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(54) Benævnelse: **FREMGANGSMÅDE OG KIT TIL FUGTNING AF OVERFLADEN AF ØJNE**

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Description

Field of the Invention

[0001] The invention pertains to the field of care of the surface of the eye, including the sclera, conjunctiva, and cornea. More particularly, the invention pertains to the application of fluids for moisturizing the surface of the eye.

BACKGROUND OF THE INVENTION

[0002] In normal situations, the surface of the eye, including the sclera, the conjunctiva, and the cornea, is kept moist by the presence of a tear film. This tear film is found in virtually all terrestrial vertebrates, with the exception of snakes.

[0003] The surface area of the eye in an adult human is about 2 cm^2. It is covered by a complex tear film having a trilaminar structure, with each of the layers having a discrete and necessary function.

[0004] Nearest to the surface of the eye is an inner layer of mucus approximately 10 to 20 μm in thickness. The mucus in this layer stabilizes the tear film and provides for attachment of the tear film to the underlying cornea and conjunctiva. The mucus also reduces the surface tension between the tear film and the eye and so permits the tear film to spread evenly across the eye.

[0005] The middle layer of the eye is an aqueous layer that is composed largely of water, electrolytes, and various proteins. This layer contains about 2 to 5 μl of aqueous fluid and forms the bulk of the tear film. Within this layer, pH, osmotic pressure, oxygen tension, and the levels of electrolytes such as potassium, calcium, chloride, inorganic phosphates, and acids such as lactic acid and citric acid, are maintained within narrow physiologic ranges. Proteins present in the aqueous layer of the tear film include albumin, and other proteins, such as immunoglobulins, interferon, β-lysin, and lysozyme which have antimicrobial activities.

[0006] Farthest from the surface of the eye is a lipid layer, which may range in thickness from a single monolayer to nearly 200 nm. Ordinarily, this layer is about 100 nm thick. This layer serves to retard evaporation of the tear film.

[0007] The tear film rapidly decreases in thickness following a blink. Without a subsequent blink, holes will begin to form in the tear film, called tear breakup, within about 30 seconds. Tear breakup times lower than 10 seconds are considered to be abnormal. This can occur with decreased tear formation or deficiencies in the mucus layer of the tear film. Other situations that can result in dryness of the eye surface include environmental aridity, contact lens wearing, and upon waking.

[0008] Typically, dryness of the eye is treated with water based solutions containing electrolytes and preservatives which maintain sterility of the solution for multiple applications. Solutions without preservatives are usually packaged in containers that provide for a single use, with disposal of the container and any residual solution following the single application.

[0009] The solutions are generally applied by drops, which provide about 20 to 25 μl of fluid to the eye surface. The application of eye drops results in rapid moisturizing of the eye. However, because the amount delivered is greater than the volume of the tear film, these drops have the disadvantage of flooding the eye, which washes away the tear film and replaces the tear film with the fluid that comprises the drops. Immediately following this flooding there exists a period of time when the normal tear film, with its three

layer structure and the constituents of each layer, is not present on the eye surface. This can result in incomplete eye moisturizing which lasts for several blink cycles.

[0010] Other methods of administration of liquids onto the surface of the eye include eye cups, aerosol and pump sprays, and misters. Eye cups are used to bathe the surface of the eye in fluid, which results in flooding and washing away the tear film that is present on the eye surface. A mister that can be used to deliver a spray of droplets to the eye is described in Hahn, U.S. Patents Nos. 5,346,132 and 5,893,515.

[0011] In these patents, Hahn discloses several disadvantages of delivering fluid to the eye by drops, including difficulty in positioning the dropper and incomplete delivery of medications due to missing the eye and spilling onto the face. Hahn does not address the issue of the quantity of fluid that is administered to the eye or the issue of washing away the tear film due to flooding. The mister of Hahn delivers a measurable quantity of fluid and can be used for household or medical purposes or to moisturize the eyes or the skin.

