(12) STANDARD PATENT (11) Application No. **AU 2002225950 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
L-histidine in ophthalmic solutions

(51) International Patent Classification(s)
A61K 31/74 (2006.01) ***A61K 47/18*** (2006.01)
A61K 9/00 (2006.01) ***A61K 47/32*** (2006.01)
A61K 31/415 (2006.01) ***A61L 12/08*** (2006.01)
A61K 31/4172 (2006.01) ***A61L 12/10*** (2006.01)
A61K 31/4415 (2006.01) ***A61L 12/12*** (2006.01)
A61K 33/40 (2006.01) ***A61L 12/14*** (2006.01)

(21) Application No: **2002225950** (22) Date of Filing: **2001.11.08**

(87) WIPO No: **WO02/38077**

(30) Priority Data

(31) Number	(32) Date	(33) Country
60/246,707	**2000.11.08**	**US**
60/246,709	**2000.11.08**	**US**
60/246,708	**2000.11.08**	**US**
60/246,689	**2000.11.08**	**US**

(43) Publication Date: **2002.05.21**
(43) Publication Journal Date: **2002.07.25**
(44) Accepted Journal Date: **2006.08.10**

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 May 2002 (16.05.2002)

PCT

(10) International Publication Number
WO 02/038077 A3

(51) International Patent Classification[7]: A61K 31/74

(21) International Application Number: PCT/US01/46762

(22) International Filing Date:
8 November 2001 (08.11.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/246,689	8 November 2000 (08.11.2000)	US
60/246,707	8 November 2000 (08.11.2000)	US
60/246,708	8 November 2000 (08.11.2000)	US
60/246,709	8 November 2000 (08.11.2000)	US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
25 July 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/038077 A3

(54) Title: L-HISTIDINE IN OPHTHALMIC SOLUTIONS

(57) Abstract: The invention relates to an aqueous ophthalmic solution comprising 0.01 to about 1.0 percent by weight L-histidine; 0.01 to 0.0001 percent by weight hydrogen peroxide; 0.1 to 500 parts per million of a cationic polymeric preservative that provides superior preservative efficacy especially as against fungal microbes. These solutions may be employed in various ways including cleaning contact lenses, rinsing lenses while in the eye, storing lenses and in delivering active pharmaceutical agents to the eye.

L-HISTIDINE IN OPHTHALMIC SOLUTIONS

Cross-Reference to Related Applications

This application claims the benefit of U. S. Provisional Patent Application Serial Nos. 60/246,689, filed November 8,2000,60/246,707, filed November 8,2000,60/246,708, filed November 8,2000, and 60/246,709, filed November 8,2000.

Field of the Invention

The present invention relates to the field of ophthalmic solutions used to treat eyes, store contact lenses, or condition medical devices used in the eye. Such solutions are well known and widely employed with numerous products available commercially. There are several types of solutions within the field depending upon specific use. For instance, there are specific solutions for disinfecting contact lenses, solutions for cleaning contact lenses, solutions for treating the surface of contact lenses, solutions for rinsing lenses, solutions for wetting eyes, etc.

While each of these lenses are formulated specifically for their intended application, each solution is formulated or handled so that it will remain free of sources of infection to the eye. Numerous approaches to this problem have been employed, from methods that call for sterilization of the solution and packaging of the solution in a container that will not allow contamination. Use of specific preservative agents employed in concentrations sufficient to prevent microbial increase have been employed. Oxidative agents have been used as well as methods of

irradiation. In the cases where chemical agents have been employed, there has been a tendency to employ one preservative agent in the formulation. It has been found that use of two or more specific agents in combination surprisingly provide greater efficacy in preserving solutions than state of the art single preservative systems and in particular the use of the combination of a cationic polymeric preservative, hydrogen peroxide and L-histidine provide increased preservative efficacy against fungal contamination.

This surprising effect is achievable with the further use of certain, but not all, contact lens solution agents. In particular, certain tonicity agents when employed decrease the preservative efficacy of the invention and should not be employed.

The discussion of the background to the invention herein is included to explain the context of the invention. This is not to be taken as an admission that any of the material referred to was published, known, or part of the common general knowledge as at the priority date of any of the claims.

