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Brief Report

# Efficacy and Safety of KeraVio Using Violet Light-Emitting Glasses and Cyanocobalamin Drops for Progressive Keratoconus: A Pilot Study

Running head: KeraVio Without Cyanocobalamin Drops

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## Abstract

**Purpose:** To evaluate the efficacy and safety of KeraVio treatment, a minimally invasive corneal cross-linking technique that combines cyanocobalamin eye drops with violet light (VL) irradiation, in patients with progressive keratoconus. **Methods:** This prospective, single-arm exploratory study included three patients (mean age,  $36.67 \pm 11.24$  years; 2 males, 1 female) with progressive keratoconus. Treatment consisted of 0.02% cyanocobalamin eye drops administered six times daily and VL irradiation via TLG-003 eyeglasses worn 4.5 hours per day for three months. Patients were followed for six months. The primary endpoint was the change in maximum keratometry (Kmax). Secondary endpoints included thinnest corneal thickness (TCT), demarcation line (DL), best-corrected visual acuity (BCVA), uncorrected visual acuity (UCVA), manifest refraction, intraocular pressure, corneal endothelial cell density, corneal haze, slit-lamp/fundus examination findings, and periocular skin changes. **Results:** The mean Kmax change at 6 months was  $-0.37 \pm 6.82$  D. The mean change in the TCT was  $-7.33 \pm 19.66$   $\mu\text{m}$ . BCVA and UCVA remained stable (mean BCVA change:  $-0.03 \pm 0.15$  logMAR; mean UCVA change:  $0.04 \pm 0.07$  logMAR). No clinically observed changes in refraction, intraocular pressure, endothelial cell density, corneal clarity, or retinal findings were detected. No adverse events occurred. **Conclusions:** KeraVio treatment appeared to be safe for use in this small cohort. However, owing to the limited sample size and variable Kmax responses, further large-scale, controlled studies are needed to determine the efficacy of this treatment in the context of halting keratoconus progression.

**Keywords:** keratoconus; corneal cross-linking; violet light; cyanocobalamin eye

## Introduction

Keratoconus is a progressive ectatic corneal disorder characterized by thinning and anterior protrusion of the cornea, leading to irregular astigmatism, myopia, and visual impairment [1]. Conventional corneal cross-linking (CXL) with ultraviolet-A (UVA) and riboflavin slows disease progression but requires epithelial removal, which is associated with pain and potential complications such as infectious keratitis [2].

To address these limitations, a noninvasive approach using violet light (VL; wavelength 360–400 nm) has been developed. VL irradiation using eyeglass-type devices influences corneal biomechanics, and the KeraVio protocol combines VL with a photosensitizer to achieve corneal cross-linking without epithelial removal [3–5].

In previous KeraVio treatments, we used flavin adenine dinucleotide (FAD), a compound similar to riboflavin [3]. However, the supply of the active ingredient will be discontinued after 2022,

thus causing FAD eye drops to become unavailable in Japan. As alternatives to riboflavin or FAD, we focus on the role of cyanocobalamin (vitamin B12), the UV-visible absorption spectrum of which peaks at the VL wavelength. The absorption spectrum of cyanocobalamin has characteristic peaks in both the visible light and ultraviolet regions at 361 nm [6]. This phenomenon is due to electronic transitions between the cobalt center and ligands within the molecule and is used for quantitative analysis in analytical chemistry and biochemistry. Cyanocobalamin eye drops improve fine movement accommodation in accommodative eye strain and are used clinically to treat eye strain in Japan [7]. These eye drops have been on the market for more than 40 years and are therefore considered sufficiently safe. Our hypothesis is that it is possible to confirm the effects of KeraVio treatment with the administration of cyanocobalamin drops and VL irradiation. In this study, riboflavin was replaced with cyanocobalamin (vitamin B12), which shares a similar absorption spectrum and has shown *ex vivo* efficacy in increasing corneal tensile strength. We conducted an exploratory clinical study to evaluate the safety and potential efficacy of cyanocobalamin-assisted KeraVio in progressive keratoconus.

## Methods

### *Ex Vivo Study*

We investigated whether cyanocobalamin and VL irradiation altered the corneal elastic modulus using porcine eyes. Porcine corneas with intact epithelium were randomly sorted into three different treatment groups (total n=15). To evaluate the corneal biomechanical properties without epithelial removal, KeraVio with cyanocobalamin and FAD drops was used (each, n=5). Corneas that received no treatment with VL irradiation or drug delivery served as the controls (n=5).

