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(54) Methods and materials for cleaning soft contact lenses.

(57) A cleaning solution for soft contact lenses is described. The solution differs from previously known solutions in that it includes a lipolytic enzyme together with a buffering substance, such as a phosphate. The cleaning solution removes any lipids present on the surface of the lens by splitting them into fatty acids and esters for removal by subsequent rinsing and, optionally, boiling in physiological saline solution.

A supplementary cleaning solution comprises, in addition to the lipolytic enzyme, a proteolytic enzyme, such as papain or bromelain, such solution providing for complete removal of all deposits from the surface of the lens. The solution of the invention is preferably hypertonic and it is applied either by using a droplet technique or by introducing the lens fully into the solution.

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TITLE OF INVENTION:

METHODS AND MATERIALS FOR CLEANING SOFT CONTACT LENSES.

TECHNICAL FIELD:

The present invention relates to methods and materials for removing from soft contact lenses deposits that are formed during use. Such deposits contain mainly Albumin, Globulins and Lipids.

BACKGROUND ART:

Deposits that occur during use of soft contact lenses generally result in an opaque film, yellow discoloration, white spots and thread-like configurations on the lenses. Investigations carried out have shown that these deposits can consist of Albumin, Ig γ-Globulin, Lysozyme and lipoproteins.

The deposits are often largely composed of Lipids and denatured Albumin, which are deposited on the lenses from the tear fluid as a result of the saline solution with which the lenses are impregnated being exchanged for the tear fluid. The drying-out of a lens, for instance through its use in a dry environment and by air flowing past it, etc. causes some Albumin to be denatured and deposited on the lens. Even when contact lenses are sterilized by boiling, Albumin is denatured which gives rise to apolar interior groups of Lipids. Other causes too, such as for example continuous use, cause Albumin and Lipids to be deposited on contact lenses in fairly large quantities.

One method of cleaning contact lenses is already known which comprises the steps of dissolving in water a proteolytic enzyme in tablet form and then placing the lenses to be cleaned in the solution for a period of at least two hours. This process has been regarded as complicated by the wearers of contact lenses so that cleaning has not always been carried out as regularly as

is required and this has resulted in lenses finally acquiring such a coating that the lenses have become unusable. Moreover, the prior art using only proteolytic enzymes does not provide for complete removal of the deposits formed in that deposits of lipid origin remain substantially unaffected by the solutions of the prior art.

SUMMARY OF THE INVENTION:

An object of the present invention is to provide cleaning solutions and methods for cleaning soft contact lenses which, on the one hand are simple for the contact lens wearer to use and which also provide an improved cleaning effect.

It is another object to provide cleaning liquids which prevent a general build-up of proteins and lipids.

Yet another object of the present invention is to provide solid compositions of matter to be dissolved in an aqueous vehicle to form soft contact lens cleaning solutions, preferably of a hypertonic character.

According to one aspect of the invention an enzyme containing cleaning liquid for soft contact lenses consists of a solution containing a lipolytic enzyme (mainly for reducing the lipids) and, optionally, a proteolytic enzyme, such as papain or bromelain, (for reducing the Albumin deposits) and, additionally, a buffering agent, such as a phosphate. Such cleaning liquid is preferably hypertonic to its nature, i.e. its osmotic pressure exceeds that of a physiological solution, so that in treatment with the solution some dewatering of the lens takes place, which seems to be beneficial to the cleaning effect. During after-treatment with an isotonic solution, for example a saline solution, the lens reversibly again takes up water to revert to its original state.

A pack for cleaning soft contact lenses comprises

a volume of a solution containing Papain or Bromelain and a Lipolytic Enzyme, a device for forming droplets of the solution for depositing same on the surface of a soft contact lens and a volume of a sterile isotonic physiological saline solution in which the lens can be rinsed and subsequently boiled.

A method of cleaning a soft contact lens in accordance with the invention to remove deposits on the surface of the lens by enzymatic action comprises the steps of placing at least one drop of a solution containing Papain or Bromelain and in addition a Lipolytic Enzyme, on the contact lens which is to be cleaned to reduce both Albumin and Lipids present to water soluble peptones, fatty acids and esters, and subsequently removing the resulting products by rinsing and boiling in a physiological saline solution.