Summary of the Invention

The invention relates to an aqueous ophthalmic solution comprising 0.01 to about 1.0 percent by weight L-histidine; 0.0001 to 0.01 percent by weight hydrogen peroxide; 0.1 to 500 parts per million of a cationic polymeric preservative that provides superior preservative efficacy especially as against fungal microbes. These solutions may be employed in various ways including cleaning contact lenses, rinsing lenses while in the eye, storing lenses and in delivering active pharmaceutical agents to the eye. It should be noted that

the term "comprises" and variations thereof do not have a limiting meaning where these terms appear in the description and the claims.

The invention may also further comprise a surface-active agent chosen from those known in the art, but in particular might be a hydroxy-ethoxylated castor oil.

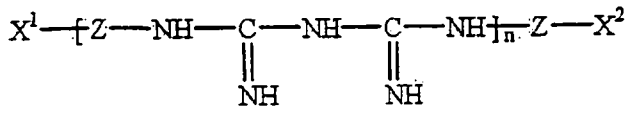
The solution can be used to deliver a pharmaceutical agent to the eye by providing the agent to the solution and then contacting the eye with the resultant solution. Or the solution can be used to clean, treat or store contact lenses by contacting the solution with the contact lens.

Detailed Description

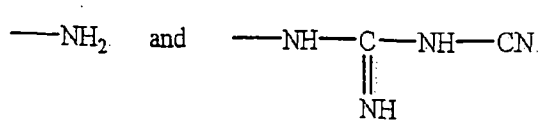
The invention relates to an aqueous ophthalmic solution comprising 0.01 to about 1.0 percent by weight L-histidine; 0.01 to 0.0001 percent by weight hydrogen peroxide; and 0.1 to 500 parts per parts by weight of a cationic polymeric preservative that provides superior preservative efficacy, especially as against fungii. These solutions may be employed in various ways including cleaning contact lenses, rinsing lenses while in the eye, storing lenses and in delivering active pharmaceutical agents to the eye. The invention may also further comprise a surface-active agent chosen from those known in the art, but in particular might be a hydroxy-ethoxylated castor oil.

Histidine is a basic amino acid well known in the chemical arts and available from numerous commercial sources. Histidine is known to be used in ophthalmic ointments and the like in very concentrated forms.

The cationic polymeric preservatives: The cationic polymeric preservative includes polymeric biguanides such as polymeric hexamethylene biguanides (PHMB), and combinations thereof. Such cationic polymeric biguanides, and water-soluble salts thereof, having the following formula :

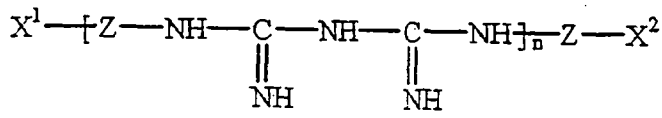


wherein Z is an organic divalent bridging group which may be the same or different throughout the polymer, n is on average at least 3, preferably on average 5 to 20, and X^1 and x^2 are



One preferred group of water-soluble polymeric biguanides will have number average molecular weights of at least 1,000 and more preferably will have number average molecular weights from 1,000 to 50,000. Suitable water-soluble salts of the free bases include, but are not limited to hydrochloride, borate, acetate, gluconate, sulfonate, tartrate and citrate salts.

Most preferred are the polymeric hexamethylene biguanides, commercially available, for example, as the hydrochloride salt from Zeneca (Wilmington, Del.) under the trademark CosmocilTM CQ. Such polymers and water-soluble salts are referred to as polyhexamethylene (PHMB) or polyaminoptopyl biguanide (PAPB). The term polyhexamethylene biguanide, as used herein, is meant to encompass one or more biguanides have the following formula:



wherein Z, X^1 and X^2 are as defined above and n is from 1 to 500.

Depending on the manner in which the biguanides are prepared, the predominant compound falling within the above formula may have different X^1 and X^2 groups or the same groups, with lesser amounts of other compounds within the formula. Such compounds are known and are disclosed in U. S. Pat. No. 4, 758, 595 and British Patent 1,432,345, which patents are hereby incorporated. Preferably, the water-soluble salts are compounds where n has an average value of 2 to 15, most preferably 3 to 12.

