspension, for example, using a spectrophotometer at a preselected wavelength, for example 490 nm. One tube was prepared containing a minimum of 10 mL of test solution per challenge organism. Each tube of the solution to be tested was inoculated with a suspension of the test organism sufficient to provide a final count of 1 x 10^5 to 1 x 10^6 cfu/mL, the volume of the inoculum not exceeding 1 percent of the sample volume. Dispersion of the inoculum was ensured by vortexing the sample for at

least 15 seconds. The inoculated product was stored at 10 to 25 degrees Celsius. Aliquots in the amount of 1.0 mL were taken of the inoculated product for determination of viable counts after certain time periods of disinfection. The time points for the bacteria were, for example, 1, 2, 3 and 4 hours when the proposed regimen soaking time was four hours. Yeast and mold were tested at an additional timepoint of 16 hours (4 times the regimen time). The suspension was mixed well by vortexing vigorously for at least 5 seconds. The 1.0 mL aliquots removed at the specified time intervals were subjected to a suitable series of decimal dilutions in validated neutralizing media. The suspensions were mixed vigorously and incubated for a suitable period of time to allow for neutralization of the microbial agent. The viable count of organisms was determined in appropriate dilutions by preparation of triplicate plates of trypticase soy agar (TSA) for bacteria and Sabouraud dextrose agar (SDA) for mold and yeast. The bacterial recovery plates were incubated at 30 to 35 degrees Celsius for two to four days. The yeast recovery plates were incubated at 20 to 30 degrees Celsius for two to four days. The mold recovery plates were incubated at 20 to 25 degrees Celsius for three to seven days. The average number of colony forming units was determined on countable plates. Countable plates refer to 30 to 300 cfu/plates for bacteria and yeast, and 8 to 80 cfu/plates for mold

except when colonies are observed only for the 10^0 or 10^{-1} dilution plates. The microbial reduction was then calculated at the specified time points and recorded as set forth below in Table 2. In order to demonstrate the suitability of the medium used for growth of test organisms and to provide an estimation of the initial inoculum concentration, inoculum controls were made by dispersing an identical aliquot of the inoculum into a suitable diluent, for example DPBST, using the same volume of diluent used to suspend the organism listed above. Following inoculation in a validated neutralizing broth and incubation for an appropriate period of time, the inoculum control must be between 1.0×10^5 to 1.0×10^6 cfu/mL. The solutions were evaluated based on the performance requirement referred to as the "Stand-Alone Procedure for Disinfecting Products" (Stand-Alone Test) and is based on the Disinfection Efficacy Testing for contact lens care products under the Premarket Notification (510(k)) Guidance Document for Contact Lens Care Products dated May 1, 1997, prepared by the U.S. Food and Drug Administration, Division of Ophthalmic Devices. This performance requirement does not contain a rub procedure. This performance requirement is comparable to current ISO standards for disinfection of contact lenses (revised 1995). The Stand-Alone Test challenges a disinfecting product with a standard inoculum of a representative range of microorganisms and establishes the extent

of viability loss at predetermined time intervals comparable with those during which the product may be used. The primary criteria for a given disinfection period, corresponding to a potential minimum recommended disinfection period, is that the number of bacteria recovered per mL must be reduced by a mean value of not less than 3.0 logs within the given disinfection period. The number of mold and yeast recovered per ml must be reduced by a mean value of not less than 1.0 log within the minimum recommended disinfection time with no increase at four times the minimum recommended disinfection time.

TABLE 1

Test Solutions With and Without Triethanolamine

Ingredients (w/w%)	A	B	C	D	E	F
Triethanolamine HCL	0.7	0.7	0.7	0	0.7	0.7
Pluronic F127	1	0	1	1	1	1
Pluronic P123	0.2	0	0.2	0.2	0.2	0.2
EDTA	0.025	0.025	0.025	0.025	0.025	0.025
Glycerin	0.6	0.6	0	0.6	0.6	0.6
NaCl	0.132	0.132	0.327	0.358	0.202	0.132
AMPD	0.2107	0.2107	0.2107	0.2107	0	0
PHMB (ppm)	1	1	1	1	1	1
pH	7.1	7.12	7.09	7.13	7.11	7.07
Osmolality (mOsm/Kg)	226	216	219	231	222	238

