(CONVENTION. By one or more persons and/or a Company)

PATENT OFFICE 100 ONE HUNDRED DOLLARS

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COMMONWEALTH OF AUS

Patents Act 1952-1969

CONVENTION APPLICATION FOR A PATENT

FEE STAMP TO VALUE OF $ 200 ATTACHED
MAIL OFFICER

(1) Here insert (in full) Name or Names of Applicant or Applicants, followed by Address (es).

K/We (1) CIBA-GEIGY AG

of Klybeckstrasse 141, 4002 Basle, Switzerland

hereby apply for the grant of a Patent for an invention entitled: (2)

(2) Here insert Title of Invention.

DISINFECTING COMPOSITION FOR SOFT CONTACT LENSES CONTAINING A STABILIZED HYDROGEN PEROXIDE SOLUTION

(3) Here insert number(s) of basic application(s)

which is described in the accompanying complete specification. This application is a Convention application and is based on the application numbered (3)

917,947

(4) Here insert Name of basic Country or Countries, and basic date or dates

for a patent or similar protection made in (4) United States of America on 14th October 1986

COMPLETE ACCEPTED AND AMENDMENTS ALLOWED 9-8-90

ADDRESS FOR SERVICE ALTERED

AUSTRALIAN PATENT OFFICE Reg'd 12

~~My~~/Our address for service is ~~Messrs. Edwd. Waters & Sons, Patent Attorneys, 50 Queen Street, Melbourne, Victoria~~, Australia.

ARTHUR S CAVE & CO SYDNEY NSW

DATED this 12th day of October 19 87

(5) Signature (s) of Applicant (s) or Seal of Company and Signatures of its Officers as prescribed by its Articles of Association.

(5)

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CIBA-GEIGY AG

by

Registered Patent Attorney.

To:

THE COMMISSIONER OF PATENTS.

P246250/GH

AU Case V-16127/+-CGV 1225 Regulation 12(2)

PATENT DECLARATION FORM (CONVENTION)

COMMONWEALTH OF AUSTRALIA

Patents Act 1952

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION FOR A PATENT

In support of the Convention application made for a patent for an invention entitled: Disinfecting composition for soft contact lenses containing a stabilized hydrogen peroxide solution

I/~~We~~ Ernst Altherr ..... (full name of declarant)
of CIBA-GEIGY AG, Klybeckstrasse 141, 4002 Basle, Switzerland (full address)
do solemnly and sincerely declare as follows:-

1. I am/~~are~~ authorised by CIBA-GEIGY AG the applicant for the patent to make this declaration on its behalf.

2. The basic Application(s) as defined by Section 141 of the Act was/were made in the following country or countries on the following date namely:-
in USA on October 14, 1986 by FU-PAO TSAO

3. FU-PAO TSAO
of 1361 Pinehurst Hunt, Lawrenceville, GA 30245, USA
is the actual inventor of the invention and the facts upon which the applicant(s) are entitled to make the application are as follows:

The Applicant is the Assignee of the said invention from the actual inventor.

4. The basic application(s) referred to in paragraph 2 of this Declaration was the first application(s) made in a Convention country in respect of the invention the subject of the application.

Declared at Basle this 28th day of June , 1990.

CIBA-GEIGY AG

E. Ernst

To:
The Commissioner of Patents

ARTHUR S. CAVE & CO.
PATENT AND TRADE MARK ATTORNEYS
SYDNEY

Signature of Declarant(s)
Ernst Altherr
Single Signature, by special power

2090W/AMP

(12) PATENT ABRIDGMENT (11) Document No. AU-B-79703/87
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 602926

(54) Title
METHOD OF DISINFECTING SOFT CONTACT LENSES USING A STABILISED AQUEOUS HYDROGEN PEROXIDE SOLUTION

International Patent Classification(s)
(51)[4] A61L 002/18

(21) Application No. : 79703/87 (22) Application Date : 13.10.87

(30) Priority Data

(31) Number (32) Date (33) Country
917947 14.10.86 US UNITED STATES OF AMERICA

(43) Publication Date : 21.04.88

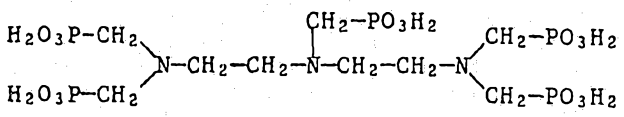
(44) Publication Date of Accepted Application : 01.11.90

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(57) The present invention relates to a stabilized aqueous hydrogen peroxide solution for use in the disinfection of a soft contact lens having a hydrogen peroxide content from about 0.5 to about 6 % by weight hydrogen peroxide wherein the stabilized solution contains from about 0.003 to about 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) of the formula



or a physiologically compatible salt thereof, and to an improved method of disinfecting a soft contact lens with such solution.

