

DEGRADABLE TEAR DUCT PLUG, PREPARATION METHOD THEREFOR AND APPLICATION THEREOF

Cross-reference to related application

The present application claims priority to Chinese Patent Application No. 201910927365.1, entitled “Degradable tear duct plug, preparation method therefor and application thereof”, and filed on September 27, 2019, the entire disclosure of which is incorporated herein by reference in its entirety.

Technical Field

The present invention relates to the technical field of medicine, specifically, to a degradable tear duct plug, a preparation method therefor and an application thereof.

Background Art

Dry eye is a multifactorial tear and ocular surface disorder that can cause symptoms of ocular discomfort (severe dry eye, foreign body sensation, dryness, burning sensation, photophobic lacrimation), impaired vision (visual fatigue, blurred vision or fluctuant vision), tear film instability and potential damage to the ocular surface, and is often accompanied by increased tear film osmotic pressure and ocular surface inflammation, and also can cause rapid decline in visual function and even blindness in severe cases. For a long time, with the change of people's living and working environment, the popularization of computers, air pollution and other factors, the prevalence of dry eye has gradually increased. The dry eye has become one of the most common diseases in ophthalmology clinics, and the age of onset tends to be younger.

Existing epidemiological studies show that about one in five of people in the United States suffers from dry eye of varying degrees, and the prevalence rate increases significantly with age increasing. It has been reported that about 50% of middle-aged women aged 35 to 60 in the United States suffer from dry eye, and 14.6 % of the elderly suffer from severe dry eye. In modern society, the incidence rate of dry eye is increasing due to significant changes in living environment and patterns, and the dry eye has seriously threatened the patients' normal life, including reading, work, and driving and so on. Aiming at this disease, the more common methods for clinical treatment of dry eye are artificial tears, lacrimal punctum closure and lacrimal duct embolization. Among them, the treatment method of artificial tears requires a longer treatment time and can only treat mild dry eye, and the dry eye is prone to recurrence. Although the lacrimal punctum closure is simple and effective, it is easy to cause scarring and it

is accompanied by pain, and the operation is also irreversible. At present, the lacrimal duct embolization is the most effective method for treating dry eye. The lacrimal duct embolization is a relatively new technique of lacrimal duct closure, which reduces tear drainage by mechanically blocking the lacrimal duct and prolongs its residence time on the ocular surface, so as to improve the ocular surface environment and relieve dry eye symptoms, or prolong the time of the drug on the ocular surface, thereby improving the drug treatment effect and significantly reducing the symptoms of dry eye in patients.

The tear duct plug used in clinic can be mainly divided into two categories, degradable type and permanent type. The permanent tear duct plug is usually made of silicone or polyacrylate materials, and the materials themselves are not degradable. The degradable tear duct plug is mainly made of animal collagen, which can be automatically degraded in a short period of time (about one week) after implantation in the lacrimal duct, and mainly used for short-term experimental treatment and seasonal dry eye. When exposing to tears, the degradable tear duct plug becomes larger in volume, and its length and diameter increase, which requires a relatively deep implantation position, thus the degradable tear duct plug has the defects of easy slippage after implantation, short maintenance time and high price.

In this regard, Chinese patent application CN109077993A discloses a lacrimal canaliculus sustained-release hydrogel implant and a preparation method thereof to cope with the above-mentioned defects. The implant adopts PEG derivative material as a carrier, and in addition to having a drug loaded to achieve drug treatment effect, it also has the function of lacrimal duct embolization in form. The implant has intelligent characteristics that it will automatically shorten and thicken when encountering water, and can retract into the depth of the tear duct, effectively avoiding slipping. However, the preparation method of the implant involves secondary drying, and the production cycle is long. In addition, during the preparation process, the polyethylene glycol (PEG) derivative phase and the trilycine acetate phase are mixed first, which may cause bubbles to be generated in the mixed system during the preparation process. Moreover, because the cross-linking reaction occurs immediately after mixing, the viscosity gradually increases, and once the gel is formed, the fluidity is lost, and the subsequent pouring cannot be carried out. Therefore, it is necessary to mix well quickly and perform pouring quickly, which causes the bubbles to exist in the gel because there's no enough time to eliminate bubbles, resulting in the phenomenon of uneven surface of a part of the dry gel obtained after vacuum drying and affecting the uniformity of the product. Moreover, the subsequent hydrogel stretching requires secondary drying, which is not conducive to industrial production.