In another embodiment, a polymeric biguanide is used in combination with a bis(biguanide) compound. Polymeric biguanides, in combination with bisbiguanides such as alexidine, are effective in concentrations as low as 0.00001 weight percent (0.1 ppm). It has also been found that the bactericidal activity of the solutions may be enhanced or the spectrum of activity broadened through the use of a combination of such polymeric biguanides with alexidine or similar biguanides.

An optional non-biguanide disinfectant/gennicide can be employed as a solution preservative, but it may also function to potentiate, complement or broaden the spectrum of microbiocidal activity of another germicide. This includes microbiocidally effective amounts of germicides which are compatible with and do not precipitate in the solution, in concentrations

ranging from about 0.00001 to about 0.5 weight percent, and more preferably, from about 0.0001 to about 0.1 weight percent. Suitable complementary germicidal agents include, but are not limited to, quaternary ammonium compounds or polymers, thimerosal or other phenylmercuric salts, sorbic acid, alkyl triethanolamines, and mixtures thereof. Representative examples of the quaternary ammonium compounds are compositions comprised of benzalkonium halides or, for example, balanced mixtures of n-alkyl dimethyl benzyl ammonium chlorides. Other examples include polymeric quaternary ammonium salts used in ophthalmic applications such as poly [(dimethyliminio)-2-butene-1, 4-diyl chloride], [4-tris (2-hydroxyethyl) ammonio]-2-butenyl-w-[tris(2-hydroxyethyl) ammonio] dichloride (chemical registry number 75345-27-6) generally available as polyquaternium 1 (r) from ONYX Corporation.

Peroxide sources may also be included in the formulations of the present invention and are exemplified by hydrogen peroxide, and such compounds, which provide an effective resultant amount of hydrogen peroxide, such as sodium perborate decahydrate, sodium peroxide, urea peroxide and peracetic acid, an organic peroxy compound.

The pH of the present solutions should be 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. Suitable buffers may be added, such as boric acid, sodium borate, potassium citrate, citric acid, sodium bicarbonate, bis-tris propane, TRIS, and various mixed phosphate buffers (including combinations of Na_2HPO_4, NaH_2PO_4 and KH_2PO_4) and mixtures thereof. Borate buffers are preferred, particularly for enhancing the efficacy of PAPB. Generally, buffers will be used in amounts ranging from about 0.05 to 2.5 percent by weight, and preferably, from 0.1 to 1.5 percent.

The solutions of the present invention may further contain other additives including but not limited to buffers, tonicity agents, demulcents, wetting agents, preservatives, sequestering agents (chelating agents), surface active agents, and enzymes.

Ophthalmologically acceptable chelating agents useful in the present invention include amino carboxylic acid compounds or water-soluble salts thereof, including ethylenediaminetetraacetic acid, nitrilotriacetic acid, diethylenetriamine pentaacetic acid, hydroxyethylethylenediaminetriacetic acid, 1,2-diaminocyclohexanetetraacetic acid, ethylene glycol bis (beta-aminoethyl ether) in N, N, N', N' tetraacetic acid (EGTA), aminodiacetic acid and hydroxyethylamino diacetic acid. These acids can be used in the form of their water soluble salts, particularly their alkali metal salts. Especially preferred chelating agents are the di-, tn- and tetra-sodium salts of ethylenediaminetetraacetic acid (EDTA), most preferably disodium EDTA (Disodium Edetate).

Other chelating agents such as citrates and polyphosphates can also be used in the present invention. The citrates which can be used in the present invention include citric acid and its mono-, di-, and tri-alkaline metal salts. The polyphosphates which can be used include pyrophosphates, triphosphates, tetraphosphates, trimetaphosphates, tetrametaphosphates, as well as more highly condensed phosphates in the form of the neutral or acidic alkali metal salts such as the sodium and potassium salts as well as the ammonium salt.

The solutions of the invention are compatible with both rigid gas permeable and hydrophilic contact lenses and other ophthalmic devices and instruments during storage, cleaning, wetting, soaking, rinsing and disinfection.