CLAIM

1. A method of disinfecting a soft contact lens with a stabilized aqueous hydrogen peroxide solution having a pH between 5.5 and 7.5, a hydrogen peroxide content of between 0.5 and 6 % by weight, and containing between 0.003 and 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof, as a stabilizer, such that the solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

.../2

13. A stabilized aqueous hydrogen peroxide solution adapted for use in the disinfection of a soft contact lens, having a pH of between 5.5 and 7.5, a hydrogen peroxide content of between 0.5 and 6 % by weight, and containing between 0.003 and 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof as a stabilizer, wherein said solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

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602926

Form 10

PATENTS ACT 1952-69

COMPLETE SPECIFICATION

(ORIGINAL)

Class Int. Class

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

This document contains the amendments made under Section 49 and is correct for printing.

Priority :

Related Art :

Name of Applicant : CIBA-GEIGY AG

AUSTRALIAN PATENT OFFICE

Address of Applicant : Klybeckstrasse 141, 4002 Basle, Switzerland

Actual Inventor: FU-PAO TSAO

Address for Service : ~~EDWD. WATERS & SONS,~~ ARTHUR S. CAVE & Co. SYDNEY NSW ~~50 QUEEN STREET, MELBOURNE,~~ AUSTRALIA, ~~3000.~~

Complete Specification for the invention entitled:

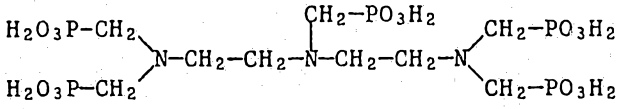
DISINFECTING COMPOSITION FOR SOFT CONTACT LENSES CONTAINING A STABILIZED HYDROGEN PEROXIDE SOLUTION

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

V-16127/+/CGV 1225

Disinfecting Composition For Soft Contact Lenses Containing A Stabilized Hydrogen Peroxide Solution

The present invention relates to a stabilized aqueous hydrogen peroxide solution for use in the disinfection of a soft contact lens having a hydrogen peroxide content from about 0.5 to about 6 % by weight hydrogen peroxide wherein the stabilized solution contains from about 0.003 to about 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) of the formula



or a physiologically compatible salt thereof, and to an improved method of disinfecting a soft contact lens with such solution.

Soft contact lenses are characteristically prepared from hydrophilic polymers, such as polymers of hydroxyethyl methacrylate (HEMA), crosslinked with a conventional crosslinking agent, such as ethylene glycol dimethacrylate (EGDMA), or more complex copolymer systems including copolymers of HEMA, EGDMA, methacrylic acid and/or poly-N-vinylpyrrolidone, and the like. Other hydrophilic monomers conventionally employed in varying amounts in the manufacture of soft contact lenses include, for example, N-vinylpyrrolidone, glyceryl methacrylate, diethylene glycol monomethacrylate, triethylene glycol monomethacrylate, allyl 2-hydroxyethyl ether, acrylic acid, acrylamide, N,N-dimethylacrylamide, and the like. Other conventional crosslinking agents commonly employed include,

inter alia, diallyl ether, divinyl benzene, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, diallyl succinate, allyl methacrylate, glycerin tri-methacrylate, and the like. Moreover, various amounts of relatively hydrophobic monomer units can be employed in the manufacture of soft contact lens materials, as long as the final copolymer network exhibits the desired hydrophilic characteristics. Typical hydrophobic monomers include methyl methacrylate, glycidyl methacrylate, N-(1,1-dimethyl-3-oxobutyl)acrylamide, siloxane methacrylates, perfluoroalkyl methacrylates, perfluoroalkoxyperfluoroalkyl methacrylates, and the like. In general, such lenses exhibit marked hydrophilic properties and, when wet, absorb water and are soft and flexible.