Therefore, there is a need to provide a new degradable tear duct plug and its preparation method and application to solve the problems of the prior art.

Summary of the Invention

In order to solve the problems existing in the prior art, one of the purposes of the present invention is to provide a method for preparing a degradable tear duct plug with a short production cycle and uniform product quality.

In order to realize the purpose of the present invention, the technical solutions of the present invention are as follows:

A method for preparing a degradable tear duct plug comprises: first, putting a component A containing a polyethylene glycol derivative into a first material channel, and putting a component B containing a trilycine acetate into a second material channel; and then, extruding the component A from the first material channel and the component B from the second material channel, respectively, into a same mixing channel for static mixing to form a hydrogel, and heating and stretching the hydrogel after drying.

The present invention does not specifically define the first material channel, the second material channel and the mixing channel, as long as they can achieve the purpose of the present invention. For example, the first material channel and the second material channel can be conventional syringes, double drug mixers, pipes and the like, but are not limited thereto; and the mixing channel can be silicone tubes, static mixers and the like, but is not limited thereto.

When the tear duct plug is conventionally prepared, the gel contains air after the polyethylene glycol derivative phase and the trilycine acetate phase are mixed, resulting in the phenomenon of uneven surface of the dried gel obtained by vacuum drying, thus it is unable to obtain uniform products. The preparation method of the present invention can avoid the mixing of bubbles, so that the uniformity property of product is greatly improved. Moreover, the polyethylene glycol derivative phase and the trilycine acetate phase do not need to be totally mixed together, but are gradually micro-mixed as the two phases continue to be extruded separately from the material channels. Due to the small mixing volume, the mixing efficiency is high and the uniformity is good. Instantly mixing and pouring can be achieved, and the whole process is not affected by the gelation time.

In addition, it is found through research that the chemically cross-linked gel prepared by the method of the present invention can be suitable for direct heating and stretching treatment after drying, and has good stretching performance and uniform stress on the whole gel, so that the

prepared dry gel can be quickly and easily stretched for forming. This avoids the problems that the stretching properties of the existing conventional dry gel is poor when it is stretched in a silicone tube; it is difficult to maintain the stretched state because the two ends are easily broken during the drying process; the dry gel bends and is not easy to be taken out from the silicone tube and cut after the silicone tube is retracted; and the difference between batches is large, the industrial production is difficult, and so on. Moreover, compared with the existing method of drying the hydrogel first, then taking it out, placing it in a high-humidity environment for stretching, and then drying it again, the present method avoids secondary drying, shortens production cycle, and saves production cost.

In the method of the present invention, the hydrogel is dried at a temperature of 60°C to 80°C for 4 to 8 h.

The continuous mixing process of the polyethylene glycol derivative solution and the trilycine acetate solution of the present invention can be performed by using a double syringe (double drug mixer) or a microchannel reactor. The microchannel reactor can be T-shaped or Y-shaped, and the diameter or width of the channel is 0.1 to 2.0 mm, preferably 0.4 to 1.0 mm, so as to control the mixing rate more easily.

In the method of the present invention, a speed ratio of the component A and the component B entering the mixing channel is (2 to 5):1, preferably (3 to 4):1, so that the gel cross-linked space network structure is more uniform, which further ensures the uniformity of the diameter of the dry gel during heating and stretching subsequently. A speed of the static mixing is 10 to 100 ml/min, preferably 30 to 60 ml/min so as to facilitate uniform mixing.

The mixing of the component A and the component B of the present invention can be carried out directly at normal temperature.

In the method of the present invention, the temperature for heating and stretching the hydrogel is 40°C to 80°C, preferably 50°C to 70°C.