Preferably the enzyme activity in the cleaning solution is of the order of 100 tyrosine units per ug of protein.

The fluid activity is allowed to occur for a period of the order of 15 minutes.

Preferably the physiological saline solution has a particle size below 0.2 microns, and is isotonic, has a pH-value of 7.0 with a buffer capacity of 6-8 and is also sterile.

A preferred enzyme solution for cleaning the lens consists of Bromelain, Mannitol, Sorbitol, Ethylenediaminetetraacetic acid, Sodium Metabisulphite, and a lipolytic enzyme.

A preferred cleaning solution may consist of:

Purified fruit bromelain	50-500 g,	e.g. about	100 g.
Sorbitol	100-1000 g,	" "	500 g.
Mannitol	10-100 g,	" "	50 g.
Sodium hydrogen sulphite	8-12 g,	" "	10 g.
Ethylenediaminetetraacetic acid disodium salt	0.8-1.2 g,	" "	1 g.
Potassium sorbate	10-1000 mg,	" "	100 mg.

diluted to 1 litre aqua dest., together with Lipase from cand. cylindracae, preferably in an amount corresponding to about 50000 units, in 1000 ml. 0.1 M Phosphate buffer in an aqueous polymer complex.

An alternative cleaning solution (which comprises another aspect of the invention) which may be used to clean a soft contact lens consists of a solution of Lipase and a phosphate buffer.

When a proteolytic enzyme and a lipolytic enzyme are used in combination it is preferred in order to avoid undue interaction between the enzymes to include in the solution a so-called "aqueous polymer complex", which is conventional in the art and have for a purpose to bind the lipolytic enzymes so that it will not be unduly destroyed by the proteolytic enzyme. The nature of this polymer complex is not critical and any commercial product may be used, such as polyethylene glycol , polyvinyl alcohol, polyvinyl pyrrolidone and the like. As a fully non-limiting example one may mention the polymer complex "Kollodon" 25 or 30 from BASF, West Germany.

In order to obtain a fully understanding of the invention, its background and its underlying problems, some further explanation will be given below.

The polymers used in the manufacturing of soft contact lenses at the present time, PMMA, HEMA and PvP all have a common factor, that is, they are lipid and protein retensive. New materials have been introduced

such as silicone, even in this material there is lipid retention.

At the present time it does not seem possible to present a material for the manufacturing of soft contact lenses that does not present this problem.

This problem of fatty deposits from tear fluids has been demonstrated in numerous investigations. The insidious, relentless accumulation of fatty deposits on and in the matrix of the lens material can appear after a short period of time, it seems that the amount of lipids in tear fluid varies from one person to the next.

The lipid deposits appear either as yellowish tinting of the lens or as a whitish haze.

Chemically the deposits are composed of phospholipids, probably in the form of lecitin, forming together with the protein a lecitoprotein, (lecitin on exposure to heat and light tends to autooxidise or decompose into yellowish substances) or cholesterol and fat esters which are white in colour.

Plaques or what one might call lesions also appear on the lenses after a period of time. Typically the plaque consists of a central core of lipid lying free on the polymer and protruding into the material matric causing a sand grain sensation when the lens lies in the eye.

Unfortunately, we have only theories to explain how fatty substances in the tear fluid are transformed into obstructive plaques. However, these plaques start from the same observation - an excess of lipids - and in particular cholesterol and lecitin.

Based on these observations it is therefore quite apparent that a method for cleaning soft contact lenses presently and in the future must be one that can remove the lipid and protein deposits formed in the soft contact lens material during wearing.

Due to the fact that new materials are being investigated it is necessary that the cleaning method must be compatible with these materials. An enzymatic method whereby a lipase is used is without doubt the most gentle method and probably the most efficient for removing fatty deposits from soft contact lenses.

It is also evident that the greater the water content of the polymer the greater the binding of protein and lipids, this binding tends to be normally a surface adsorption but in those polymers that are combined with copolymers of certain types there is a possibility that a covalent binding can occur.

This type of binding is naturally more difficult to separate than an ordinary surface adsorption. It is, however, possible with the use of lipase in combination with a tenside; the tenside in this case increases the water/oil interphase and allows the enzyme to react upon the lipids.

