doi.org/10.36721/PJPS.2025.38.6.REG.14567.1

Combined sodium aescinate and calf blood extract gel for corneal foreign body injury

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Abstract: The aim of this study was to assess the efficacy of combining sodium aescinate tablets with deproteinized calf blood extract eye gel (DCB-EG) in treating corneal foreign body injuries. This retrospective study included 270 patients divided into three groups: Combination (sodium aescinate + DCB-EG, n=90), Gel (DCB-EG, n=90) and Control (routine anti-infection, n=90). Primary outcome was clinical efficacy rate; secondary outcomes included pain scores (VAS), corneal healing metrics, inflammatory markers (IFN-γ, TNF-α, IL-17), tear film stability (BUT), corneal epithelial status (CESS), tear secretion (SIt) and ocular surface disease index (OSDI). Data were analyzed using ANOVA or Chi-square test. The research results showed that the Combination group achieved the highest efficacy (98.89%), significantly better than the Gel (91.11%) and Control (86.67%) groups ($P<0.05$). Combined intervention shortened corneal edema resolution time, corneal healing time and pain relief time, while also reducing VAS scores and inflammatory factor levels (all $P<0.05$). Additionally, the Combination group demonstrated superior tear film stability, corneal epithelial repair and subjective symptom improvement compared to the Control group (all $P<0.05$). No significant differences in adverse events were observed ($P>0.05$). The combination therapy provided a safe and optimized treatment method for corneal foreign body injuries.

Keywords: Corneal foreign body injury; Deproteinized calf blood extract; Eye gel; Sodium aescinate

Submitted on 08-05-2025 - Revised on 01-08-2025 - Accepted on 06-08-2025

INTRODUCTION

Corneal foreign body injury is a common, preventable ophthalmic emergency that can lead to visual impairment. It accounts for about 30% to 40% of ophthalmic emergencies, often affecting industrial workers, welders, farmers and those without adequate eye protection (Ay İ *et al.*, 2022; Heath Jeffery *et al.*, 2022). Typically caused by foreign objects like metal debris, sand, glass, or plant materials splashing into the eye (Ambikkumar *et al.*, 2022), its symptoms vary based on the object and injury severity, potentially causing abrasions, inflammation, light sensitivity, tearing, reduced vision, infections, or serious issues like corneal ulceration and perforation (Macarie *et al.*, 2023). The cornea, the eye's frontmost clear tissue, is crucial for vision. Anatomically, it has five layers: epithelial cell, Bowman's, stroma, Descemet's membrane and endothelial cell layers (Sliwicki and Orringer, 2023). The epithelial layer regenerates well, but stroma damage can scar and impair vision. The cornea protects the eye and provides about two-thirds of its refractive power, so injuries, especially to the visual axis, can significantly affect vision (Akbaş *et al.*, 2021). Corneal foreign bodies often cause sudden eye pain, a feeling of something in the eye, redness, excessive tearing and involuntary eyelid closure (Sun *et al.*, 2021). Clinical exams may show conjunctival hyperemia, with the foreign body on the corneal surface or within the stroma, often with surrounding tissue swelling (Bourke *et al.*, 2021). Special foreign bodies may cause characteristic changes, like a rust ring from iron or copper deposition syndrome from copper (Moutei *et al.*, 2024; Wang *et al.*, 2023). Superficial foreign bodies can be removed under topical anesthesia with a sterile cotton swab or irrigation; deeper ones need specialized tools under an operating microscope (Widyanatha, 2025). Be vigilant, as occupational injuries like high-speed metal splinters may involve intraocular foreign bodies, requiring imaging like B-scan ultrasonography or CT scans to rule them out (Kumar *et al.*, 2024).

Currently, the clinical treatment of corneal foreign body injuries primarily includes foreign body removal and postoperative pharmacotherapy. The conventional pharmacotherapy regimen mainly focuses on topical antibiotics to prevent infection, supplemented by artificial tears to protect the corneal epithelium. However, this regimen has limited efficacy in promoting corneal repair and reducing tissue edema and inflammatory responses (Nukala *et al.*, 2020). The repair process following corneal injury involves complex biological mechanisms, including the regulation of inflammatory responses, epithelial cell migration and proliferation and stromal remodeling. Drugs with a single mechanism of action often struggle to comprehensively intervene in these processes (Rebattu *et al.*, 2023). Deproteinized calf blood extract eye gel (DCB-EG) is an active substance extracted from the blood of young calves, containing various components such as amino acids, nucleotides, glycolipids and low molecular weight peptides. It has the effects of promoting cellular