[0012] Another mister is described in Hutson, U.S. Patent No. 5,588,564. Like the mister of Hahn, the mister of Hutson can be used to deliver an adjustable and repeatable dose of fluid to the surface of the eye. Hutson does not address the issue of the quantity of fluid that is administered to the eye or the issue of washing away the tear film due to flooding. WO97/23177 discloses the dosage of ophthalmic treatment liquid in the form of a jet or stream of droplets.

[0013] A need exists for a method to moisturize the surface of the eye without flooding the eye or destroying the integrity of the natural tear film.

BRIEF SUMMARY OF THE INVENTION

[0014] It has been unexpectedly discovered that administering an amount of fluid to the surface of the eye at a level below that which results in flooding and washing away the tear film results in an improvement in eye moisturizing over prior art methods.

[0015] In one embodiment, the invention is a method for moisturizing the eye. The method comprises steps as disclosed in the claims. The method according to the disclosure includes obtaining an applicator that can controllably deliver an aqueous fluid to the surface of the eye in a quantity below that which will flood the eye. In this manner, the method of the disclosure serves to rehydrate the aqueous layer of the tear film and leaves the normal trilaminar tear film intact. In accordance with the method of the invention, the quantity of fluid that is administered to the eye surface is less than about two times the volume of the normal aqueous layer of the tear film, that is less than about 10 µl. Preferably, between 0.5 and 6 µl is administered, and most preferably, between 2 and 5 µl is administered. The fluid may be administered to the eye surface in a single bolus, or may be administered over time, in ten seconds or less, preferably 5 seconds or less, in accordance with the invention.

[0016] The fluid is delivered as a fine mist. It has been discovered that aqueous fluids in the form of a fine mist are extremely well suited for rehydrating the aqueous portion of the tear film, without rinsing away the tear film.

[0017] In another embodiment, the invention is a kit for delivering a composition for moisturizing the eye. In accordance with the invention, the kit contains an aqueous fluid composition, a container that holds the composition, and an applicator that, when actuated, controllably administers between about 0.5 and 10 µl of the pharmaceutical composition to a surface of about 2 cm^2 in about 10 seconds or less, preferably about 5 seconds or less. Preferably, the kit further contains instructions to controllably apply the pharmaceutical composition to the surface of the eye using the kit.

[0018] According to the present disclosure there is provided the use of an aqueous fluid consisting essentially of water for the manufacture of a product for moisturizing the eye, wherein the aqueous fluid is for spraying onto the surface of the eye in the form of a mist consisting essentially of droplets having an average diameter between 5 and 150 microns and wherein the amount of the aqueous fluid that is for spraying onto the surface of the eye is sufficient to hydrate the aqueous layer of the tear film of the eye but is below that which will wash away the tear film.

[0019] In a further aspect of the present invention, there is provided an eye-moisturizing kit comprising a sealed container, an aqueous fluid consisting essentially of water within said container, and an actuator that sprays a mist of said fluid from said container onto the surface of the eye in an amount that is sufficient to moisturize the aqueous layer of the tear film on the surface of the eye and less than an amount that washes away the tear film.

[0020] The present invention is set out in the appended dependent claims.

BRIEF DESCRIPTION OF THE DRAWING

[0021] FIG. 1 shows one embodiment of the kit of the invention for moisturizing the eye in accordance with the method of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0022] It has been discovered that a sudden increase in humidity to the tear film, as opposed to a splash of fluid such as occurs with presently available droppers and misters, increases the water content of the tear film while causing little or no displacement of the tear film.

[0023] In accordance with the invention, the volume of the tear film the surface of the eye is increased by applying a fluid in an amount not greater than about 100 to 200% of the volume of the aqueous portion of the tear film, which generally has a volume of 2 to 5 µl. Thus, in accordance with the invention, about 10 µl or less is applied to the surface of the eye. Preferably, 0.5 to 6 µl is applied, and most preferably 1 to 2 µl is applied, especially when moisturizing the eye because of the presence of dry eye, in which the total tear volume is typically between 1 to 2 µl. The volume of fluid in accordance with the invention acts to rehydrate the aqueous portion of the tear film and maintains the integrity of the overlying lipid and the underlying mucus layers.