A typical aqueous solution of the present invention may contain additional ingredients which would not affect the basic and novel characteristics of the active ingredients described earlier, such as tonicity agents, surfactants and viscosity inducing agents, which may aid in either the lens cleaning or in providing lubrication to the eye. Suitable tonicity agents include sodium chloride, potassium chloride, glycerol or mixtures thereof The tonicity of the solution is typically adjusted to approximately 240-310 milliosmoles per kilogram solution (mOsm/kg) to render the solution compatible with ocular tissue and with hydrophilic contact lenses. In one embodiment, the solution contains 0.01 to 0.35 weight percent sodium chloride.

The solutions employed in the present invention may also include surfactants such as a polyoxyethylene-polyoxypropylene nonionic surfactant which, for example, can be selected from the group of commercially available surfactants having the name poloxamine or poloxamer, as adopted by The CTFA International Cosmetic Ingredient Dictionary. The poloxamine surfactants consist of a poly(oxypropylene)-poly(oxyethylene) adduct of ethylene diamine having a molecular weight from about 7,500 to about 27,000 wherein at least 40 weight percent of said adduct is poly(oxyethylene), has been found to be particularly advantageous for use in conditioning contact lenses when used in amounts from about 0.01 to about 15 weight percent. Such surfactants are available from BASF Wyandotte Corp., Wyandotte, Mich., under the registered trademark "Tetronic". The poloxamers are an analogous series of surfactants and are polyoxyethylene, polyoxypropylene block polymers available from BASF Wyandotte Corp., Parsippany, N.J. 07054 under the trademark "Pluronic".

The HLB of a surfactant is known to be a factor in determining the emulsification characteristics of a nonionic surfactant. In general, surfactants with lower HLB values are more lipophilic, while surfactants with higher HLB

values are more hydrophilic. The HLB values of various poloxamines and poloxamers are provided by BASF Wyandotte Corp., Wyandotte, Mich. Preferably, the HLB of the surfactant in the present invention is at least 18, more preferably 18 to 32, based on values reported by BASF.

Additional compatible surfactants that are known to be useful in contact wetting or rewetting solutions can be used in the solutions of this invention. The surfactant should be soluble in the lens care solution and non-irritating to eye tissues. Satisfactory non-ionic surfactants include polyethylene glycol esters of fatty acids, e.g. coconut, polysorbate, polyoxyethylene or polyoxypropylene ethers of higher alkanes ($C_{12} - C_{18}$). Examples of the preferred class include polysorbate 20 (available from ICI Americas Inc., Wilmington, Del. 19897 under the trademark Tween ® 20), polyoxyethylene (23) lauryl ether (Brij ® 35), polyoxyethylene (40) stearate (Myrj ® 52), polyoxye thylene (25) propylene glycol stearate (Atlas ® G 2612). Brij ® 35, Myrj ® 52 and Atlas ® G 2612 are trademarks of, and are commercially available from, ICI Americas Inc., Wilmington, Del. 19897.

Various other surfactants suitable for in the invention can be readily ascertained, in view of the foregoing description, from McCutcheon's Detergents and Emulsifiers, North American Edition, McCutcheon Division, MC Publishing Co., Glen Rock, N.J. 07452 and the CTFA International Cosmetic Ingredient Handbook, Published by The Cosmetic, Toiletry, and Fragrance Association, Washington, D.C. however, the preferred surfactants are commercially available surfactants sold under the trademark Cremaphor RH40® by BASF which are polyoxyethoxylated castor oils.

Examples

The following examples illustrate the inventor but do not fully delineate the scope of the invention intended by the inventor to be claimed herein. They are intended to illustrate how the invention might be practiced in certain particulars, but are not meant to be interpreted by those of skill in this art restrictively.

Example 1

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Hydrogen Peroxide	Dequest 2010
1.25	PHMB 0.0001%	L-histidine 0.2%	none	0.006%
1.85	PHMB 0.0001%	L-histdine 0.2%	0.006%	0.006%

The results demonstrate the improved antifungal efficacy of the histidine - hydrogen peroxide combination against *C. albicans*.