If the heating temperature is lower than 40°C, the dry gel of the present invention cannot be sufficiently softened and cannot be effectively stretched, and if the heating temperature is higher than 80°C, the dry gel will be too soft and the pressure resistance will be deteriorated, and the dry gel are easy to break at two ends during the fixing process and cannot be stretched.

In the method of the present invention, a stretching rate for heating and stretching the hydrogel is 0.2 to 2.0 m/s, preferably 0.6 to 1.2 m/s, so as to obtain a dry gel with a more uniform diameter during stretching.

In the method of the present invention, the stretching ratio for heating and stretching is 1 to

5 times.

In the method of the present invention, the component A is a borax buffer containing polyethylene glycol derivative with a concentration of 5% (w/v) to 40% (w/v).

In the method of the present invention, the component B is a borax buffer containing tryllysine acetate with a concentration of 1% (w/v) to 5% (w/v).

In the method of the present invention, a mass ratio of the polyethylene glycol derivative and the tryllysine acetate is (20 to 50):1.

In a preferred embodiment of the present invention, the concentration of polyethylene glycol derivative in the component A is 30% (w/v), the concentration of tryllysine acetate in the component B is 3% (w/v), and the mass ratio of the polyethylene glycol derivative and the tryllysine acetate is 30:1.

In the method of the present invention, the concentration of the borax buffer is 0.005 to 0.05 mol/L, preferably 0.01 to 0.03 mol/L. The gelation time of the present invention can be adjusted by adjusting the concentration of the borax buffer. Within the preferred range, the time for forming a gel after mixing the component A and the component B of the present invention can be controlled within 3 to 10 minutes. If the concentration is too low, the gelation time is too long and if the concentration is too high, the gelation time is too short, which are not conducive to the control of production.

By adjusting the type and amount of the polyethylene glycol derivatives of the present invention, the density and strength of the steric crosslinking can be adjusted, so that the degradation period of the tear duct plug can be adjusted to be 3 to 90 days.

In the method of the present invention, the polyethylene glycol derivative is prepared by modifying polyethylene glycol by groups, and the group used for modifying polyethylene glycol is one or more selected from succinimidyl carbonate-SC, succinimidyl glutarate-SG, succinimidyl acetate-SCM, succinimidyl propionate-SPA, succinimidyl succinate-SS, succinimidyl valerate-SVA, and maleimide-MAL.

In the method of the present invention, the molecular weight of the polyethylene glycol derivative is 5,000 to 50,000.

In the method of the present invention, both the component A and the component B include a chromogenic reagent, and the contents of the chromogenic reagent in the component A and the component B are both 0.02% (w/v) to 0.2% (w/v).

In the method of the present invention, the chromogenic reagent is a non-toxic colored substance suitable for use in implanted medical instruments; preferably the chromogenic reagent

is N-hydroxysuccinimidyl fluorescein.

The non-toxic colored substance can be one or more selected from FD&C BLUE#1, FD&C BLUE#2, eosin, fluorescent yellow, methylene blue, indocyanine green, and N-hydroxysuccinimidyl fluorescein.

When N-hydroxysuccinimidyl fluorescein is used, since it can participate in the cross-linking reaction of the hydrogel, the color will disappear only after the gel is completely degraded. Compared to the chromogenic reagent that exists in the gel in the free molecular or ionic state, the color development effect of N-hydroxysuccinimidyl fluorescein will not decrease with tear loss.

In the method of the present invention, an ophthalmic drug can be dissolved or dispersed in component A or component B to play anti-inflammatory or anti-glaucoma effects. The ophthalmic drug is one or more selected from travoprost, latanoprost, cyclosporine, moxifloxacin, gatifloxacin, prednisolone, ibuprofen, dexamethasone, tobramycin, timolol, and atropine.