[0024] In contrast with the present state of the art in which 20 to 50 µl of fluid is applied to the eye by dropper or by spray, the method in accordance with the invention reestablishes the normal state in individuals with dry eye. Present methods merely wash away the existing tear film and replace the tear film, or at least the middle aqueous layer, with an aqueous solution. These solutions lack the structure of the intact tear film and also differs from the normal aqueous layer of the tear film.

[0025] Generally, the above amount of fluid which is applied in accordance with the invention is applied during one blink cycle, that is between blinks. However, the fluid may be applied during a period of time in which one or more blinks occurs. Preferably, the fluid is applied within a period of 5 to 10 seconds or less.

[0026] The fluid is administered as dispersed droplets in air (mist), in particular in the form of a fine mist of discrete liquid droplets in which the average size of the fluid droplets is between about 5 and 150 microns in diameter. It has been found that a fine mist composed of droplets of this size range, preferably between about 0.1 % to 1 % of the tear volume per droplet, provides optimal hydration of the tear film and moisturization of the surface of the eye. Preferably, the average size of the fluid droplets is less than 100 microns, and more preferably less than 75 microns. Most preferably, the droplets have a diameter between 10 and 50 microns,

with a most preferred range between 15 and 30 microns in diameter. Droplets above about 100 microns in diameter tend to incompletely vaporize and will fall out and produce undesirable wetting of the face and on horizontal surfaces. Droplets below about 20 microns in diameter are generally considered to be inhalable and can be aspirated into the upper and lower respiratory passages. This is acceptable when delivering a substance to the surface of the eye which is not potentially harmful to the respiratory system, such as a water.

[0027] The fluid that is delivered to the surface of the eye in accordance with the invention is a water based fluid. For moisturizing the eye, the fluid preferably is an aqueous fluid having a pH of neutral to slightly acidic, such as between about 7 to about 6.5. Preferably, the fluid has a low concentration of solutes, less than that of the normal tear film. In accordance with a preferred embodiment of the invention, the osmotic pressure of the fluid is less than 350 mOsm and most preferably less than 311 mOsm.

[0028] It is further preferred that the water be hypoallergenic and substantially free of preservatives and other chemical compounds that have a potential to irritate the surface of the eye.

[0029] The aqueous fluid delivered to the surface of the eye consists essentially of water. The water may contain trace amounts of minerals. It is most preferred, however, that the amount of minerals in the fluid be as small as possible. The water is free of constituents such as lubricants, preservatives, buffering agents and surfactants.

[0030] In another embodiment, the invention is a kit for administering a controlled dosage of between 0.5 and less than 10 µl and most preferably less than 5 µl. In the most preferred embodiment, the controlled dosage is between 1 and 2 µl of fluid. In accordance with the invention, the kit contains a container, an aqueous fluid within the container, and an actuator that delivers a spray or fine mist of fluid in the dosage described above. It is preferred that the mist be composed of discrete droplets having an average size of about 5 to 150 microns in diameter, most preferably less than 100 microns, even more preferably less than 75 microns, most preferably less between 10 and 50 microns with a most preferred range between 15 and 30 microns in diameter. The kit may further contain instructions to apply the controlled dosage of the aqueous fluid to the surface of the eye. Preferably, the container of the kit is hermetically sealed so that it may be used for multiple applications of the aqueous fluid over several days to months without the need to include a preservative in the fluid.

[0031] A preferred embodiment of the kit of the invention is shown diagrammatically in FIG. 1. FIG. 1 shows a package such as a box 101 for containing a rigid, preferably metallic, hermetically sealed container 102, inside of which is an inner hermetically sealed flexible pouch 103, which contains a fluid to be dispensed. There is a pressurization agent such as compressed air or nitrogen 104 between the hermetically sealed container 102 and the flexible pouch 103, and an actuator 105 that permits the proper dosage of the fluid in the pouch 103 to escape when depressed. The kit further contains instructions (not shown) for delivering a pre-determined dosage of the fluid into the eye.