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energy metabolism, stimulating cell proliferation and improving tissue nutrition (Li *et al.*, 2020). The DCB-EG has been widely used in the treatment of various corneal diseases, such as corneal ulcers, chemical burns and neurotrophic keratitis. Clinical studies have confirmed its significant efficacy in promoting corneal epithelial repair and reducing scar formation (Wu *et al.*, 2014). Nam *et al.* (Nam and Maeng, 2019) explored the roles of DCB-EG in regulating gene expression and corneal epithelial cell (CEC) activity. The results indicated that DCB-EG could enhance the adhesion, migration, proliferation and wound healing capabilities of corneal epithelial cells by increasing the expression of mucin family genes (such as MUC1, -5AC, -7 and -16) in these cells and elevating the activity of intracellular signaling molecules, including AKT, Focal Adhesion Kinase (FAK), Extracellular Signal-Regulated Kinase (ERK) and Src. Sodium aescinate, a natural pharmaceutical compound derived from horse chestnut seeds, exhibits multiple pharmacological properties, including anti-inflammatory, anti-exudative, venous return enhancement and microcirculation improvement (Xu *et al.*, 2023). By stabilizing lysosomal membranes and inhibiting protease activity, it can effectively reduce vascular permeability and alleviate tissue edema; simultaneously, it can increase venous tone and improve local blood circulation, creating a favorable environment for tissue repair (Mei *et al.*, 2023; Zhu *et al.*, 2024).

Despite the prevalence of corneal foreign body injuries and the existing treatment modalities, there remains a significant gap in optimizing clinical outcomes, particularly in terms of rapid corneal repair, effective inflammation control and overall improvement in ocular surface health. This study uniquely addresses these gaps by exploring the synergistic effects of sodium aescinate tablets and DCB-EG in a comprehensive manner. Unlike previous studies that have primarily focused on single-agent therapies or limited outcome measures, our research evaluates a wide range of clinical indicators, including corneal healing time, inflammatory factor levels, tear film stability and patient-reported quality of life. By demonstrating the significant benefits of this combined treatment regimen, our findings provide a novel and optimized therapeutic approach that has the potential to transform the clinical management of corneal foreign body injuries. This study not only offers robust evidence for the efficacy and safety of the combination therapy but also highlights the importance of a multi-targeted strategy in enhancing corneal repair and improving patient outcomes.

MATERIALS AND METHODS

Research object

This study employed a retrospective controlled trial design, with data collection and analysis conducted by researchers who were not involved in the treatment of the patients. A total of 270 patients with corneal foreign body injuries admitted from January 2023 to June 2024 were selected. Inclusion criteria: (1) aged 18-60 years; (2) diagnosed with corneal foreign body injuries via slit-lamp examination, with the foreign body depth not exceeding the superficial layer of the corneal stroma; (3) the time from injury to presentation was within 48 hours. Exclusion criteria included: (1) concurrent other ocular diseases such as glaucoma, cataracts, or active ocular infections; (2) severe systemic diseases such as diabetes mellitus or immunodeficiency disorders; (3) allergies to the components of the study drugs; (4) pregnant or lactating women; (5) concomitant medication use that may impact the evaluation of treatment effectiveness. Based on the therapeutic approach, participants were allocated to one of three groups: Control group, Gel Group, or Combination group, with 90 cases per group. The specific flow of this study is shown in fig. 1.

Sample size calculation

This study's sample size calculation was conducted using one-way ANOVA via G-Power software. According to previous research experience and the anticipated inter-group differences in this study, the moderate effect size (f=0.25) (Erdfelder *et al.*, 1996), a 0.05 significance level (α) and 0.95 statistical power to ensure that the study could effectively detect inter-group differences at a medium effect size. Based on the aforementioned parameters, the required sample size for each group was calculated to be 84. In this study, 90 samples were included in each group, meeting the sample size requirements.

Treatment methods

All patients initially underwent thorough one-time removal of corneal foreign bodies by the same experienced physician under surface anesthesia induced by oxybuprocaine hydrochloride eye drops, with sterile corneal foreign body needles. Rust rings formed by metallic foreign bodies were also removed as thoroughly as possible. Postoperative treatments were as follows:

(1) ***Control group***

Received conventional treatment, including levofloxacin eye drops (1 drop, 3 times daily) for infection prevention and sodium hyaluronate eye drops (1 drop, 3 times daily) for corneal epithelial protection, for a duration of 2 weeks.

(2) ***Gel group***

In addition to the Control group's treatment, DCB-EG was applied, approximately 0.5 cm in length, 3 times daily into the conjunctival sac, for 2 weeks.

(3) ***Combination group***

On the basis of the treatment administered to the Gel Group, sodium aescinate tablets (specification 30 mg/tablet, National Drug Approval Number H20051590, manufactured by Shandong Luye Pharmaceutical Co., Ltd.) were administered orally at a dose of 1 tablet, twice daily, after breakfast and dinner, for a continuous treatment period of 2 weeks. All patients were prohibited from wearing corneal contact lenses during the treatment period and were advised to avoid behaviors that could increase the risk of infection, such as rubbing their eyes and swimming. In cases of significant pain, temporary use of oral acetaminophen for pain relief was permitted, with documentation of medication usage. The use of other eye drops or systemic medications that might affect the evaluation of treatment efficacy was prohibited during the study period.