In a specific embodiment of the present invention, the method for preparing the above-mentioned degradable tear duct plug (lacrimal canalicular sustained-release hydrogel implant) of the present invention may specifically comprise the following steps:

- (1) dissolving a polyethylene glycol derivative in a borax buffer containing a chromogenic reagent, and transferring the resultant to a first material channel;
- (2) dissolving a trilycine acetate in a borax buffer containing a chromogenic reagent, and transferring the resultant to a second material channel;
- (3) pouring the resultants obtained in steps (1) and (2) into a silicone tube;
- (4) leaving the silicone tube to stand to form a hydrogel, and then vacuum drying to constant weight;
- (5) pulling out the dry gel from the silicone tube, and performing stretching (using a stretcher) after heating and softening;
- (6) naturally cooling the stretched gel to room temperature, and then cutting the gel to obtain a tear duct plug.

In yet another specific embodiment of the present invention, the method for preparing the above-mentioned degradable tear duct plug (lacrimal canalicular sustained-release hydrogel implant) of the present invention may specifically comprise the following steps:

- (1) dissolving a polyethylene glycol derivative in a borax buffer containing a chromogenic reagent, and transferring the resultant to a syringe of a double drug mixer;
- (2) dissolving a trilycine acetate in a borax buffer containing a chromogenic reagent, and

transferring the resultant to the other syringe of the double drug mixer;

(3) pushing the double drug mixer and pouring the instantly mixed solution into a silicone tube immediately;

(4) leaving the silicone tube to stand to form a hydrogel, and then vacuum drying to constant weight;

(5) pulling out the dry gel from the silicone tube, and performing stretching (using a stretcher) after heating and softening;

(6) naturally cooling the stretched gel to room temperature, and then cutting the gel to obtain a tear duct plug.

Another object of the present invention is to provide a rod-shaped intelligent degradable tear duct plug, which can automatically shorten and thicken after being inserted into the lacrimal canaliculus.

The degradable tear duct plug of the present invention is prepared by the above method.

The degradable tear duct plug matrix material of the present invention is polyethylene glycol derivatives and trily sine acetate. The tear duct plug has a diameter of 0.3 to 0.5 mm, preferably 0.35 to 0.45 mm, and a length of 2 to 6 mm, preferably 3 to 5 mm. The tear duct plug expands to 0.8 to 2.0 mm, preferably 1.0 to 1.5 mm in diameter; and is shortened in length by 10% to 60 %, preferably 20% to 40 % after encountering water. The degradable tear duct plug can be retracted deep into the tear duct, effectively avoiding slipping.

Preferably, the degradable tear duct plug of the present application may further comprise an ophthalmic drug, preferably the ophthalmic drug is one or more selected from travoprost, latanoprost, cyclosporine, moxifloxacin, gatifloxacin, prednisolone, ibuprofen, dexamethasone, tobramycin, timolol, and atropine.

Another purpose of the present invention is to provide use of the above-mentioned degradable tear duct plug in the treatment of dry eye.

The present invention also provides use of the degradable tear duct plug in the treatment of eye inflammation.

The present invention also provides use of the degradable tear duct plug in the treatment of glaucoma.

The beneficial effects of the present invention are at least as follows:

(1) Due to the use of a hot stretching method for a dry gel, the gel only needs to be cooled to room temperature naturally after stretching, and moisture absorption and secondary drying are not needed, which shortens the production cycle.

(2) In the preparation method of the present invention, the polyethylene glycol derivative phase and the trilycine acetate phase do not need to be mixed in advance, but the two phases are injected separately, and subjected to micro-mixing at the intersection, so that the mixing efficiency is high, the uniformity is good, instantly mixing and pouring can be achieved, the whole process is not affected by gelation time, and bubbles will not occur in the product, the quality of the product becomes uniform, and the product is suitable for hot stretching preparation.

(3) The degradable tear duct plug prepared by the present invention does not contain bubbles, has a smooth appearance, and has a uniform and stable quality.

(4) The degradable tear duct plug prepared by the present invention can be used for treating dry eye, improving the ocular surface environment and alleviating dry eye symptoms.

Specific Modes for Carrying Out the Embodiments

The preferred embodiments of the present invention will be described in detail below with reference to the Examples. It should be understood that the following Examples are given for illustrative purposes only, and are not intended to limit the scope of the present invention. A person skilled in the art can make various modifications and substitutions to the present invention without departing from the aim and spirit of the present invention.