VL irradiation (375 nm) was applied using a single VL diode (Nitride Semiconductors Co., Ltd., Tokushima, Japan) with an irradiance of 0.31 mW/cm<sup>2</sup> for 4.8 hours at a distance of 60 cm from the cornea (total energy dose of 5.4 J/cm<sup>2</sup>). To avoid the cytotoxic threshold of the corneal endothelium, which is 0.36 mW/cm<sup>2</sup>, we applied a VL intensity of 0.31 mW/cm<sup>2</sup> [8–10]. A collection of samples comprising the KeraVio with cyanocobalamin and FAD groups was also prepared (each, n=5). For this group, during the initial 30 minutes of VL irradiation, 0.025% cyanocobalamin and 0.05% FAD drops were applied simultaneously to the corneal epithelium every 2 minutes.

All the corneas from the three groups were allowed to rest in a wet chamber for 30 minutes after the VL or sham-VL treatment. The corneas were harvested en bloc along the sclera. A 2- to 3-mm scleral rim was preserved, and the cornea was attached along a custom-made scale. Afterward, a 5-mm-wide strip was vertically resected along the cornea. The corneal strips were clamped vertically at a distance of 5 mm between the jaws. To calculate the cross-sectional area of the corneal strip, we used the central corneal thickness of each cornea. After the prepared corneal strip was placed on a computer-controlled electronic universal testing machine (TA XTplusC Texture Analyser™; Stable Micro Systems, Ltd., London, UK), a fixture was used to hold the corneoscleral limbus of the corneal strip for a uniaxial tensile test. For the actual measurement, the sample was stretched at a velocity of 1.8 mm/min up to a maximum force of 5 N. The elastic modulus was defined as the ratio of tensile stress (amount of force causing deformation per unit transsectional area of corneal strips) to tensile strain (percentage change in the length caused by the stress). For the subsequent statistical analysis, the elastic modulus was consistently evaluated at 10% strain.

### *Clinical Pilot Study*

A prospective, single-arm, open-label exploratory clinical trial (jRCTs032230104) was conducted at Minami Aoyama Eye Clinic, Tokyo, Japan. Our aim was to assess the efficacy and safety outcomes of KeraVio treatment with the administration of cyanocobalamin drops. Institutional review board approval was obtained. The study adhered to the tenets of the Declaration of Helsinki. The study participants completed a written informed consent form. This study was approved by the Review Board at Hattori Clinic and registered in the Japan Registry of Clinical Trials (jRCT): jRCTs032230104.

### *Inclusion and Exclusion Criteria*

The inclusion criteria were as follows: male or female sex, any race or ethnicity, an age of 15 years or older, and a diagnosis of keratoconus as documented by topography or tomography. Subjects were also required to have experienced progression within 6 months before baseline to receive KeraVio treatment, as defined by one or more of the following: (1) an increase of  $\geq 0.50$  diopters (D) in the maximum keratometry value (Kmax); (2) an increase of  $\geq 0.50$  D in cylinder power on subjective manifest refraction; (3) an increase of  $\geq 0.50$  D in myopia on subjective manifest refraction; and (4) a decrease of  $\geq 5$   $\mu\text{m}$  in the thinnest corneal thickness. The contact lenses were removed for a period before each visit to avoid changes in corneal shape. This period was 3 weeks for rigid gas-permeable lenses and 1 week for soft contact lenses. The exclusion criteria included photosensitivity, a history of epilepsy, an allergy to fluorescein, or other ophthalmic/systemic conditions deemed inappropriate for participation.

### *KeraVio Treatment*

The subjects wore VL-emitting glasses, and their corneas were aligned and exposed to VL (375 nm) for 4.5 hours daily for 3 months; 0.02% cyanocobalamin drops were administered onto the corneal epithelium every 30 min during each 3-hour VL irradiation session to permeate the cornea. In eyes with KeraVio with VL irradiation and cyanocobalamin drops, the subjects wore VL-emitting glasses [3], and their corneas were aligned and exposed to VL (375 nm) for 4.5 hours daily for 3 months. Before each treatment, the desired irradiance of  $0.31 \text{ mW/cm}^2$  was verified with a UVA meter (LaserMate-Q; LASER 2000, Wessling, Germany) at a distance of 1.2 cm from the cornea and, if necessary, regulated with a potentiometer. The aforementioned KeraVio protocol in this clinical study using cyanocobalamin drops and VL-emitting glass was continued daily for 3 months (total energy dose of  $301.3 \text{ J/cm}^2$ ). Patients could have both eyes treated if the investigator thought the KeraVio treatment could be beneficial in both eyes. Only the more severely affected eye of each patient was considered in the efficacy and safety analysis.