Observation indicators

- *Main outcome measures*

Clinical efficacy evaluation criteria: ①Cured: After treatment, the patient's clinical symptoms such as ocular pain, conjunctival hyperemia and edema disappear and tear inflammatory indicators approach or reach the normal range. ②Effectivet: After treatment, the patient's aforementioned clinical symptoms exhibit some degree of improvement, with an improvement rate of tear inflammatory indicators. ③Ineffective: After treatment, there is no discernible difference in clinical symptoms compared to before treatment and tear inflammatory indicators show no significant improvement or have worsened. Total Effective Rate = (Cured Cases + Effectivet Cases) / Total Number of Cases × 100%.

- ***Secondary outcome measures***

Pain Assessment: Evaluations were conducted before treatment, 1 week after treatment initiation and 2 weeks after treatment initiation. The time to pain relief was recorded and patients' pain levels were assessed using the Visual Analog Scale (VAS) (Toyota *et al.*, 2022), which ranges from 0 to 10 points, corresponding to "no pain" to "intolerable pain," with higher scores indicating more severe pain.

Corneal Healing Status: Observations were made using a slit-lamp microscope to record the time for corneal edema resolution and corneal wound healing before treatment, 1 week after treatment initiation and 2 weeks after treatment initiation.

Inflammatory Factor Levels: Tear samples were collected from patients using sterile capillary tubes or specialized tear collectors before treatment, 1 week after treatment initiation and 2 weeks after treatment initiation. The tear content of IFN-γ, TNF-α and IL-17 was analyzed by ELISA.

Tear Film Break-Up Time (BUT) (Yazdani et al., 2021): Fluorescein was added to the tear film and patients blinked fully to ensure even distribution. The tear film was examined under cobalt blue slit-lamp light and the time from the last blink to the first dry spot was recorded with a stopwatch. The test was repeated three times and the average was calculated. BUT was measured before treatment, at 1 week and at 2 weeks post-treatment.

Corneal Epithelial Status Score (CESS) (Amparo et al., 2018): Corneal epithelial staining was assessed at baseline, 1 week and 2 weeks post-treatment. Staining severity was graded as: 0 (none), 1 (mild punctate), 2 (moderate punctate with partial confluence), or 3 (dense punctate with confluence). The cornea was divided into four quadrants (superior nasal, inferior nasal, superior temporal, inferior temporal), with total scores calculated by summing quadrant scores.

Tear Secretion Test (Schirmer I Test, SIt) (Wang et al., 2022): Tear secretion was measured pre-treatment, at 1 week and 2 weeks post-treatment using a test strip placed in the outer third of the lower conjunctival sac. After 5 minutes of eye closure, wetting length <10 mm indicated reduced secretion.

Ocular-Related Quality of Life: The Ocular Surface Disease Index (OSDI) (Martin and Emo Research, 2023) evaluated ocular-related quality of life at 1 and 2 weeks post-treatment. It includes three dimensions: "ocular symptoms," "visual function," and "environmental triggers," with a total of 12 items, each scored from 0 to 4 points. Ocular symptoms include five indicators: photophobia, grittiness, eye pain, visual fluctuation and poor vision. Visual function includes the impact on four activities: reading, night driving, using electronic devices and watching television. Environmental triggers include three scenarios: windy weather, very dry environments and air-conditioned rooms. Scoring criteria: 0 (none), 1 (minimal), 2 (half), 3 (most), 4 (always). The total score ranges from 0 to 48 points, with higher scores indicating more severe dysfunction.

Adverse Reaction Monitoring: A systematic monitoring protocol was employed to capture any uncomfortable symptoms or signs that occurred during treatment. Specifically, participants were asked to maintain a daily log to document any mild or transient events, such as eyelid itching, eye irritation and eye pain. All reported symptoms were reviewed and documented by the study team during each follow-up visit.

Statistical analysis

Data were analyzed using SPSS 25.0. Normally distributed measurement data [e.g., corneal healing, inflammatory factors (IFN-γ, TNF-α, IL-17), BUT, SIt, OSDI] were expressed as mean ± SD; ANOVA (LSD-t for pairwise comparisons) was used for multi-group comparisons with homogeneity of variance. Non-normally distributed data (e.g., VAS, CESS) were presented as [M (Q1, Q3)] and analyzed via Kruskal-Wallis H test. Categorical data (e.g., clinical efficacy, adverse reactions) were reported as n (%) and compared using χ^2, corrected χ^2, or Fisher's exact test. Two-tailed tests were applied, with $P<0.05$ considered significant.

RESULT

Comparison of baseline characteristics

The comparison results of baseline data among the three groups of patients are shown in table 1. Statistical analysis indicated that there were no significant differences between the Control group , the Gel Group and the Combination group in terms of gender (χ^2=0.578, P=0.749), age (F=0.309, P=0.734), BMI (F=0.176, P=0.840), education level (χ^2=0.408, P=0.815), underlying diseases (χ^2=0.876, P=0.928), affected eye (χ^2=0.563, P=0.755), disease duration (F=0.584, P=0.558), depth of corneal foreign body (χ^2=0.856, P=0.931) and Corneal foreign body components (χ^2=3.903, P=0.690) suggesting that the three groups of patients were comparable.