While these lenses are not actually perforate, they do have a sufficient degree of molecular porosity to permit water, oxygen and tear fluids to permeate the lens structure. In order for the disinfection of such lenses to be effective after they have been worn, it is important that contaminants be removed from both surfaces, and the interior of the lens, to the extent contaminants are present therein. Hydrogen peroxide in the form of a dilute solution, e.g. about 0.5 to 6 % by weight in water, is known to be effective for use with contact lenses in order to kill any contaminating microorganisms.

One drawback with unstabilized dilute hydrogen peroxide solutions, however, is that without the use of a stabilizer or a combination of stabilizers, the aqueous peroxide solutions characteristically decompose over a period of time. The rate at which such dilute hydrogen peroxide solutions decompose will, of course, be dependent upon such factors as pH and the presence of trace amounts of various metal impurities, such as copper or chromium, which may act to catalytically decompose the same.

Moreover, at moderately elevated temperatures the rate of decomposition of such dilute aqueous hydrogen peroxide solutions is greatly accelerated.

A large variety of stabilizers has been proposed for use with hydrogen peroxide to deactivate trace catalytic impurities, including stannous salts, ethylene diamine tetraacetic acid, and the like.

For example, U.S. Patent 3,860,391 discloses bleaching compositions containing hydrogen peroxide and, as a stabilizer, amino lower alkylene polyphosphonates, including diethylene triamine penta-(methylenephosphonic acid) or salts thereof, and/or hydroxy alkane phosphates, with or without additional stabilizer constituents, and adjusted to a pH of between about 9.0 and 12.0 with, e.g. sodium hydroxide, for the bleaching of cellulose materials. Exemplified are compositions having a pH of 12.0.

Unfortunately, such highly basic compositions are undesirable in a contact lens environment and especially in the disinfection of contact lenses.

Thus, it is essential that the hydrogen peroxide containing solutions employed be, upon disinfection of the contact lenses and decomposition of the hydrogen peroxide, sufficiently compatible with the ocular environment so as not to occasion ocular irritation or damage if the disinfected contact lens containing the residual solution absorbed by the lens, is placed into the eye.

Caustic compositions, for example, can occasion severe ocular irritation and damage to the ocular tissue.

It is thus an object of the present invention to provide a method of disinfecting a soft contact lens with a stabilized aqueous hydrogen peroxide solution having a pH of about 5.5 to about 7.5, employing diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof, as a stabilizer, such that upon disinfection of such contact lens and decomposition of residual

hydrogen peroxide, the resulting solution, absorbed by and adhering to said lens, is physiologically tolerable to the ocular environment.

It is a further object of the present invention to provide stabilized aqueous hydrogen peroxide solutions for use in such method.

These and other objects of the present invention are apparent from the following more specific disclosures.

One embodiment of the present invention relates to a method of disinfecting a soft contact lens with a stabilized aqueous hydrogen peroxide solution having a pH between about 5.5 and about 7.5, a hydrogen peroxide content of between about 0.5 and about 6 % by weight, and containing between about 0.003 and about 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof, as a stabilizer, such that the solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

An alternate embodiment of the present invention relates to a stabilized aqueous hydrogen peroxide solution adapted for use in the disinfection of a soft contact lens, having a pH of between about 5.5 and about 7.5, a hydrogen peroxide content of between about 0.5 and about 6 % by weight, and containing between about 0.003 and about 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof as a stabilizer, wherein said solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

Physiologically compatible salts of diethylene triamine penta(methylenephosphonic acid) include, for example, water soluble salts with conventional pharmaceutically acceptable cationic moieties, including the alkali metal, alkaline earth metal, ammonium and amine cations. Suitable amine salts include, for example, mono-, di- and

tri-lower alkyl amines, such as methylamine, ethylamine, diethylamine, triethylamine, dimethylamine, trimethylamine, propylamine, and the like; and mono-, di- and tri-lower hydroxyalkyl amines, such as ethanolamine, diethanolamine, triethanolamine, glucamine, 2-hydroxypropylamine, and the like.

By "lower", e.g. in the context of an alkyl group, is meant a group having up to 6 carbon atoms, preferably up to 4 carbon atoms.

Preferably, the concentration of hydrogen peroxide in the stabilized solution is between about 2 % and 6 % by weight, based upon the weight of the formulation.