With regard to the enzymes used in the liquid or solution according to the invention any lypolitic enzyme hydrolyzing the lipids to yield fatty acids and glycerol are useful. A preferred variety is lipase derived from cand. cylindracae, suitably prepared by lyophilization. As a proteolytic enzyme any protein-digesting enzyme is useful, preferred examples being bromelain and papain. When using in combination both a lipolytic enzyme and a proteolytic enzyme, the latter being papain, it will be noted that the beneficial effect of free sulfhydryl groups on the activity of papain will be satisfied by the presence of the lipase containing sulfhydryl groups. Thus, such combination of enzymes is particularly preferred, especially when used in solutions of a hypertonic character.

EXAMPLES:

The invention will now be further described by non-limiting examples.

Example I.

A soft contact lens cleaning fluid (known as PROLEN) is made up as follows:-

Purified fruit bromelain	100 g
Sorbitol	500 g
Mannitol	50 g
Sodium hydrogen sulphite	10 g
Ethylenediaminetetraacetic acid disodium salt	1 g
Potassium sorbate	100 mg

Dilute to 1 litre aqua dest.

Then add:-

Lipase from cand. cylindracae 50000 units in 1000 ml. 0.1 M Phosphate buffer in an aqueous polymer complex.

Example II.

A second soft contact lens cleaning fluid (known as LIPREN) is made up as follows:-

Lipase derived from cand. cylindracae, lyophilised	100 units.
0.1 M phosphate buffer	10 ml.

Methods of use

PROLEN

A few drops (0.3 ml) of the fluid are placed on a lens and left on the lens for 15 minutes. The lens is then rinsed in a saline solution and thereafter boiled in the saline solution for 20 minutes. Finally the lens is rinsed once more in the saline solution before reinserting.

LIPREN

(a) For regular periodic cleaning.

A freeze dried lipase is reconstituted with a phosphate buffer (0.1 M). The lenses are placed in this solution and allowed to remain in the solution for 30 minutes.

After this time the lenses are removed and rinsed in a saline solution and then boiled in the saline solution for 20 minutes. After boiling the lenses they are once again rinsed in saline solution before reinserting.

(b) For lenses that have not previously been treated with Lipren and have visual deposits or are discoloured.

A freeze dried Lipase is reconstituted with a phosphate buffer (0.1 M). The lenses are placed in the fluid and allowed to remain in the fluid for 8-10 hours.

The lenses are removed and rinsed in dest. water.

The lenses are then heated in a saline solution to 40°C for 30 minutes.

The lenses are then rinsed in dest.water and boiled in saline solution for 30 minutes.

Finally the lenses are rinsed in saline solution before reinserting.

The cleaning of soft contact lenses using cleaning liquids of the invention.

After use a lens is usually coated with deposits of protein, lipoproteins and lipids. In accordance with one aspect of the invention the lens is treated with a preparation having a high enzymatic effect which contains a stabilised protease and a high activity lipase. Drops of the preparation are placed on the lens in accordance with the invention and it is left for the preparation to take effect, for 15 minutes.

This cleaning preparation is, as described above, preferably formed from Bromelain, Mannitol, Sorbitol, Ethylenediaminetetraacetic acid, Sodium Metabisulphate and lipolytic enzyme.

Complete removal of lipids from the lens is achieved by using a stabilised enzyme in fluid form and this may be applied either separately or as a

second step. This is typically dripped onto the contact lens so as to remove any lipid deposits.

The stabilised enzyme in fluid form is, as described above, preferably a lipase with a phosphate buffer.

A further step in the cleaning operation involves rinsing the contact lens in a physiological saline solution and then boiling the lens in the same or a similar solution.

The saline solution should be particle-free (i.e. have a particle size below 0.2 micron), should be isotonic, should have a pH-value of 7.0 and a buffer capacity of 6-8 and should also be sterile. The pH-value which is indicated is that value which will avoid smarting when the lens is subsequently inserted. An incorrect pH-value will cause smarting to occur. An incorrect pH-value will also cause the protein in the tear fluid to become denatured spontaneously which is not, of course, desirable.

In order to fulfil the conditions imposed as to purity and sterility, the solution is preferably packed in a disposable pack and is sterilised by means of Gamma radiation.