The experimental methods used in the following Examples are conventional methods unless otherwise specified. The materials, reagents and the like used in the following Examples can be obtained from commercial sources unless otherwise specified.

Example 1

The specific steps for preparing the degradable tear duct plug of the present invention are as follows:

(1) 5000 mg four-arm PEG-SS (chemical name: 4-arm succinimidyl succinate, molecular weight 10000 ± 1000) was dissolved in 20 ml of 0.015 M borax buffer containing 20 mg N-hydroxysuccinimidyl fluorescein to obtain a component A, and the component A was transferred to one syringe of a double drug mixer (the diameter of the corresponding channel is 0.8 mm);

(2) 200 mg trilycine acetate was dissolved in 10 ml of 0.015 M borax buffer containing 10 mg N-hydroxysuccinimidyl fluorescein to obtain a component B, and the component B was transferred to the other syringe of the double drug mixer (the diameter of the corresponding channel is 0.8 mm);

(3) two syringes of the double drug mixer were pushed respectively, wherein the speed of the component A entering the mixing channel was 20 ml/min, and the speed of the component B entering the mixing channel was 10 ml/min; the instantly mixed solution was immediately poured in a silicone tube with an inner diameter of 2.0 mm;

(4) the silicone tube was left to stand to form a hydrogel, the resultant was cut into sections with about 30 cm of a length of each section, and then vacuum-dried at a temperature of 60°C for 6 h;

(5) the dry gel was pulled out from the silicone tube, heated for softening and stretched (using a stretcher), wherein the heating temperature was 60°C, the stretching ratio was 2 times, the stretching rate was 0.2 m/s, and the diameter of the tear duct plug was 0.5 mm;

(6) after the stretched gel was naturally cooled to room temperature, the stretched gel was cut to obtain a tear duct plug with a length of 3.0 mm.

The prepared tear duct plug has a yellow rod-like appearance, a smooth surface and a uniform diameter (0.5 ± 0.07 mm). After being placed in water for 10 minutes, the tear duct plug is shortened to 2.0 mm in length, and expanded to 1.5 mm in diameter. The degradation cycle in normal saline at 37°C is 14 days.

Example 2

The specific steps for preparing the degradable tear duct plug of the present invention are as follows:

(1) 9000 mg four-arm PEG-SG (chemical name: 4-arm succinimidyl glutarate, molecular weight 20000 ± 2000) was dissolved in 30 ml of 0.015 M borax buffer containing 30 mg N-hydroxysuccinimidyl fluorescein to obtain a component A, and the component A was transferred to one syringe of a double drug mixer (the diameter of the corresponding channel is 0.8 mm);

(2) 300 mg trilycine acetate was dissolved in 10 ml of 0.015 M borax buffer containing 10 mg N-hydroxysuccinimidyl fluorescein to obtain a component B, and the component B was transferred to the other syringe of the double drug mixer (the diameter of the corresponding channel is 0.8 mm);

(3) two syringes of the double drug mixer were pushed respectively, wherein the speed of the component A entering the mixing channel was 22.5 ml/min, and the speed of the component B entering the mixing channel was 7.5 ml/min; the instantly mixed solution was immediately poured in a silicone tube with an inner diameter of 2.0 mm;

(4) the silicone tube was left to stand to form a hydrogel, the resultant was cut into sections with about 30 cm of a length of each section, and then vacuum-dried at a temperature of 60°C for 6 h;

(5) the dry gel was pulled out from the silicone tube, heated for softening and stretched (using a stretcher), wherein the heating temperature was 60°C, the stretching ratio was 2 times, the stretching rate was 0.8 m/s, and the diameter of the tear duct plug was 0.5 mm;

(6) after the stretched gel was naturally cooled to room temperature, the stretched gel was cut to obtain a tear duct plug with a length of 3.0 mm.