### *Outcome Measures*

Tomographic data were obtained using anterior segment optical coherence tomography (AS-OCT) (CASIA, Tomey Corporation, Nagoya, Japan) at baseline and at 1, 3 and 6 months after KeraVio. To quantify the keratometric parameters, the thinnest corneal thickness and stromal demarcation line (DL) identified by the AS-OCT system were analyzed. Kmax was chosen as the primary efficacy outcome because it measures a salient feature of corneal ectasia, that is, the steepness of ectatic tomographic distortion. Moreover, Kmax afforded an objective, quantitative endpoint and allowed the use of consistent hardware and software among the study sites. Keratometry values along the flat (K1) and steep (K2) meridians were also evaluated. To evaluate the success rate, significant corneal flattening 6 months after KeraVio treatment was defined as a decrease in the Kmax of more than 1.00 D compared with the baseline value. If we recognized the demarcation line using the AS-OCT scans, the measurements of the DL depth were taken by two independent observers 3 months after treatment, as analytically reported in our previous studies [11,12]. The DL was also visually assessed.

Uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA) and manifest refraction spherical equivalent (MRSE) were measured at baseline and 3 and 6 months after KeraVio. Visual acuity measurements were obtained as the logarithm of the minimal angle of resolution (logMAR) units using a Landolt C chart.

### *Safety Outcomes*

The safety analysis included all treated eyes. The safety outcomes of endothelial cell density and intraocular pressure were measured at each time point using a specular microscope (NonconRobo, Konan, Nishinomiya, Japan) and a tonometer (TONOREF, Nidek Co.), respectively. Slit-lamp

examination was also performed to evaluate adverse events, such as secondary cataracts, conjunctivitis and eyelid adverse events.

### Statistical Analysis

Statistical analysis was performed with the assistance of Statistical Analysis Software (version 9.4; SAS Institute, Cary, NC). The differences in the elastic modulus among the three treatment groups were tested using the Friedman nonparametric test coupled with Scheffe's multiple comparison test. A P value of less than 0.05 was considered to indicate statistical significance. With respect to clinical data, statistical analysis was not performed because of the small number of cases included in the current study.

## Results

### Ex Vivo Study

The elastic modulus and percentage strain of the treated corneas at 10% strain were determined for each of the three groups (**Table 1**). The average elastic moduli at 10% strain in the KeraVio without cyanocobalamin, KeraVio with FAD, and control groups were  $285.20 \pm 83.71$  kPa,  $181.80 \pm 99.98$  kPa, and  $47.50 \pm 19.66$  kPa, respectively. The elastic modulus at 10% exhibited significant differences among the groups according to the nonparametric Friedman test performed with respect to the four groups ( $P = 0.135$ ).

**Table 1.** Elastic modulus at 10% strain in each group.

|                     | KeraVio with cyanocobalamin | KeraVio with flavin adenine dinucleotide | Control           |
|---------------------|-----------------------------|--|-------------------|
| Mean $\pm$ SD (kPa) | $285.20 \pm 83.71$          | $181.80 \pm 99.98$                       | $47.50 \pm 19.66$ |
| Range               | 226.03 to 344.31            | 111.10 to 252.50                         | 33.60 to 61.40    |

### Clinical study

Three eyes belonging to 3 patients were treated with KeraVio and cyanocobalamin. All included patients had progressive keratoconus and met the eligibility criteria. The participant demographics are presented in **Table 2**. All patients remained in the study through the 6-month follow-up.