Report of experiments to determine effectiveness of invention.

With a view to determining the cleansing effect of the solutions and methods proposed by the invention, investigations were carried out as follows. For protein determination, the method according to Lowry as modified by Wedler was used. For determining the lipid quantity present, the method according to Boyer et al was used.

Analysis of tear fluid according to several different sources shows that the fluid consists of Lysozyme, Ig γ-globulin, 1-lipoprotein, small amounts of carbohydrates and phospholipids. A similar solution

was therefore prepared from the following:- γ-chymotrypsin, serum albumin, lysozyme, bovine mucin, globulin II, β-globulin III, globulin and β-lipoprotein in 0.9 % NaCl solution. Lenses were placed in this prepared solution and left over night. Control lenses were kept in a sterile saline solution instead of the prepared solution. At the end of the period of storage the lenses were divided into four groups:-

Group 1. The lenses in this first group were rinsed and then boiled in a sterile saline solution.

Group 2. The lenses in the second group were rinsed in a "cleaning solution" and then stored in a saline solution containing preservatives.

Group 3. The lenses in Group 3 were treated with an enzyme solution and subsequently rinsed and boiled.

Group 4. The lenses from the saline solution were treated in the same way.

After treatment the protein and lipid content of each of the four groups was found to be as follows:-

Group 1 - Protein content 3-8 µg per lens. Total lipid content

100-250 µg per lens.

Group 2 - Protein content 1-4 µg per lens. Lipid content

60-120 µg per lens.

Group 3 - Protein content 0-0.5 µg per lens. Lipid content

0-30 µg per lens.

Group 4 - Protein content 0.02 µg per lens. Lipid content

0 µg per lens.

The invention allows soft contact lenses to be cleaned rapidly and effectively and in general the cleaning operation should be carried out daily. However, where lenses are worn day and night, the interval

between cleanings may be extended to every other or even every third day.

The invention therefore provides for a simpler cleaning process than the known technique which requires the dissolving of tablets in water and also provides for a shorter cleaning period than hitherto. What is more important, however, is that the invention allows a more complete cleaning of the contact lens on account of the higher enzymatic activity. Unlike previously known cleaning preparations, the method according to the present invention is also designed to be used daily on the one hand for cleaning the lenses and on the other hand as a preventative measure to present the build-up of larger deposits of protein and lipids which after a time are difficult to remove and affect the properties of the lens.

The types of enzymes which can be utilised may be Papain or Bromelain in each case together with a lipolytic enzyme. Cysteine and Polysaccharides may be used as substrate materials.

Enzymatic activity should be of the order of 100 tyrosine units per µg of protein (substrate).

By splitting the albumin into water-soluble peptones by enzymatic action, the latter can be rinsed or boiled away using a physiological saline isotonic solution.

The invention provides a stable liquid cleaning agent for cleaning soft contact lenses which can be stored under normal environmental conditions without loss of enzymatic activity thereby obviating the need to dissolve a tablet or quantity of powder in water so as to produce the cleaning solution for the lens. In this way just sufficient quantity of the cleaning liquid need be used to cover the surface of the lens and it is with this in mind that the invention provides for the

application of the cleaning liquid by means of droplet applicator or the like.

Typically the PROLEN solution described above is used as a regular daily cleaning agent. This will remove most of the deposits normally found on the lens but will not completely remove the Lipid deposits. The steady build-up of Lipids is conveniently removed by periodically (e.g. monthly) cleaning the lens in LIPREN as described above. The Lipase in a phosphate buffer forming the LIPREN effectively removes the Lipid build-up.

CLAIMS:

1. An enzyme containing liquid for cleaning soft contact lenses consisting of a solution containing a lipolytic enzyme and a phosphate buffer.