The prepared tear duct plug has a yellow rod-like appearance, a smooth surface and a uniform diameter (0.5 ± 0.04 mm). After being placed in water for 10 minutes, the tear duct plug is shortened to 2.2 mm in length, and expanded to 1.4 mm in diameter. The degradation cycle in normal saline at 37°C is 35 days.

Example 3

(1) 8000 mg four-arm PEG-SS (chemical name: 4-arm succinimidyl succinate, molecular weight 20000 ± 2000) was dissolved in 40 ml of 0.015 M borax buffer containing 40 mg N-hydroxysuccinimidyl fluorescein to obtain a component A;

(2) 160 mg tryllysine acetate was dissolved in 10 ml of 0.015 M borax buffer containing 10 mg N-hydroxysuccinimidyl fluorescein to obtain a component B;

(3) the component A and the component B were respectively input into the two microchannels in a Y-type microchannel device through a constant-flux pump (both widths of the two microchannels were 0.4 mm, and the channel width after mixing is 0.8 mm), wherein the speed of the component A entering the mixing channel was 40 ml/min, and the speed of the component B entering the mixing channel was 10 ml/min; the instantly mixed solution was immediately poured in a silicone tube with an inner diameter of 3.0 mm;

(4) the silicone tube was left to stand to form a hydrogel, the resultant was cut into sections with about 30 cm of a length of each section, and then vacuum-dried at a temperature of 60°C for 6 h;

(5) the dry gel was pulled out from the silicone tube, heated for softening and stretched (using a stretcher), wherein the heating temperature was 60°C, the stretching ratio was 2.5 times, the stretching rate was 2 m/s, and the diameter of the tear duct plug was 0.4 mm;

(6) after the stretched gel was naturally cooled to room temperature, the stretched gel was cut to obtain a tear duct plug with a length of 4.0 mm.

The prepared tear duct plug has a yellow rod-like appearance, a smooth surface and a uniform diameter (0.4 ± 0.04 mm). After being placed in water for 10 minutes, the tear duct plug is shortened to 2.8 mm in length, and expanded to 1.2 mm in diameter. The degradation cycle in normal saline at 37°C is 7 days.

Comparative Example 1

The tear duct plug was prepared by the same method as that in Example 1 of the present invention, except that the polyethylene glycol derivative phase and the trilysine acetate phase were mixed by a shaking-mixing method, and the specific method is as follows: the trilysine acetate solution (component B) was poured into a syringe containing a polyethylene glycol derivative solution (component A), shaken by hand and turned upside down 10 times. The prepared tear duct plug has uneven appearance and nonuniform diameter (0.4 ± 0.15 mm) after hot stretching, with a large deviation range.

Comparative Example 2

The tear duct plug was prepared by the same method as that in Example 1 of the present invention, except that the speed of the component A entering the mixing channel was 15 ml/min, and the speed of the component B entering the mixing channel was 15 ml/min. The dry gel obtained after drying was easily broken during the stretching process after being heated, which does not meet the preparation requirements.

Comparative Example 3

The tear duct plug was prepared by the same method as that in Example 1 of the present invention, except that the addition of four-arm PEG-SS in step (1) was 2000 mg.

After the gel was dried, the dry gel was pulled out from the silicone tube, and it was found that the dry gel was obviously flat, and the ratio of the long diameter to the short diameter was about 2.0, which did not meet the product quality requirements.

Although the present invention has been described in detail above with general description and specific embodiments, some modifications or improvements can be made on the basis of the present invention, which will be obvious to a person skilled in the art. Therefore, these modifications or improvements made without departing from the spirit of the present invention fall within the scope of the claimed protection of the present invention.

Industrial applicability

The present invention provides a degradable tear duct plug, a preparation method therefor, and application thereof. The degradable tear duct plug of the present invention is prepared by the

following method, comprising: first, putting a component A containing a polyethylene glycol derivative into a first material channel, and putting a component B containing a trilysine acetate into a second material channel; and then, extruding the component A from the first material channel and the component B from the second material channel, respectively, into a same mixing channel for static mixing to form a hydrogel, and heating and stretching the hydrogel after drying. The method of the present invention adopts a continuous micro-mixing approach, instantly mixing and pouring can be achieved, and the pouring process is not affected by the gelation time, and the product does not generate bubbles and has uniform quality; due to the use of a hot stretching method for a dry gel, moisture absorption and secondary drying are not needed, and the process is simple. The degradable tear duct plug prepared by the present application contains no bubbles, has a smooth appearance and uniform quality, and is suitable for treating dry eye, and has good economic value and application prospect.