Comparison of clinical efficacy

The comparison results of clinical efficacy among the three groups of patients are shown in table 2. Statistical analysis revealed that the total effective rate in the Combination group [98.89% (89/90)] was higher than that in the Control group [86.67% (78/90)] and the Gel Group [91.11% (82/90)], with statistically significant differences between groups (χ^2=9.604, P=0.008). This indicates that the combined treatment regimen of sodium aescinate tablets and DCB-EG has a significant synergistic effect in the treatment of corneal foreign body injuries.

Comparison of pain intensity

Table 3 shows that the pain relief time in the Combination group was shorter than that in the Control group and the Gel Group (F=75.602, P<0.05). The VAS pain scores of the Combination group at 1 week and 2 weeks post-treatment were lower than those of the Control group and the Gel Group (P<0.05). This result confirms that the combined treatment regimen can alleviate pain symptoms caused by corneal foreign body injuries more quickly and effectively.

Comparison of corneal healing status

The comparison results of corneal repair status among the three groups of patients are detailed in table 4. Statistical analysis indicates that the average time for corneal edema resolution in the Combination group was 2.41±0.35 days, which was 28.9% shorter than that in the Control group (3.39±0.45 days) and 15.7% shorter than that in the Gel group (2.86±0.37 days), with all differences being statistically significant (F=148.462, P<0.05). The average time for corneal wound healing in the Combination group was 5.82±1.55 days, shorter than that in the Control group (9.01±2.14 days, a reduction of 35.4%) and the Gel Group (7.89±2.37 days, a reduction of 26.2%) (F=56.468, P<0.05). These findings suggest that the combined use of sodium aescinate and DCB-EG can accelerate the process of corneal edema resolution and wound healing, with its efficacy being markedly superior to single-drug regimens and conventional treatment protocols.

Comparison of tear inflammatory factor levels

Fig. 2 compares the changes in the levels of inflammatory factors (IFN-γ, TNF-α, IL-17) in tears among three groups of patients with corneal foreign body injuries before and after treatment. The research results show that before treatment, there were no statistically significant differences in the levels of IFN-γ, TNF-α and IL-17 in the tears among the three groups (P>0.05), indicating that the baseline levels were balanced and comparable across the groups. At 1 week and 2 weeks post-treatment, the levels of IFN-γ, TNF-α and IL-17 in the tears of the Combination group were lower than those in the other two groups, with the differences being statistically significant (P<0.05). This indicates that the combined treatment regimen is more effective than the use of DCB-EG alone or conventional local anti-infective treatment in reducing the levels of inflammatory factors in tears, suggesting that the combined treatment has a more pronounced efficacy in alleviating the inflammatory response caused by corneal foreign body injuries.

Comparison of BUT

Table 5 compares the BUT values of patients with corneal foreign body injuries in the three groups at different time points. The results show that there were no statistically significant differences in the BUT values among the three groups at baseline (F=0.341, P=0.711). 1 week after treatment, the BUT value in the Combination group was higher than those in the Gel Group and the Control group (F=266.387, P<0.05), indicating that the combined treatment can improve tear film stability in the early stage. 2 weeks after treatment, the BUT value in the Combination group further increased and remained higher than those in the other two groups (F=200.284, P<0.05), while the BUT value in the Gel Group, although higher than that in the Control group, showed a limited increase. This suggests that the combined treatment regimen may be more suitable for clinical treatment in patients with corneal foreign body injuries.

Comparison of CESS

Table 6 compares the CESS values of the three groups before and after treatment. The results show that there were no statistically significant differences in the CESS values among the three groups before treatment (F=0.921, P=0.631), indicating that the corneal epithelial status of the three groups was similar at baseline. 1 week after treatment, the CESS value in the Combination group was lower than those in the Gel Group and the Control group (F=185.722, P<0.05), suggesting that the combined treatment can improve the corneal epithelial status in the early stage. 2 weeks after treatment, the CESS value in the Combination group further decreased to 0 (0,0) and was lower than those in the other two groups (F=72.960, P<0.05), whereas the CESS values in the Gel Group and the Control group showed improvement, but some patients still had corneal epithelial issues. This indicates that the combined treatment regimen has a significant advantage in promoting corneal epithelial healing.