2. A liquid according to claim 1, in which the Lipase is derived from cand. cylindracae, lyophilised.

3. A liquid according to claim 2 in which there are 100 units of the Lipase in 10 ml of 0.1M phosphate buffer.

4. A liquid according to any of the preceding claims containing additionally a proteolytic enzyme.

5. A liquid according to claim 4 in which the proteolytic enzyme is Papain or Bromelain..

6. A liquid according to claim 5 consisting of

Purified fruit bromelain	50-500 g, e.g. about	100 g.
Sorbitol	100-1000 g, " "	500 g.
Mannitol	10-100 g, " "	50 g.
Sodium hydrogen sulphite	8-12 g, " "	10 g.
Ethylenediaminetetraacetic acid disodium salt	0.8-12 g, " "	1 g.
Potassium sorbate	10-1000 mg, e.g. "	100 mg.

diluted to 1 litre aqua dest., together with Lipase from cand. cylindracae, preferably in an amount corresponding to about 50000 units, in 1000 ml. 0.1 M Phosphate buffer in an aqueous polymer complex.

7. A liquid according to any of the preceding claims, which is hypertonic.

8. A method of cleaning a soft contact lens by removing deposits from the surface of the lens by enzymatic action comprising the steps of

a) placing at least one drop of a solution containing a lipolytic enzyme and in addition, optionally, a proteolytic enzyme, such as Papain or Bromelain, on

the surface of the lens which is to be cleaned, to reduce both the Albumin and Lipids present on the surface to water soluble peptones, and fatty acids and esters and

b) subsequently removing the resulting products by rinsing and boiling the lens in a physiological saline solution.

9. A method as claimed in claim 8 wherein the enzymatic activity of the said solution is of the order of 100 tyrosine units per µg of protein.

10. A method as claimed in claim 8 or 9 in which the said at least one drop of solution containing a lipolytic enzyme and, optionally a proteolytic enzyme is left on the surface of the lens to be cleaned for a period of about 15 minutes.

11. A method as claimed in any one of claims 8 to 10 wherein the physiological saline solution has a particle size below about 0.2 micron, is isotonic, has a pH-value of about 7.0 and a buffer capacity of 6-8 and is also sterile.

12. A method as claimed in any one of claims 8 to 11 wherein the enzyme solution which is applied to the lens consists of Bromelain, Mannitol, Sorbitol, Ethylenediaminetetraacetic acid, Sodium Metabisulphite and a Lipase.

13. A method as claimed in any of claims 8 to 11 in which the enzyme solution consists of:

Purified fruit bromelain	50-500 g,	e.g. about	100 g.
Sorbitol	100-1000 g,	" "	500 g.
Mannitol	10-100 g,	" "	50 g.
Sodium hydrogen sulphite	8-12 g,	" "	10 g.
Ethylenediaminetetraacetic acid disodium salt	0.8-1.2 g,	" "	1 g.
Potassium sorbate	10-1000 mg,	" "	100 mg.

diluted to 1 litre aqua dest., together with Lipase from cand. cylindracae, preferably in an amount corresponding to about 50000 units, in 1000 ml. 0.1 M Phosphate buffer in an aqueous polymer complex.

14. A method of cleaning a soft contact lens comprising the steps of placing the lens in contact with a solution as claimed in any of claims 1-6 for a first specified period of time, rinsing it in a saline solution, removing it and boiling it for a second specified period of time in a saline solution and thereafter rinsing it again in a saline solution.

15. A method as claimed in claim 14 in which the first specified period of time is 30 minutes and the second specified period of time is 20 minutes.

16. A method of cleaning a soft contact lens comprising the steps of placing the lens in contact with a solution as claimed in any of claims 1-6 for a specified period of time, removing it from the solution and rinsing it in dest. water, heating it in a saline solution to a given temperature for a second specified period of time, subsequently rinsing it in dest. water and thereafter boiling it in saline solution for a third specified period of time and rinsing it in saline solution.

17. A method as claimed in claim 16 in which the first specified period of time is 8 to 10 hours, the second specified period of time is 30 minutes, the given temperature is 40°C and the third specified period of time is also 30 minutes.

18. Dry composition of matter comprising a lipolytic enzyme, buffer and additional substances so as to form, when dissolved in water, a hypertonic soft contact lens cleaning liquid.

19. Composition according to claim 18, further comprising a proteolytic enzyme.

20. Composition according to claim 19, comprising Bromelain, Mannitol, Sorbitol, Ethylenediaminetetraacetic acid, Sodium Metabisulphite and a Lipase.

21. Composition according to any of claims 18-20, comprising as a buffer a phosphate buffer.