What is claimed is:

1. A method for preparing a degradable tear duct plug, characterized by comprising first, putting a component A containing a polyethylene glycol derivative into a first material channel, and putting a component B containing a trylisine acetate into a second material channel; and then, extruding the component A from the first material channel and the component B from the second material channel, respectively, into a same mixing channel for static mixing to form a hydrogel, and heating and stretching the hydrogel after drying.

2. The method according to claim 1, wherein a speed ratio of the component A and the component B entering the mixing channel is (2 to 5):1, preferably (3 to 4): 1, and a speed of the static mixing is 10 to 100 ml/min, preferably 30 to 60 ml/min.

3. The method according to claim 1 or claim 2, wherein the temperature for heating and stretching the hydrogel is 40°C to 80°C, preferably 50°C to 70°C; and/or a stretching rate for heating and stretching the hydrogel is 0.2 to 2.0 m/s, preferably 0.6 to 1.2 m/s.

4. The method according to any one of claims 1 to 3, wherein the component A is a borax buffer containing the polyethylene glycol derivative with a concentration of 5% (w/v) to 40% (w/v).

5. The method according to any one of claims 1 to 4, wherein the component B is a borax buffer containing the trylisine acetate with a concentration of 1% (w/v) to 5% (w/v).

6. The method according to any one of claims 1 to 5, wherein a mass ratio of the polyethylene glycol derivative and the trylisine acetate is (20 to 50):1.

7. The method according to any one of claims 1 to 6, wherein the polyethylene glycol derivative is prepared by modifying polyethylene glycol by a group, and the group used for modifying polyethylene glycol is one or more selected from succinimidyl carbonate, succinimidyl glutarate, succinimidyl acetate, succinimidyl propionate, succinimidyl succinate, succinimidyl valerate, and maleimide.

8. The method according to any one of claims 1 to 7, wherein the component A and/or the component B respectively further comprises a chromogenic reagent, and the chromogenic reagent is preferably N-hydroxysuccinimidyl fluorescein.

9. The method according to any one of claims 1 to 8, wherein the component A and/or the component B respectively further comprises an ophthalmic drug, and the ophthalmic drug is preferably one or more selected from travoprost, latanoprost, cyclosporine, moxifloxacin,

gatifloxacin, prednisolone, ibuprofen, dexamethasone, tobramycin, timolol, and atropine.

10. A degradable tear duct plug, characterized by being prepared by the method according to any one of claims 1 to 9.

11. The degradable tear duct plug according to claim 10, wherein the degradable tear duct plug has a diameter of 0.3 to 0.5 mm, preferably 0.35 to 0.45 mm, and a length of 2 to 6 mm, preferably 3 to 5 mm.

12. The degradable tear duct plug according to claim 10 or 11, wherein after encountering water, the degradable tear duct plug expands to 0.8 to 2.0 mm in diameter, preferably 1.0 to 1.5 mm; and is shortened in length by 10% to 60%, preferably 20% to 40%.

13. The degradable tear duct plug according to any one of claims 10 to 12, wherein the degradable tear duct plug comprises an ophthalmic drug, preferably the ophthalmic drug is one or more selected from travoprost, latanoprost, cyclosporine, moxifloxacin, gatifloxacin, prednisolone, ibuprofen, dexamethasone, tobramycin, timolol, and atropine.

14. Use of the degradable tear duct plug according to any one of claims 10 to 13 in the treatment of dry eye.

15. Use of the degradable tear duct plug according to any one of claims 10 to 13 in the treatment of eye inflammation.

16. Use of the degradable tear duct plug according to any one of claims 10 to 13 in the treatment of glaucoma.