**Table 2.** Demographic characteristics of patients included in the KeraVio treatment with a decrease in cyanocobalamin concentration (n=3).

| Case          | Age (years)       | Sex (female/male) | Kmax (diopters)   |
|---------------|-------------------|-------------------|-------------------|
| # 1           | 34                | Male              | 50.70             |
| # 2           | 49                | Male              | 82.47             |
| # 3           | 27                | Female            | 76.46             |
| Mean $\pm$ SD | $36.67 \pm 11.24$ | n/a               | $69.88 \pm 16.88$ |

SD=standard deviation; n/a = not applicable.

**Table 3** shows the changes in corneal parameters from baseline to the 6-month observation period after treatment. The mean change in Kmax during the 6-month observation period was  $-0.37 \pm 6.82$  D. However, in three cases, Kmax increased and decreased, resulting in variability. Similarly, the K1, K2, and thinnest corneal thickness results also varied, and no consistent trend was observed. The success rate (flattening of the Kmax  $>1.00$  D) was 33% (one-eye). No DL was observed after KeraVio with cyanocobalamin at 3 months.

**Table 3.** Changes in corneal parameters after KeraVio with a decrease in cyanocobalamin concentration.

|                 | Baseline | 3 months | 6 months | Change from baseline to 6 months |
|-----------------|----------|----------|----------|----------------------------------|
| <b>Kmax (D)</b> |          |          |          |                                  |
| # 1             | 50.70    | 50.83    | 51.04    | 0.34                             |
| # 2             | 82.47    | 73.63    | 74.96    | -7.51                            |

|  |                 |                 |                 |               |
|--|-----------------|-----------------|-----------------|---------------|
| # 3                                    | 76.46           | 86.97           | 82.53           | 6.07          |
| Mean ± SD                              | 69.88 ± 16.88   | 70.48 ± 18.28   | 69.51 ± 16.44   | -0.37 ± 6.82  |
| <b>K1 (D)</b>                          |                 |                 |                 |               |
| # 1                                    | 42.25           | 42.60           | 42.47           | 0.22          |
| # 2                                    | 53.18           | 51.82           | 52.47           | -0.71         |
| # 3                                    | 64.07           | 66.04           | 68.33           | 4.26          |
| Mean ± SD                              | 53.17 ± 10.91   | 53.49 ± 11.81   | 54.42 ± 13.04   | 1.26 ± 2.64   |
| <b>K2 (D)</b>                          |                 |                 |                 |               |
| # 1                                    | 45.70           | 45.58           | 45.54           | -0.16         |
| # 2                                    | 60.71           | 59.35           | 58.12           | -2.59         |
| # 3                                    | 71.62           | 75.01           | 73.20           | 1.58          |
| Mean ± SD                              | 59.34 ± 13.01   | 59.98 ± 14.73   | 58.95 ± 13.85   | -0.39 ± 2.09  |
| <b>Thinnest corneal thickness (µm)</b> |                 |                 |                 |               |
| # 1                                    | 442             | 446             | 445             | 3.00          |
| # 2                                    | 427             | 405             | 397             | -30.00        |
| # 3                                    | 225             | 226             | 230             | 5.00          |
| Mean ± SD                              | 364.67 ± 121.19 | 359.00 ± 116.99 | 357.33 ± 112.86 | -7.33 ± 19.66 |

D=diopeters.

**Table 4** shows the changes in the UCVA, BCVA, MESE, and cylindrical refraction from baseline to the 6-month observation period after treatment. In all three patients, visual acuity and subjective refraction were clinically unchanged.