[0032] The invention is further described in the following non-limiting examples.

Example 1

[0033] The volume of the tear film on the eyes of three adult human subjects is measured and determined to average 2.26 µl. The subjects are then treated by administering to surface of their eyes fine mist of between 50 and 100 micron average droplet size, with a total volume of between 2 to 5 µl within a period of 10 seconds per eye. Following administration, the tear volume is again measured and is determined to average 2.96 µl.

Example 2

[0034] Samples of the tear film from three adult human subjects are obtained and subjected to HPLC chromatography to determine the baseline level of proteins and other constituents in the tear film. One eye from each of the subjects is then moisturized by administration of a standard drop of artificial tears of between 25 and 50 µl. Samples of the tear film from the three treated eyes are then obtained and subjected to HPLC chromatography. After obtaining the second group of samples, the opposite eye of each of the subjects is then moisturized by administration of the same artificial tears but in a fine mist made of droplets having a size between 50 and 100 microns for a total volume of about 5 µl. Samples of the tear film from the mist-treated eyes are then obtained and subjected to HPLC chromatography. The artificial tears are also subjected to HPLC chromatography.

[0035] The initial HPLC chromatography provides a profile of the constituents found in the normal tear film. It is found to contain various lipids, mucus, proteins, and electrolytes.

[0036] The HPLC chromatography following moisturization by a single large drop reveals that most if not all of the lipids and mucus remain in the tear film. The proteins and electrolytes that are present in the normal tear film are no longer present and the tear film has a chromatography profile similar to that of the artificial tears, minus the lipids and mucus.

[0037] The HPLC chromatography following moisturization by the fine mist reveals that the lipids and mucus remain in the tear film. The proteins and electrolytes that are present in the normal tear film are demonstrated by the chromatography to remain in the tear film following moisturization by the fine mist.

Patentkrav

1. Ikke-terapeutisk fremgangsmåde til fugtning af øjne, hvilken fremgangsmåde omfatter indgivelse af et vandigt fluid, der består af vand og, eventuelt, spormængder af mineraler, på overfladen af øjet i form af en em, der består af dispergerede vandige fluidsmådråber i luft, hvilke dråber har en gennemsnitlig diameter på mellem 5 og 150 µm, hvor mængden af det vandige fluid er på mellem 0,5 og 10 µl.

2. Fremgangsmåde ifølge krav 1, hvor det vandige fluid har en osmolaritet, der er mindre end den for det normale vandige lag af tårefilmen.

3. Fremgangsmåde ifølge et hvilket som helst af kravene 1 og 2, hvor det vandige fluids osmolaritet er mindre end 311 mOsm.

4. Fremgangsmåde ifølge et hvilket som helst af kravene 1 til 3, hvor det vandige fluids pH er på mellem 7 og 6,5.

5. Fremgangsmåde ifølge krav 4, hvor pH'et er 6,5.

6. Fremgangsmåde ifølge et hvilket som helst af kravene 1 til 5, hvor det vandige fluid indgives inden for en periode på 5 sekunder.

7. Fremgangsmåde ifølge et hvilket som helst af kravene 1 til 6, hvor mellem 0,5 og 10 µl indgives på overfladen af øjet.

8. Fremgangsmåde ifølge krav 7, hvor mellem 0,5 og 6 µl indgives på overfladen af øjet.

9. Fremgangsmåde ifølge krav 8, hvor mellem 2 og 5 µl indgives på overfladen af øjet.

10. Fremgangsmåde ifølge et hvilket som helst af de foregående krav, hvor emmen indgives fra en anordning, der omfatter en forseglet beholder, et vandigt fluid, der består af vand og, eventuelt, spormængder af mineraler, inde i beholderen, og en aktuator til indgivelse af en em af det vandige fluid fra beholderen, og hvor det vandige fluid indgives til overfladen af øjet inden for en periode på 5 sekunder eller mindre.