Example 2

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Sodium chloride, Hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Sodium Chloride	Hydrogen Peroxide	Dequest 2010
0.50	PHMB 0.0001%	L-histdine 0.2%	0.4%	none	0.006%
1.08	PHMB 0.0001%	L-histdine 0.2%	0.4%	0.006%	0.006%

The results demonstrate the improved antifungal efficacy of the histidine - hydrogen peroxide combination against *C. albicans*.

Example 3

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Glycerin, hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Glycerin	Hydrogen Peroxide	Dequest 2010
1.60	PHMB 0.0001%	L-Histidine 0.2%	none	none	none
2.38	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	none
1.27	PHMB 0.0001%	L-Histidine 0.2%	none	none	0.006%
2.25	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	0.006%
1.08	PHMB 0.0001%	L-Histidine 0.2%	none	none	0.003%
2.04	PHMB 0.0001%	L-Histidine 0.2%	none	0.006%	0.003%
1.57	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	none
2.15	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	none
1.25	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	0.006%
2.04	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	0.006%
1.08	PHMB 0.0001%	L-Histidine 0.2%	0.50%	none	0.003%

1.93	PHMB 0.0001%	L-Histidine 0.2%	0.50%	0.006%	0.003%

The results demonstrate the improved antifungal against *C. albicans* in each paired formulation, when 0.006% hydrogen peroxide is added. The data demonstrates that the increased activity is independent of the presence of Dequest 2010.

Example 4

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Hydrogen Peroxide	Dequest 2010
2.01	PHMB 0.0001%	Histidine 0.2%	none	none
2.42	PHMB 0.0001%	Histidine 0.2%	0.006%	0.003%
0.73	Marketed Product 1			
1.95	Marketed Product 2			

* marketed product 1 having the general composition: A sterile isotonic aqueous solution containing sodium chloride, polyoxyethylene polyoxypropylene block copolymer, sodium phosphate dibasic, sodium phosphate monobasic, and preserved with edetate disodium dihydrate 0.025% and polyhexanide 0.0001%.

** marketed product 2 having the general composition: A sterile, isotonic

solution that contains HYDRANATE (hydroxyalkylphosphonate), boric acid, edetate disodium, poloxamine, sodium borate and sodium chloride; preserved with DYMED (polyaminopropyl biquanide) 0.0001%.

The results demonstrate the improved antifungal efficacy of the histidine - hydrogen peroxide combination. The effectiveness was superior to that found in either commercially marketed products.

Example 5

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. Cremophor RH40, hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl (PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Additive	Hydrogen Peroxide	Dequest 2010
2.51	PHMB 0.0001%	L-Histidine 0.2%	Cremophor RH 40	none	none
3.27	PHMB 0.0001%	L-Histidine 0.2%	Cremophor RH 40	0.006%	0.003%

The results demonstrate the improved antifungal efficacy of the histidine - hydrogen peroxide combination against *C. albicans*.

Example 6

Histidine - Peroxide

Formulations were prepared by dissolving L-histidine in water. The pH of the solutions were adjusted to 7.3 with 1N hydrochloric acid. The tonicity agent, hydrogen peroxide, Dequest 2010 and polyhexamethylenebiguanide HCl

(PHMB) were added to these solutions. The formulations were diluted to volume with water. Each of these solutions were tested for their activity against *C. albicans* (ATCC 10231) following a two hour exposure. The activity is expressed as a log reduction from the initial inoculum. The compositions, concentrations and activity of each of the solutions are summarized in the following table.

Log Reduction	Preservative	Buffer	Tonicity Agent	Wetting Agent	Hydrogen Peroxide	Dequest 2010
2.42	PHMB 0.0001%	L-Histidine 0.2%	none	Cremophor RH 40		
3.34	PHMB 0.0001%	L-Histidine 0.2%	none	Cremophor RH 40	0.006%	0.003%
2.19	PHMB 0.0001%	L-Histidine 0.2%	glycerin 3%	Cremophor RH 40		
2.94	PHMB 0.0001%	L-Histidine 0.2%	glycerin 3%	Cremophor RH 40	0.006%	0.003%
2.19	PHMB 0.0001%	L-Histidine 0.2%	propylene glycol 3%	Cremophor RH 40		
2.95	PHMB 0.0001%	L-Histidine 0.2%	propylene glycol 3%	Cremophor RH 40	0.006%	0.003%
3.36	PHMB 0.0001%	L-Histidine 0.2%	sorbitol 5%	Cremophor RH 40		
3.92	PHMB 0.0001%	L-Histidine 0.2%	sorbitol 5%	Cremophor RH 40	0.006%	0.003%