Table 1: Comparison of baseline characteristics in 3 groups

Variable	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	χ^2/F	*P-value*
Gender					
Male	55 (61.11)	50 (55.56)	52 (57.78)	0.578	0.749
Female	35 (38.89)	40 (44.44)	38 (42.22)		
Age	39.64±8.44	40.08±7.64	39.14±7.81	0.309	0.734
BMI/(kg/m²)	23.12±2.24	23.25±2.46	23.32±2.51	0.176	0.840
Education level					
Below junior college level	58 (64.44)	54 (60.00)	55 (61.11)	0.408	0.815
College degree or above	32 (35.56)	36 (40.00)	35 (38.89)		
Underlying diseases					
Hypertension	19 (21.11)	17 (18.89)	19 (21.11)		
Diabetes	20 (22.22)	21 (23.33)	16 (17.78)	0.876	0.928
Smoking history	22 (24.44)	25 (27.78)	20 (22.22)		
Affected eye					
Left eye	48 (53.33)	43 (47.78)	46 (51.11)	0.563	0.755
Right eye	42 (46.67)	47 (52.22)	44 (48.89)		
Duration (h)	26.23±8.44	25.46±7.64	26.73±7.87	0.584	0.558
Depth of corneal foreign body					
Epithelial layer	31 (34.44)	28 (31.11)	32 (35.56)		
Bowman's layer	34 (37.78)	35 (38.89)	36 (40.00)	0.856	0.931
Superficial stroma	25 (27.78)	27 (30.00)	22 (24.44)		
Corneal foreign body components					
Sand grains	21 (23.33)	17 (18.89)	22 (24.44)		
Glass fragments	22 (24.44)	25 (27.78)	19 (21.11)	3.903	0.690
Cement residues	27 (30.00)	20 (22.22)	24 (26.67)		
Iron filings	20 (22.22)	28 (31.11)	25 (27.78)		

Table 2: Comparison of clinical efficacy in 3 groups [n, (%)]

Variable	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	χ^2	*P-value*
Cured	41 (45.56)	52 (57.78)	76 (84.44)		
Effective	37 (41.11)	30 (33.33)	13 (14.44)		
Ineffective	12 (13.33)	8 (8.89)	1 (1.11)		
Total effective rate	78 (86.67)	82 (91.11)	89 (98.89)	9.604	0.008

Table 3: Comparison of pain in 3 groups ($\bar{x}\pm s$)

Variable		Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Pain relief time (days)		3 (3, 3)	2 (2, 3)	2 (2, 2)	75.602	0.000
VAS (scores)	Baseline	6 (5, 6)	6 (5, 6)	6 (5, 6)	0.464	0.793
	Week 1	3 (3, 3)	3 (2, 3)	2 (1, 2)	182.483	0.000
	Week 2	1 (0, 1)	1 (0, 1)	0 (0, 1)	22.144	0.000

Table 4: Comparison of corneal healing in 3 groups ($\bar{x}\pm s$, days)

Variable	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Corneal edema resolution time	3.39±0.45	2.86±0.37	2.41±0.35	148.462	0.000
Corneal wound healing time	9.01±2.14	7.89±2.37	5.82±1.55	56.468	0.000

Table 5: Comparison of BUT in 3 groups ($\bar{x}$±s, s)

Timepoint	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Baseline	5.45±0.76	5.49±0.46	5.41±0.71	0.341	0.711
Week 1	6.77±1.22	8.48±1.34	11.46±1.56	266.387	0.000
Week 2	10.75±1.89	12.69±1.46	15.65±1.58	200.284	0.000

Table 6: Comparison of CESS in 3 groups ($\bar{x}$±s, s)

Timepoint	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Baseline	7 (6,8)	7 (6,8)	7 (6,8)	0.921	0.631
Week 1	6 (5,6)	5 (5,5)	4 (3, 4)	185.722	0.000
Week 2	1 (0, 2)	1 (0,1)	0 (0, 0)	72.960	0.000

Table 7: Comparison of SIt in 3 groups ($\bar{x}$±s, mm)

Timepoint	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Baseline	7.44±1.22	7.54±1.34	7.49±1.19	0.144	0.866
Week 1	8.06±1.21	9.44±1.34	10.88±1.05	123.146	0.000
Week 2	9.33±1.35	10.66±1.22	12.44±0.75	170.025	0.000

Table 8: Comparison of OSDI score in 3 groups ($\bar{x}$±s, scores)

Timepoint	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	*F*	*P-value*
Week 1	16.14±2.48	14.33±2.11	11.64±2.46	83.029	0.000
Week 2	12.33±2.04	7.11±2.16	5.04±1.41	351.517	0.000

Table 9: Comparison of incidence of adverse reactions in 3 groups [n, (%)]

Variable	Control group (n=90)	Gel Group (n=90)	Combination group (n=90)	χ^2	*P-value*
Eye irritation	1 (1.11)	1 (1.11)	1 (1.11)		
Eye pain	1 (1.11)	0 (0.00)	1 (1.11)		
Eyelid itching	1 (1.11)	1 (1.11)	0 (0.00)		
Total incidence	3 (3.33)	2 (2.22)	2 (2.22)	0.282	0.868