**Table 4.** Changes in visual acuity and refraction after KeraVio with a decrease in cyanocobalamin concentration.

|   | Baseline     | 3 months     | 6 months     | Change from baseline to 6 months |
|---|--------------|--------------|--------------|----------------------------------|
| <b>Uncorrected visual acuity (logMAR)</b>           |              |              |              |                                  |
| # 1   | 1.10         | 1.22         | 1.10         | 0.00                             |
| # 2   | 0.70         | 0.70         | 0.82         | 0.12                             |
| # 3   | 2.00         | 2.00         | 2.00         | 0.00                             |
| Mean ± SD   | 1.27 ± 0.67  | 1.31 ± 0.65  | 1.31 ± 0.62  | 0.04 ± 0.07                      |
| <b>Best-corrected visual acuity (logMAR)</b>        |              |              |              |                                  |
| # 1   | 0.15         | 0.05         | 0.05         | -0.11                            |
| # 2   | 0.15         | 0.22         | 0.30         | 0.15                             |
| # 3   | 1.22         | 1.30         | 1.10         | -0.12                            |
| Mean ± SD   | 0.51 ± 0.62  | 0.52 ± 0.68  | 0.48 ± 0.55  | -0.03 ± 0.15                     |
| <b>Manifest refraction spherical equivalent (D)</b> |              |              |              |                                  |
| # 1   | -4.50        | -4.50        | -4.50        | 0.00                             |
| # 2   | -4.00        | -4.00        | -4.25        | -0.25                            |
| #3  | -21.00       | -18.50       | -20.00       | 1.00                             |
| Mean ± SD   | -9.83 ± 9.67 | -9.00 ± 8.23 | -9.58 ± 9.02 | 0.25 ± 0.66                      |
| <b>Cylindrical refraction (D)</b>                   |              |              |              |                                  |
| # 1   | -2.00        | -2.00        | -2.00        | 0.00                             |
| # 2   | -6.00        | -6.00        | -5.50        | 0.50                             |
| # 3   | -6.00        | -5.00        | -6.00        | 0.00                             |
| Mean ± SD   | -4.67 ± 2.31 | -4.33 ± 2.08 | -4.50 ± 2.18 | 0.17 ± 0.29                      |

logMAR=logarithm of the minimal resolution angle; D=diopeters.

**Table 5** presents the safety profile of KeraVio with cyanocobalamin treatment. Two patients demonstrated errors in corneal endothelial cell density and intraocular pressure, but all eyes remained clinically unchanged. With respect to adverse events, no vision-threatening complications were reported in this study, indicating the safety of this treatment. No pterygium, skin melanoma, lenticular opacity or transient corneal haze was noted in either eye at the 6-month follow-up.

**Table 5.** Safety profile after KeraVio with a decrease in cyanocobalamin concentration.

|  | Baseline | 3 months | 6 months |
|--|----------|----------|----------|
| <b>Endothelial cell density (cells/mm<sup>2</sup>)</b> |          |          |          |

|                                    |              |              |              |
|------------------------------------|--------------|--------------|--------------|
| # 1                                | 3130         | 3021         | 3153         |
| # 2                                | 3034         | 3088         | 2924         |
| # 3                                | unmeasurable | unmeasurable | unmeasurable |
| <b>Intraocular pressure (mmHg)</b> |              |              |              |
| # 1                                | 13           | 15.0         | 10.0         |
| # 2                                | unmeasurable | 7.0          | 10.0         |
| # 3                                | 9            | 9.0          | 8.0          |

## Discussion

In this exploratory study, KeraVio treatment with cyanocobalamin and VL irradiation exhibited a favorable safety profile, with no adverse events or detrimental changes in ocular health parameters over six months. However, Kmax outcomes were highly variable among patients, and the small sample size precluded statistical analysis. Although the concept of replacing riboflavin with cyanocobalamin is supported by preclinical data, its clinical efficacy in keratoconus progression remains unproven. Notably, in our study, we investigated the therapeutic effects of cyanocobalamin and VL irradiation on progressive keratoconus; no similar studies have been reported to date.

In a tensile strength test that used porcine eyes treated with cyanocobalamin eye drops and VL irradiation, no statistically significant differences in the elastic modulus were observed among the three groups. However, the cyanocobalamin and FAD groups presented higher values compared with the control group. This finding is consistent with our previous basic and clinical study using FAD eye drops and VL irradiation [3].

Cyanocobalamin is a drug that has an absorption peak at 361 nm and is therefore logically expected to have a corneal cross-linking effect [6]. However, in this study, corneal epithelial peeling was not performed in all porcine eyes. Thus, penetration of the drug into the corneal stroma was limited, and the extent to which cyanocobalamin penetrated the corneal stroma was unclear. Future studies should evaluate cyanocobalamin concentrations in the corneal stroma in the presence or absence of epithelial peeling. Unlu et al. reported that the combination of citicoline and vitamin B12 for keratoconus effectively promoted corneal nerve healing after CXL [13]. Furthermore, a report produced by Romano et al. revealed that vitamin B12 treatment promotes not only corneal re-epithelialization but also reinnervation after mechanical injury [14]. These findings suggest that cyanocobalamin is effective for corneal epithelial regeneration and is also an effective drug for treating keratoconus.