Preferably, diethylene triamine penta(methylenephosphonic acid) or a salt thereof is present in the stabilized composition in an amount between about 0.006 and about 0.02 % by weight of the composition, and most preferably between about 0.006 and about 0.0120 % by weight of the composition.

If desired, additional conventional stabilizers may be employed in conjunction with the diethylene triamine penta(methylenephosphonic acid) or salt stabilizer in accordance with the present invention.

Suitable conventional stabilizers include: water soluble stannates, such as alkali metal or ammonium stannates, for example sodium stannate, alone or in combination with a water soluble phosphate, polyphosphate or metaphosphate salt, such as an alkali metal or ammonium salt thereof; or an amino polycarboxylic acid chelating agent, such as ethylene diamine tetraacetic acid, nitrilo triacetic acid or a water soluble salt thereof, such as an alkali metal or ammonium salt, especially the sodium salt, or mixtures thereof. Where such additional stabilizers are employed, they are generally employed in a physiologically tolerable amount, e.g. in an amount of about 0.002 to about 0.1 % by weight.

However, the presence of additional stabilizers is on no account essential. In contrast to the prior art where diethylene triamine penta(methylenephosphonic acid), when used as a stabilizer of hydrogen peroxide solutions, as in U.S. patents 4,294,575; 4,525,291 or 4,614,646, is generally used in a combination with other stabilizers, the presence of additional stabilizers is preferably limited in the solutions and methods according to the present invention.

Thus, a preferred embodiment of the invention is a solution or a method as defined hereinbefore wherein diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof is the substantially effective stabilizer. In a more preferred embodiment the additional presence of stabilizing alkali metal polyphosphates or polyalkylenepolycarboxylic acids is excluded. An even more preferred embodiment relates to solutions and methods as defined hereinbefore wherein diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof is the only effective stabilizer.

The pH of the stabilized solution is, as stated above, between about 5.5 and about 7.5. Preferably, the pH of the stabilized hydrogen peroxide solution is between about 6 and about 7, most preferably between about 6.2 and about 6.8. The pH can be adjusted as desired by incorporation of suitable amounts of acid or base of a physiologically tolerable nature in the amounts employed.

Also, there may be present in the stabilized hydrogen peroxide solution according to the present invention, one or more conventional, substantially inert, physiologically acceptable tonicity enhancing agents. Suitably such agents include, for example alkali metal halides, phosphates, hydrogen phosphates, and borates. Preferred are sodium chloride, sodium phosphate monobasic and sodium phosphate dibasic. The function of such tonicity enhancing agents is to increase the comfort level of the solution, after decomposition

of the hydrogen peroxide during or subsequent to contact lens disinfection, which adheres to the contact lens, in the eye of the patient.

Preferably sufficient tonicity enhancing agents are present in the solution, such that, upon decomposition of the hydrogen peroxide therein, the resulting solution is substantially isotonic, e.g. substantially equivalent to a 0.9 % by weight aqueous sodium chloride solution.

In use, the contact lens to be disinfected is removed from the eye of the patient and placed into a solution of the stabilized hydrogen peroxide to disinfect the lens. Upon disinfection the hydrogen peroxide is decomposed, e.g. by the use of a conventional catalyst, such as a platinum catalyst on a support, or catalase, or by the use of a physiologically acceptable hydrogen peroxide decomposition agent, such as a physiologically acceptable reducing agent, including pyruvic acid or suitable salts thereof, e.g. the sodium salt. The lens can thereafter be stored in the resulting solution until reinsertion into the eye.

In general, the stabilized hydrogen peroxide solutions of the present invention are characterized by their extraordinary stability, even under accelerated conditions, for example by heating the solutions to 100°C for 24 hours. Moreover, the instant compositions are characterized by their physiological tolerability subsequent to hydrogen peroxide decomposition.

The following examples are presented for illustrative purposes and are not intended to limit the scope of this invention. All parts are by weight unless otherwise indicated.

Example 1: Into 80 ml distilled deionized water there is added 0.8655 g sodium chloride, 0.0622 g sodium phosphate dibasic (anhydrous), 0.0072 g sodium phosphate monobasic (monohydrate) and 0.006 g diethylene triamine penta(methylenephosphonic acid) with stirring.