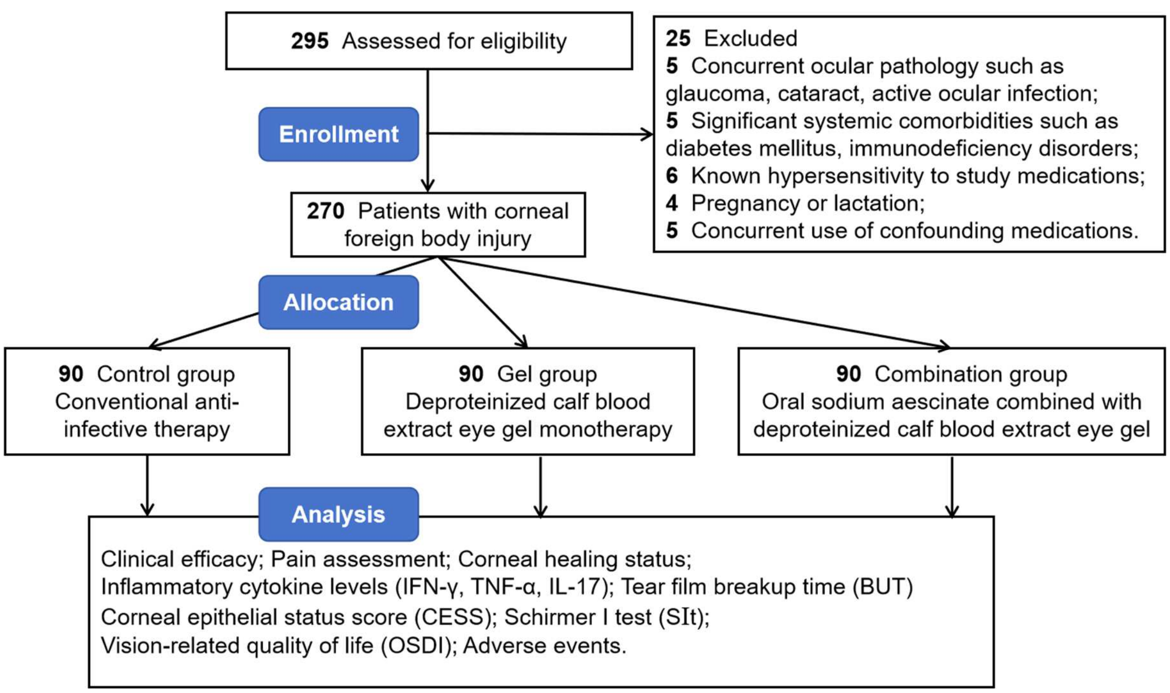

Fig. 1: Flow diagram of the study

This experiment was approved

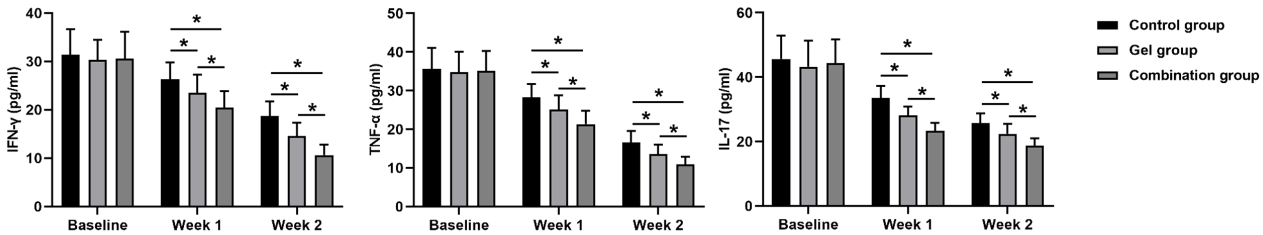

Fig. 2: Comparison of levels of inflammatory factors in tears in 3 groups
Note: *P<0.05.

Comparison of SIt

Table 7 shows that there were no statistically significant differences in the SIt results among the three groups of patients before treatment (F=0.144, P=0.866), suggesting that the tear secretion function of the groups was comparable before treatment. 1 week after treatment, the SIt value in the Combination group (10.88±1.05 mm) was higher than those in the Gel Group (9.44±1.34 mm) and the Control group (8.06±1.21 mm) (F=123.146, P<0.05). At 2 weeks, the SIt value in the Combination group further increased to (12.44±0.75 mm) and remained superior to those in the Gel Group (10.66±1.22 mm) and the Control group (9.33±1.35 mm) (F=170.025, P<0.05). This result indicates that the combined treatment regimen of sodium aescinate and DCB-EG has a synergistic effect in improving tear secretion function in patients with corneal foreign body injuries and its efficacy is better than that of single gel therapy or conventional treatment.

Comparison of ocular-related daily life quality

Table 8 shows that at 1 week (F=83.029, P<0.05) and 2 weeks (F=351.517, P<0.05) after treatment, the OSDI scores in the Combination group were lower than those in the Control group and the Gel Group, indicating that the combined treatment regimen has a significant advantage in improving ocular surface symptoms in patients with corneal foreign body injuries and its efficacy is superior to that of single gel therapy or conventional anti-infective treatment. This synergistic effect may stem from the complementary effects of sodium aescinate's anti-inflammatory and tissue edema-reducing actions and DCB-EG's promotion of corneal epithelial repair function. This result supports the clinical application value of combined medication, particularly for patients who require rapid symptom relief and promotion of ocular surface repair.