0.68 Marketed Product 1

2.99 Marketed Product 2

2.98 Marketed Product 3 (Opti-Free Express)

* marketed product 1 having the general composition: A sterile isotonic aqueous solution containing sodium chloride, polyoxyethylene polyoxypropylene block copolymer, sodium phosphate dibasic, sodium phosphate monobasic, and preserved with edetate disodium dihydrate 0.025% and polyhexanide 0.0001%.

** marketed product 2 having the general composition: A sterile, isotonic solution that contains HYDRANATE (hydroxyalkylphosphonate), boric acid, edetate disodium, poloxamine, sodium borate and sodium chloride; preserved with DYMED (polyaminopropyl biquanide) 0.0001%.

The data shows that the addition of 0.006% hydrogen peroxide to histidine provides increased antifungal ctivity against *C. albicans*. Consistent results were found in the presence of Cremophor RH40 with glycerin, propylene glycol, and soribitol. All formulations with dilute hydrogen peroxide added to hisitidine were equal to or superior to marketed products.

2002225950 28 Jul 2006

The Claims Defining the Invention are as Follows:

1. An ophthalmic solution comprising:

0.01 to about 1.0 percent by weight L-histidine;

0.0001 to 0.01 percent by weight hydrogen peroxide; and

0.1 to 500 parts per million of a cationic polymeric preservative.

2. A method for supplying a rinsing solution to an eye comprising the step of:

contacting an eye with a solution comprising:

0.01 to about 1.0 percent by weight L-histidine;

0.0001 to 0.01 percent by weight hydrogen peroxide; and

0.1 to 500 parts per million of a cationic polymeric preservative.

3. A method of delivering an active pharmaceutical agent to the eye comprising the steps of:

providing a solution of 0.01 to about 1.0 percent by weight L-histidine; 0.0001 to 0.01 percent by weight hydrogen peroxide; and 0.1 to 500 parts per million of cationic polymeric preservative; and

contacting the eye with said solution.

4. A method of treating contact lenses comprising the step of:

contacting a solution of 0.01 to about 1.0 percent by weight L-histidine;

0.0001 to 0.01 percent by weight hydrogen peroxide; and 0.1 to 500 parts per million of a cationic polymeric preservative with a contact lens.

5. The use of a solution comprising:

0.01 to about 1.0 percent by weight L-histidine;

0.0001 to 0.01 percent by weight hydrogen peroxide; and

0.1 to 500 parts per million of a cationic polymeric preservative

for rinsing an eye.

6. The use of a solution of 0.01 to about 1.0 percent by weight L-histidine; 0.0001 to 0.01 percent by weight hydrogen peroxide; and 0.1 to 500 parts per million of cationic polymeric preservative for delivering an active pharmaceutical agent to the eye.

7. The use of a solution of 0.01 to about 1.0 percent by weight L-histidine; 0.0001 to 0.01 percent by weight hydrogen peroxide: and 0.1 to 500 parts per million of a cationic polymeric preservative for treating contact lenses.

8. An ophthalmic solution comprising L-histidine, hydrogen peroxide and a cationic polymeric preservative, substantially as herein described with reference to any one of the Examples.

9. A method for supplying a rinsing solution to an eye comprising the step of contacting the eye with a solution of claim 8.

10. A method of delivering an active pharmaceutical agent to an eye comprising providing a solution of claim 8 and contacting the eye with the solution.

11. A method of treating contact lenses comprising the step of contacting a solution of claim 8 with a contact lens.

12. The use of a solution of claim 8 for rinsing an eye.

13. The use of a solution of claim 8 for delivering an active pharmaceutical agent to the eye.

14. The use of a solution of claim 8 for treating contact lenses.