TABLE 2

Log Reduction After 4 Hour Exposure to Test Solutions

Agent	A	B	C	D	E	F
S. aureus	4.2	3.5	>4.5	>4.5	>4.5	4.5
P. aeruginosa	>4.5	4.0	>4.5	>4.6	>4.5	>4.5
S. marcescens	>4.6	3.4	4.3	1.4	4.4	>4.6
C. albicans	2.2	2.1	1.1	>4.5	1.7	2.1
F. solani	4.1	3.3	3.2	2.7	3.7	>4.3

Denaturing of tear proteins on soft contact lenses is a common problem. Once proteins denature on the lens, they are difficult to remove, reduce lens clarity, may cause allergic reactions for the wearer, and can act as attachment sites for infectious microorganisms. Lysozyme, especially is a potentially troublesome tear protein insofar as high water, about 55 percent water, contact lenses are concerned because lysozyme is a positively charged protein that is readily attracted to the negatively charged lens surface. An in vitro assay was developed to determine the ability of a test solution to retard lysozyme

denaturing. In this assay, a 1% stock solution of lysozyme in isotonic borate buffered saline (pH = 7.0) is freshly prepared, and an aliquot of this stock solution is mixed with an equal aliquot of a test solution. The resulting mixture is heated at 75 degrees Celsius for 15 minutes in a hot water bath. After the mixture is removed from the heating bath, it is allowed to cool to room temperature before it is visually inspected for signs of protein denaturing as evidenced by the formation of a white precipitate. The following scale was used to measure the extent of protein stabilization.

+++++	Clear solution
++++	Slightly hazy solution
+++	Hazy solution
++	Slight precipitation
+	Significant precipitation

The results obtained for solutions of Table 1 above are set forth below in Table 3.

TABLE 3

Protein Stabilization

	A	B	C	D	E	F
Protein Stabilization	+++++	++++	+++++	+++	+++++	+++++

Example 2 - Preparation and Testing of Biguanide-Based Compositions With Mono- vs. Di- vs. Tri- Ethanolamine Buffers:

A test was conducted to study the microbiocidal efficacy of solutions prepared according to the present invention with mono-, di- or tri-ethanolamine. The test solutions are identified below in Table 4. The antimicrobial efficacy of each of the solutions for the chemical disinfection of contact lenses was evaluated. Microbial challenge inoculums were prepared as described above in Example 1. The microbial reduction was then calculated at the specified time points and recorded as set forth below in Table 5. In order to demonstrate the suitability of the medium used for growth of test organisms and to provide an estimation of the initial inoculum concentration, inoculum controls were made as described above in Example 1.

TABLE 4

Test Solutions With Mono- vs. Di- vs. Tri- Ethanolamine

Ingredients (w/w%)	G	H	I
Triethanolamine 99%	1.356	0	0
Diethanolamine 99.9%	0	0.947	0
Monoethanolamine 99.9%	0	0	0.55
Pluronic F127	1	1	1
Pluronic P123	0.2	0.2	0.2
EDTA	0.025	0.025	0.025
NaCl	0.159	0.069	0.126
1 N HCL	Adjust to pH 7.1	Adjust to pH 7.1	Adjust to pH 7.1
PHMB (ppm)	1	1	1
pH	7.14	7.16	7.07
Osmolality (mOsm/Kg)	220	218	217

TABLE 5

Log Reduction After 4 Hour Exposure to Test Solutions

Agent	G	H	I
S. aureus	>4.7	>4.7	>4.7
P. aeruginosa	4.5	>4.5	>4.5
S. marcescens	4.5	>4.5	3.9
C. albicans	1.5	1.5	1.2
F. solani	3.4	4.2	>4.4

An in vitro assay was developed as described above in Example 1 to determine the ability of a test solution to retard lysozyme denaturing. The same scale was used to measure the extent of protein stabilization as that used in Example 1. The results obtained for the solutions of Table 4 above, are set forth below in Table 6.

TABLE 6

Protein Stabilization

	G	H	I
Protein Stabilization	+++++	++++	+

EXAMPLE 3 - Preparation and Testing of Biguanide-Based Compositions With Triethanolamine Buffer and Aminoalcohol Buffer Combination:

A test was conducted to study the microbiocidal efficacy of solutions prepared according to the present invention with TEA buffer in combination with another aminoalcohol buffer. The test solutions are identified below in Table 7. The antimicrobial efficacy of each of the solutions for the chemical disinfection of contact lenses was evaluated. Microbial challenge inoculums were prepared as described above in Example 1. The microbial reduction was then calculated at the specified time points and recorded as set forth below in Table 8. In order to demonstrate the suitability of the medium used for growth of test organisms and to provide an estimation of the initial inoculum concentration, inoculum controls were made as described above in Example 1.