Comparison of adverse reaction occurrence

In the Control group, there was 1 case of eye irritation, 1 case of eye pain and 1 case of eyelid pruritus, with an incidence rate of 3.33% (3/90). In the Gel Group, there was 1 case of eye irritation and 1 case of eyelid pruritus, with an incidence rate of 2.2% (2/90). In the Combination group, there was 1 case of eye irritation and 1 case of eye pain, with an incidence rate of 2.2% (2/90). No special interventions were performed in any of the three groups and the symptoms resolved spontaneously within 1 to 3 days. There was no statistically significant difference in the incidence of adverse reactions among the three groups (χ^2=0.282, P=0.868). See table 9.

DISCUSSION

Corneal foreign body injury is a common ocular emergency in clinical practice and the key to its treatment lies in rapidly alleviating symptoms, promoting corneal tissue repair and reducing secondary damage (Guarin *et al.*, 2023). Although the current clinical approach primarily involves foreign body removal combined with anti-infective treatment, monotherapies still have limitations in terms of inflammation control, corneal repair speed and functional recovery (Shrestha *et al.*, 2022). In recent years, multi-target combined treatment strategies have gradually become a research focus, aiming to enhance efficacy through the synergistic effects of different mechanisms. This study innovatively applied a combination of sodium aescinate tablets and DCB-EG. The results showed that this regimen was superior to the single gel treatment group and the conventional anti-infective Control group in terms of pain relief, corneal healing speed, inflammation regulation and ocular surface function recovery.

This study found a 98.89% total effective rate in the Combination group, surpassing that of the group using DCB-EG alone (91.11%) and the conventional anti-infective treatment Control group (86.67%). This difference in efficacy not only confirms the clinical advantages of the combined treatment strategy but also reveals a potential synergistic mechanism between sodium aescinate and DCB-EG in the treatment of corneal foreign body injuries. An in-depth analysis of efficacy indicators reveals that the combined treatment exhibits significant advantages in key metrics such as pain relief time, VAS pain scores, corneal edema resolution time and corneal wound healing time. Sodium aescinate, a triterpene saponin derived from aesculus seeds, possessing multiple pharmacological effects, including anti-inflammatory, anti-exudative, microcirculation-improving and antioxidant properties (Huang *et al.*, 2022). These characteristics make it widely used in clinical practice for treating conditions such as cerebral edema, postoperative edema, chronic venous insufficiency and inflammation caused by trauma or burns (Li *et al.*, 2020; Wang *et al.*, 2024; Zhang *et al.*, 2023). Following corneal injury, inflammatory response is one of the primary factors contributing to pain and tissue damage. At the molecular level, sodium aescinate effectively inhibits the activation process of proteases by stabilizing lysosomal membrane structures, thereby reducing vascular permeability and the release of inflammatory mediators (Xie *et al.*, 2024). This anti-inflammatory effect creates a favorable microenvironment for tissue repair. Meanwhile, its ability to enhance venous tension improves local microcirculation, providing adequate oxygen and nutrient supply to damaged tissues and facilitating the clearance of metabolic wastes. These effects collectively form the foundational conditions for tissue repair. DCB-EG, an ophthalmic drug, mainly consists of deproteinized calf blood extract with free amino acids, low-MW peptides and oligosaccharides (Li *et al.*, 2020). DCB-EG directly participates in the repair process through its rich bioactive components, with amino acids and nucleotides providing the material basis for corneal epithelial cell migration and proliferation, while various growth factors and low-molecular-weight peptides activate cellular metabolic processes, promoting collagen synthesis and remodeling in the stromal layer (Wu *et al.*, 2021). Additionally, the eye gel formulation forms a protective film on the corneal surface, reducing secondary damage to the injured area from external stimuli such as blinking friction. The synergistic effects of the two drugs manifest in the optimization of multiple treatment stages. In terms of pain control, inflammation inhibition and accelerated epithelial repair effectively reduce stimulation of exposed nerve endings; in tissue repair, improved microcirculation and enhanced cellular metabolism jointly promote edema resolution and wound healing. This multi-target intervention strategy not only enhances treatment efficiency but also reduces the risk of complications by shortening the disease course.

The results of BUT, CESS and SIt indicate that the Combination group demonstrated significant superiority over the other two groups after treatment. This suggests that combined therapy not only accelerates the repair of corneal structure but also improves ocular surface function. Sodium aescinate effectively inhibits the inflammatory cascade following corneal injury through its anti-inflammatory properties (Chen *et al.*, 2024). The reduction in inflammatory factors lowers the tear evaporation rate and alleviates the inhibitory effect of inflammation on meibomian gland function. Additionally, sodium aescinate enhances local blood circulation by improving microcirculation, providing better nutritional support to the cornea. A favorable nutritional state helps maintain tear film stability and reduces tear evaporation. DCB-EG promotes goblet cell regeneration and increases mucin secretion, both of which contribute to the perfection of the tear film's three-layer structure, particularly strengthening the outermost lipid layer and the innermost mucin layer, thereby prolonging BUT (Nam and Maeng, 2019). DCB-EG directly stimulates corneal epithelial cell proliferation and migration, accelerating the closure of epithelial defects; sodium aescinate, on the other hand, improves the microenvironment of corneal limbal stem cells, providing a continuous source of cells for epithelial regeneration. This dual action results in complete structural and functional repair of the corneal epithelium, as evidenced by significant improvements in CESS scores. An intact epithelial barrier not only reduces fluorescein staining but, more importantly, re-establishes the mechanical protection and immune defense functions of the ocular surface. Sodium aescinate enhances tear gland perfusion and nutritional supply by improving ocular microcirculation, while the neurotrophic factors in DCB-EG promote the recovery of parasympathetic nerve function innervating the tear gland. These two effects synergistically enhance tear gland secretory function, leading to a significant increase in SIt values. Increased tear secretion not only alleviates ocular surface dryness but also removes more inflammatory mediators and metabolic wastes through the tear circulation. This comprehensive improvement in ocular surface function forms a positive feedback loop. The advantage of combined therapy lies in its simultaneous action on multiple links of this loop, whereas single therapies often only improve one aspect. Therefore, the Combination group outperforms the other two groups in all indicators, demonstrating a more comprehensive therapeutic effect.