Limitations of this study include its single-arm design, the lack of a control group, and the minimal sample size. Further randomized controlled trials with larger cohorts are necessary to validate the efficacy and determine the long-term safety of this approach.

In conclusion, cyanocobalamin-assisted KeraVio appears to be a safe, noninvasive option for patients with progressive keratoconus. Given the variability in Kmax responses and limited sample size, its efficacy requires confirmation on the basis of well-powered, controlled studies.

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## References

1. Rabinowitz YS. Keratoconus. *Surv Ophthalmol.* 1998;42(4):297-319.
2. Sorkin N, Varssano D. Corneal collagen crosslinking: a systematic review. *Ophthalmologica.* 2014;232(1):10-27.
3. Kobashi H, Torii H, Toda I, Kondo S, Itoi M, Tsubota K. Clinical outcomes of KeraVio using violet light-emitting glasses and riboflavin drops for corneal ectasia: a pilot study. *Br J Ophthalmol.* 2021 Oct;105(10):1376-1382. doi: 10.1136/bjophthalmol-2020-316974.
4. Kobashi H, Yunoki S, Kato N, Shimazaki J, Ide T, Tsubota K. Evaluation of the Physiological Corneal Intrastromal Riboflavin Concentration and the Corneal Elastic Modulus After Violet Light Irradiation. *Transl Vis Sci Technol.* 2021 Apr 29;10(5):12.
5. Kobashi H, Kumanomido T, Ide T, Kato N, Shimazaki J, Itoi M, Tsubota K. Ineffectiveness of KeraVio Treatment with Violet Light-Emitting Glasses Without Riboflavin Drops for Progressive Keratoconus. *J Clin Med.* 2025 Jan 24;14(3):773.
6. Zobi F, Blacque O, Jacobs RA, Schaub MC, Bogdanova AY. 17 e- rhenium dicarbonyl CO-releasing molecules on a cobalamin scaffold for biological application. *Dalton Trans.* 2012 Jan 14;41(2):370-8.
7. Nakashima K, Yamasaki H, Shimoda R, Kuroda N, Akiyama S, Baeyens WR. Flow-injection analysis of cobalt(II) utilizing enhanced lophine chemiluminescence with hydroxylammonium chloride. *Biomed Chromatogr.* 1997 Mar-Apr;11(2):63-4.
8. Wollensak G, Spoerl E, Reber F, Seiler T. Keratocyte cytotoxicity of riboflavin/UVA-treatment in vitro. *Eye.* 2004;18:718-722.
9. Wollensak G, Spoerl E, Wilsch M, Seiler T. Keratocyte apoptosis after corneal collagen cross-linking using riboflavin/UVA treatment. *Cornea.* 2004;23:43-49.
10. Wollensak G, Spoerl E, Wilsch M, Seiler T. Endothelial cell damage after riboflavin-ultraviolet-A treatment in the rabbit. *J Cataract Refract Surg.* 2003;29:1786-1790.
11. Kymionis GD, Grentzelos MA, Plaka AD, Tsoulnaras KI, Diakonios VF, Liakopoulos DA, Kankariya VP, Pallikaris AI. Correlation of the corneal collagen cross-linking demarcation line using confocal microscopy and anterior segment optical coherence tomography in keratoconic patients. *Am J Ophthalmol.* 2014 Jan;157(1):110-115.e1.
12. Kymionis GD, Tsoulnaras KI, Grentzelos MA, Plaka AD, Mikropoulos DG, Liakopoulos DA, Tsakalis NG, Pallikaris IG. Corneal stroma demarcation line after standard and high-intensity collagen crosslinking determined with anterior segment optical coherence tomography. *J Cataract Refract Surg.* 2014 May;40(5):736-40.
13. Unlu M, Ozer F, Sahin Aslan E, Sener H, Erkilic K. Can the combination of citicoline and vitamin B12 be beneficial in the healing of corneal nerves after corneal cross-linking? *Int Ophthalmol.* 2025 Jan 31;45(1):54.
14. Romano MR, Biagioni F, Carrizzo A, Lorusso M, Spadaro A, Micelli Ferrari T, Vecchione C, Zurria M, Marrazzo G, Mascio G, Sacchetti B, Madonna M, Fornai F, Nicoletti F, Lograno MD. Effects of vitamin B12 on the corneal nerve regeneration in rats. *Exp Eye Res.* 2014 Mar;120:109-17.

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