To the resulting solution there is added 31 % aqueous hydrogen peroxide in an amount of 10 ml, and sufficient distilled deionized water is added to result in a total volume of 100 ml. Thereupon the pH is adjusted to 6.5 by the dropwise addition of dilute aqueous hydrogen chloride or sodium hydroxide.

The resulting stabilized 3 % hydrogen peroxide is then heated to 100°C for a period of 24 hours. The solution possesses a "hot stability" of above 95 %, i.e. the amount of the hydrogen peroxide present in the after-heated sample related to the before-heated sample exceeds 95 %.

Example 2: The procedure of example 1 is duplicated, except that typical deionized water is employed. Again, the hot stability of the resulting stabilized hydrogen peroxide solution is above 95 %.

Example 3: The procedure of example 1 is duplicated, except that conventional soft tap water is employed. Once again, the hot stability of the resulting stabilized hydrogen peroxide solution is above 95 %.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of disinfecting a soft contact lens with a stabilized aqueous hydrogen peroxide solution having a pH between 5.5 and 7.5, a hydrogen peroxide content of between 0.5 and 6 % by weight, and containing between 0.003 and 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof, as a stabilizer, such that the solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

2. A method according to claim 1, wherein said solution has a hydrogen peroxide content of 2 to 6 % by weight, based upon the weight of solution.

3. A method according to claim 1, wherein the pH is between 6 and 7.

4. A method according to claim 1, wherein the pH is between 6.2 and 6.8.

5. A method according to claim 1, in which the concentration of diethylene triamine penta(methylenephosphonic acid) is between 0.006 and 0.02 % by weight of the composition.

6. A method according to claim 1, wherein said solution, upon decomposition of the hydrogen peroxide therein, is substantially isotonic.

7. A method according to claim 2, wherein said solution, upon decomposition of the hydrogen peroxide therein, is substantially isotonic.

8. A method according to claim 1, wherein, upon disinfection of said lens, the hydrogen peroxide in said solution is decomposed by the use of an effective amount of a hydrogen peroxide decomposition catalyst or agent.

9. A method according to claim 8, wherein upon hydrogen peroxide decomposition, said solution is substantially isotonic.

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10. A method according to claim 1, in which said solution additionally contains between 0.002 and 0.1 % of a water soluble stannate or amino polycarboxylic acid chelating agent.

11. A method according to claim 1, wherein in said solution the presence of alkali metal polyphosphates or polyalkylene polycarboxylic acids as additional stabilizer is excluded.

12. A method according to claim 1, wherein in said solution diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof is the only effective stabilizer.

13. A stabilized aqueous hydrogen peroxide solution adapted for use in the disinfection of a soft contact lens, having a pH of between 5.5 and 7.5, a hydrogen peroxide content of between 0.5 and 6 % by weight, and containing between 0.003 and 0.03 % by weight of diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof as a stabilizer, wherein said solution, upon decomposition of the hydrogen peroxide, is physiologically tolerable to the ocular environment.

14. A solution according to claim 13, wherein said solution has a hydrogen peroxide content of 2 to 6 % by weight, based upon the weight of solution.

15. A solution according to claim 13, wherein the pH is between 6 and 7.

16. A solution according to claim 13, wherein the concentration of diethylene triamine penta(methylenephosphonic acid) is between 0.006 and 0.02 % by weight based upon the weight of solution.

17. A solution according to claim 13, wherein said solution, upon decomposition of the hydrogen peroxide therein, is substantially isotonic.

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18. A solution according to claim 14, wherein said solution, upon decomposition of the hydrogen peroxide therein, is substantially isotonic.

19. A solution according to claim 17, wherein the pH is between 6 and 7.

20. A solution according to claim 19, which additionally contains between 0.002 and 0.1 % of a water soluble stannate salt or amino polycarboxylic acid chelating agent.

21. A solution according to claim 13, wherein the presence of alkali metal polyphosphates or polyalkylene polycarboxylic acids as additional stabilizer is excluded.

22. A solution according to claim 13, wherein diethylene triamine penta(methylenephosphonic acid) or a physiologically compatible salt thereof is the only effective stabilizer.

DATED this 3rd day of August, 1990.

CIBA-GEIGY AG

By its Patent Attorneys

ARTHUR S CAVE & CO.

AUSTRALIAN PATENT OFFICE