In terms of ocular-related daily life quality, the OSDI scores of the Combination group at 1 week and 2 weeks post-treatment were lower than those of the Control group and the Gel Group. OSDI score is a key measure for evaluating ocular surface diseases' effect on quality of life, covering multiple dimensions such as ocular symptoms, visual function and environmental triggers (Ashrafizadeh, 2024; Ren, 2024). The significant reduction in OSDI scores in the Combination group indicates that this treatment regimen can more effectively alleviate patients' clinical symptoms, improve visual function and reduce the adverse effects of environmental factors on the eyes, thereby enhancing patients' ocular-related quality of life. This holds significant clinical importance for patients with corneal foreign body injuries, as such injuries not only affect patients' vision but also exert a substantial negative impact on their daily lives and work (Sumual *et al.*, 2023). By improving patients' quality of life, the combined treatment regimen not only aids in patients' recovery but also reduces the social and economic burdens associated with ocular diseases. Additionally, no significant differences in adverse reaction rates were observed between the groups and the symptoms were mild, mostly resolving spontaneously within 1-3 days. This suggests that the treatment of corneal foreign body injuries with sodium aescinate tablets combined with DCB-EG is safe and does not increase the occurrence of adverse reactions in patients. In clinical practice, safety is a crucial consideration when selecting treatment regimens and the excellent safety profile of this combined treatment regimen provides strong support for its widespread application.

Current treatment for corneal foreign body injuries mainly involves local antibiotics and artificial tears, which have limitations in promoting repair and reducing inflammation. This study shows that combining sodium aescinate and DCB-EG can enhance corneal repair and symptom relief. This optimized regimen may transform clinical practice, offering a more effective and comprehensive option for clinicians and improving patient satisfaction.

Study limitations

Despite the promising findings of this study on the combined treatment of sodium aescinate tablets and DCB-EG for corneal foreign body injury, several limitations must be acknowledged. The retrospective cohort design lacks randomization and blinding, which may introduce selection and information biases, thereby compromising the accuracy and reliability of the results. Additionally, the relatively short follow-up period of only 2 weeks restricts the comprehensive assessment of long-term therapeutic outcomes, particularly regarding long-term visual prognosis, for which no data are available. The safety discussion is superficial, with no stratified analysis of adverse reactions and insufficient consideration of the potential risks associated with systemic absorption of sodium aescinate. The conclusion may overstate the clinical applicability without adequately exploring potential differences in treatment response among various patient subgroups (e.g., varying ages or injury severities) or under different clinical conditions. Future research should validate the therapeutic effects through prospective, randomized controlled trials and conduct stratified analyses across different patient populations to provide a more comprehensive assessment of the safety and efficacy of this combined treatment regimen.

CONCLUSION

In summary, sodium aescinate tablets combined with DCB-EG demonstrate significant clinical advantages in the treatment of corneal foreign body injuries. Through their synergistic effects of anti-inflammation, promotion of repair and improvement of ocular surface function, they provide patients with a rapid and safe treatment option.

Acknowledgment

Not applicable.

Authors' contributions

[Xiaoyu Wang]: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions.

[Yake Sun]: Participated in collecting, assessing and interpreting the date. Made significant contributions to date interpretation and manuscript preparation.

[Qingliang Zhao]: Provided substantial intellectual input during the drafting and revision of the manuscript.

Funding

There was no funding.

Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

This clinical study strictly adhered to the Declaration of Helsinki (Wen *et al.*, 2025) and relevant ethical guidelines. The research protocol was approved by Suzhou Ideal Eye Hospital Ethics Committee (Ethical Approval Number: SLER2022201). During the research process, researchers will fully inform the participants or their legal representatives about the study objectives, implementation procedures, potential risks and safeguards for their rights and interests. Only after obtaining their voluntary written informed consent can participants be included in the study. Meanwhile, the study will strictly protect the personal information and data privacy of participants, in compliance with relevant requirements for medical ethics and data security.

Consent to publish

The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.

Conflicts of interest

The authors declare that they have no financial conflicts of interest.

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