TABLE 7

Test Solutions With Triethanolamine and Aminoalcohol Combination

Ingredients (w/w%)	J	K	L	M
Triethanolamine HCL	0.7	0.7	0.7	0.7
Pluronic F127	1	1	1	1
Pluronic P123	0.2	0.2	0.2	0.2
EDTA	0.025	0.025	0.025	0.025
Glycerin	0.6	0.6	0.6	0.6
NaCl	0.132	0.132	0.132	0.159
PHMB (ppm)	1	1	1	1
Tris	0.2428	0	0	0
AMPD	0	0.2107	0	0
AMP	0	0	0.1787	0
Bis-Tris	0	0	0	0.4193
pH	7.1	7.11	7.11	7.11
Osmolality (mOsmo/Kg)	218	221	222	223

TABLE 8

Log Reduction After 4 Hour Exposure to Test Solutions

Agent	J	K	L	M
S. aureus	>4.5	>4.5	>4.5	>4.5
P. aeruginosa	3.1	>4.6	>4.6	>4.6
S. marcescens	3.6	4.4	>4.6	4.4
C. albicans	1.7	3.2	3.9	3.4
F. solani	3.7	>4.4	>4.4	3.7

An in vitro assay was developed as described above in Example 1 to determine the ability of a test solution to retard lysozyme denaturing. The same scale was used to measure the extent of protein stabilization as that used in Example 1 above. The results obtained for solutions of Table 7 above are set forth below in Table 9.

TABLE 9

Protein Stabilization

	J	K	L	M
Protein Stabilization	+++++	+++++	+++++	+++++

EXAMPLE 4 - Preparation and Testing of Alexidine-Based Compositions With Borate Buffer, Surfactant and Polyquaternium-10 (Polymer JR) Combination:

A test was conducted to study the microbiocidal efficacy of alexidine-based solutions with borate, surfactant and polyquaternium-10 (Polymer JR). The test solutions are identified below in Table 10. The antimicrobial efficacy of each of the solutions for the chemical disinfection of contact lenses was evaluated. Microbial challenge inoculums were prepared as described above in Example 1. The microbial reduction was then calculated at the specified time points and recorded as set forth below in Table 11. In order to demonstrate the suitability of the medium used for growth of test organisms and to provide an estimation of the initial inoculum concentration, inoculum controls were made as described above in Example 1.

TABLE 10

Test Solutions With Borate, Surfactant And Polymer JR Combination

Ingredients (w/w%)	O	P	Q	R	S
TEA HCl 99.5%	0.937	0.937	0.937	0.937	0.937
TEA 98%	0.149	0.149	0.149	0.149	0.149
Sodium Borate	0	0	0.1	0.1	0.1
Boric Acid	0	0	0.66	0.66	0.66
Pluronic F127	1	1	1	2	2
Pluronic P123	0.2	0.2	0.2	0	0
Tetronic 1107	0	0	0	1	1
EDTA	0.025	0.025	0.025	0.025	0.025
Glycerin	0.6	0.6	0	0	0
NaCl	0.114	0.114	0	0	0
Polymer JR 30 M	0	0	0	0	0.02
PHMB (ppm)	1	0	0	0	0
Alexidine (ppm)	0	4.5	4	4	4
pH	7.17	7.14	6.69	6.72	6.71
Osmolality (mOsm/Kg)	217	220	223	229	231

TABLE 11

Log Reduction After 4 Hour Exposure to Test Solutions

Agent	O	P	Q	R	S
S. aureus	>4.6	>4.7	>4.7	>4.7	>4.7
P. aeruginosa	>4.6	>4.6	>4.6	>4.6	>4.6
S. marcescens	>4.5	>4.7	>4.7	>4.7	>4.7
C. albicans	3.0	4.7	>4.7	>4.7	>4.7
F. solani	>4.3	>4.2	>4.2	>4.2	>4.2

A sodium fluorescein permeability assay was conducted on Solution O of Table 10. To do this, a 0.5 mL cell suspension containing 2 x 10^5 cells was seeded in Millicell™ HA 13 mm inserts (Millipore, Bedford, Massachusetts). The inserts were transferred into 24 well plates containing 0.5 mL of minimum essential medium (MEM) (BioWittaker, Walkersville, Maryland) per well. The plates were then incubated at 37 degrees Celsius with 5 percent carbon dioxide for six days. Fresh media was added to the wells on days 2 through 6. On day 6 the inserts were used for the sodium fluorescein permeability assay.