11. Fremgangsmåde ifølge krav 10, hvor anordningen endvidere omfatter en forseglet fleksibel pose, der indeholder det vandige fluid i beholderen og et tryksætningsmiddel mellem beholderen og posen.

12. Kit til fugtning af øjne, der omfatter en forseglet beholder, et vandigt fluid, der består af vand og, eventuelt, spormængder af mineraler, inde i beholderen, og en aktuator, der sprøjter en em af det vandige fluid fra beholderen på overfladen af øjet, hvilken em består af dispergerede vandige fluidsmådråber i luft, der har en gennemsnitlig diameter på mellem 5 og 150 µm i en styret dosering på mellem 0,5 og 10 µl.

13. Kit ifølge krav 12, der endvidere omfatter en forseglet fleksibel pose inde i beholderen, hvilken pose indeholder det vandige fluid, og et tryksætningsmiddel mellem beholderen og posen.

14. Kit ifølge kravene 12 eller 13, hvor aktuatoren på en kontrolleret måde administrerer mellem 0,5 og 10 µl af det vandige fluid til en overflade på 2 cm^2 på 5 sekunder eller mindre.

15. Kit ifølge et hvilket som helst af kravene 12 til 14, der endvidere omfatter en emballage, der rummer den forseglede beholder og instruktioner til påføring af det vandige fluid til overfladen af øjet.

16. Kit ifølge et hvilket som helst af kravene 12 til 15, hvor emmen består af smådråber af det vandige fluid, der har en gennemsnitlig diameter på mindre end 100 µm.

17. Kit ifølge et hvilket som helst af kravene 12 til 16, hvor beholderen er en ubøjelig beholder.

18. Kit ifølge krav 17, hvor den ubøjelige beholder er metallisk.

Drawing

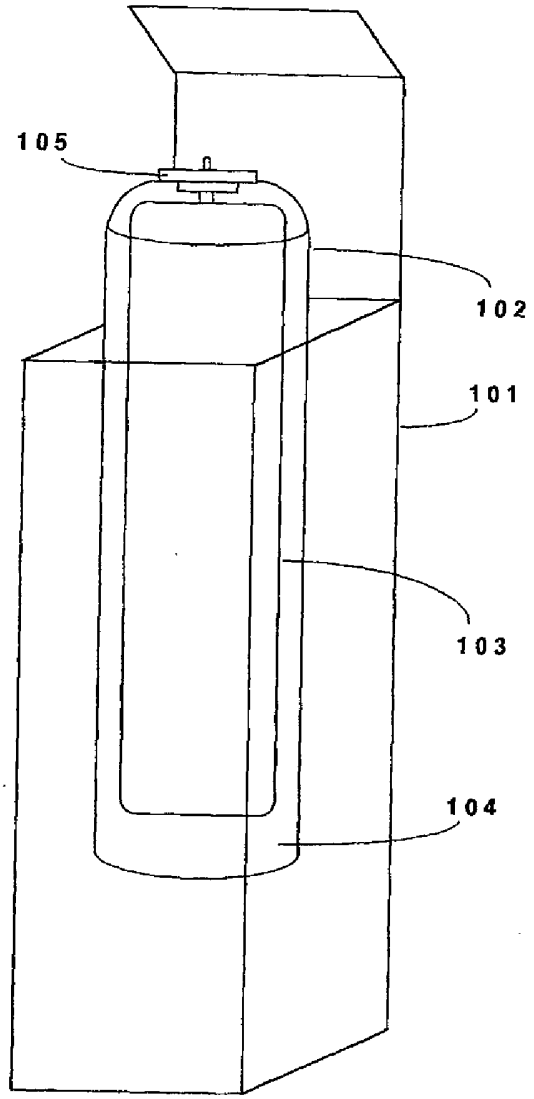


FIGURE 1