Each insert was gently rinsed three times with 1 mL of Hank's balanced salt solution (HBSS) using a 10 mL syringe, without a needle. An amount of 0.5 mL of test solution was added to separate inserts that had been placed in a fresh 24 well plate. Triplicate inserts were used for each test solution. The inserts were incubated in a 100 percent humidified chamber at 37 degrees Celsius for twenty minutes. Each series of triplicate samples was handled sequentially to allow exact timing of the treatment and subsequent steps. After incubation, each insert was individually rinsed five times with 1 mL HBSS using a 10 mL syringe without a needle, and then placed in a fresh 24 well plate containing 0.5 mL HBSS in each well. To each insert was added 0.5 mL of sodium fluorescein (3 mg/100 mL in HBSS). The inserts were incubated at room temperature for twenty minutes, removed from the wells, and the amount of sodium fluorescein was measured using a fluorometer at 540 nm excitation and 590 nm emission. The results obtained from solutions of Table 10 are recorded below in Table 12. Triplicate negative controls (HBSS solution) and positive controls consisting of sodium dodecyl sulfate (SDS) in water were included during these evaluations.

TABLE 12

Formulation	Fluorescence Units
HBSS (Negative Control)	55 ± 3
SDS (Positive Control)	1457 ± 102
Solution O	41 ± 2

Ethanolamine and biguanide compositions of the present invention are useful as antimicrobial agents in contact lens care solutions for disinfecting contact lenses. A disinfecting amount of antimicrobial agent is an amount that will at least partially reduce the microorganism population in the formulations employed. Preferably, a disinfecting amount is that which will reduce the microbial burden of representative bacteria 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 according to its 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 percent weight/volume (w/v), and more preferably, from about 0.00003 to about 0.5 percent w/v.

As stated above, contact lenses are disinfected by contacting the lens with a solution of the present composition. Although this may be accomplished by simply soaking a lens in the subject solution, greater cleaning can be achieved if a few dorps of the solution are initially placed on each side of the lens, and rubbing the lens for a period of time, for example, approximately 20 seconds. The lens can then be subsequently immersed within several milliliters of the subject solution. Preferably, the lens is permitted to soak in the solution for at least four hours. The lenses are then removed from the solution, rinsed with the same or a different solution, for example a preserved isotonic saline solution and then replaced on the eye.

Solutions containing one or more compositions of the present invention may be formulated into specific contact lens care products for use as customary in the field of ophthalmology. Such products include but are not limited to wetting solutions, soaking solutions, cleaning and conditioning solutions, as well as multipurpose type lens care solutions and in-eye cleaning and conditioning solutions.

While the invention has been described in conjunction with specific examples thereof, this is illustrative only. Accordingly, many alternatives, modifications, and variations will be apparent to those skilled in the art in the light of the foregoing description and it is, therefore, intended to embrace all such alternatives, modifications, and variations as to fall within the spirit and scope of the appended claims.

We claim:

1. Compositions comprising:

one or more aminoalcohol buffers and one or more antimicrobial agents.

2. Compositions comprising:

one or more ethanolamine buffers and one or more antimicrobial agents.

3. Compositions comprising:

triethanolamine buffer and poly(hexamethylene biguanide) or polyquaternium-1.

4. A method of producing a composition of claim 1 comprising:

combining one or more aminoalcohol buffers with one or more antimicrobial agents.

5. The method of claim 4 wherein said one or more aminoalcohol buffers include one or more ethanolamine buffers.

6. A solution comprising:

one or more aminoalcohol buffers and one or more antimicrobial agents in solution.

7. The solution of claim 6 wherein said solution includes one or more buffers or a buffering system.

8. The solution of claim 6 wherein said solution includes one or more tonicity agents.

9. The solution of claim 6 wherein said solution includes one or more surfactants.

10. The solution of claim 6 wherein said solution includes one or more viscosity agents.

11. A method of using the solution of claim 6 comprising:

contacting a surface of a contact lens with said solution for a period of time suitable to eliminate a microbial burden on said contact lens.

12. A method of producing the solution of claim 6 comprising:
adding an effective disinfecting amount of said one or more antimicrobial agents and said one or more aminoalcohol buffers to a solution.

13. A method of producing the solution of claim 6 comprising:
adding an effective preservative amount of said one or more antimicrobial agents and said one or more aminoalcohol buffers to a solution.

14. A method of using the solution of claim 6 comprising:
contacting a surface of a medical device with said solution for a period of time suitable to eliminate a microbial burden on said medical device.