Assessment of ocular irritation and tear fluid drug levels following administration of antibiotics suspended in a self-emulsifying eye drops

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INTRODUCTION

Cefuroxime sodium (CEF) and vancomycin hydrochloride (VAN) are antibiotics used in ophthalmic therapy however they are unstable in aqueous eye drops. To enhance stability, an anhydrous self-emulsifying oil (SEO) system was used as a carrier. Previous studies demonstrated high stability of both antibiotics in SEO (1 year at 40 °C and 2 years at 25 °C) [1,2]. **This study aimed to evaluate the *in vivo* elimination kinetics and ocular irritation of SEO suspensions containing 5% CEF or VAN, as well as to determine antibiotic concentrations in tear fluid.**

CONCLUSION

SEO suspensions were well tolerated and classified as non-irritating. CEF and VAN administered in SEO achieved tear fluid concentrations comparable to currently used aqueous eye drops, despite high inter- and intra-individual variability. Unexpectedly, both SEO and aqueous formulations remained detectable up to 14 h after administration. These findings indicate that the anhydrous SEO system stabilizes antibiotics that are unstable in aqueous media while maintaining ocular drug residence time similar to aqueous solutions, highlighting its potential for clinical application.

METHODS

🧪 FORMULATION
CEF or VAN (5% w/w)
+ sodium citrate (2%)
in SEO system
(Miglyol + Tween 20 5%)

- Ultra-Turrax mixing
- High-pressure homogenization
- Microscopic verification

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🐖 IN VIVO STUDY
60 healthy pigs
1 drop per eye
3× daily for 3 days
Tested formulations:
CEF-SEO | VAN-SEO
Controls:
CEF and VAN (aqueous)
Miglyol | SEO placebo
Ethic approval:
WAW2/093/2025

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👁️ IRRITATION TEST
Draize irritation test

Cornea (0–80)
Conjunctiva (0–20)
Iris (0–10)
Maximum score: 110

Evaluation:
30 min after administration

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💧 TEAR FLUID ANALYSIS
Schirmer strips collection
2 h | 5 h | 14 h

Extraction in mobile phase
HPLC-UV analysis
CEF 273 nm
VAN 210 nm

Student's t-test
$p < 0.05$

Figure 1. Collection of tear fluid from a pig using Schirmer strips.

RESULTS

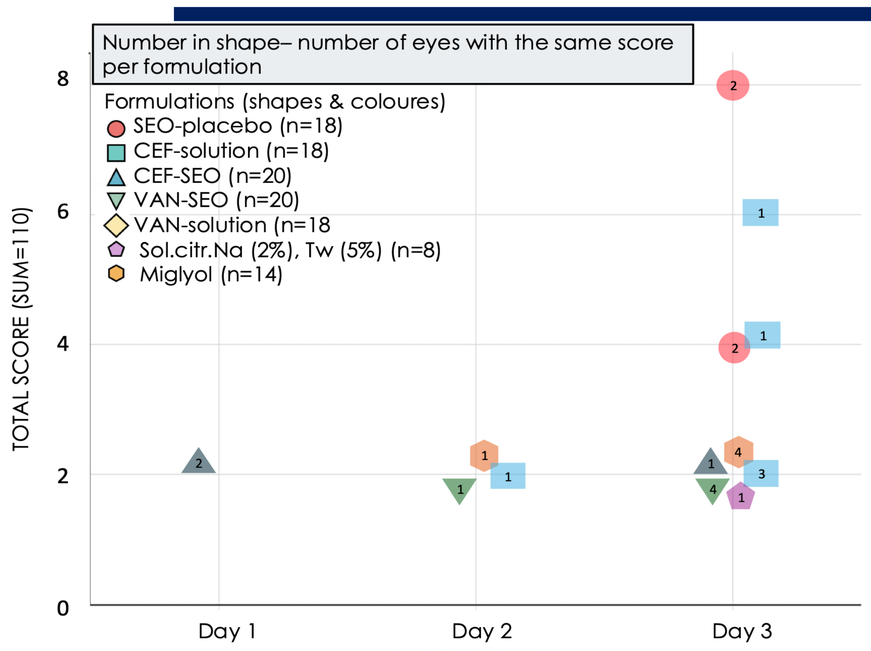

Figure 2. Number of eyes showing changes in conjunctiva depending on the type of formulation and days of application.

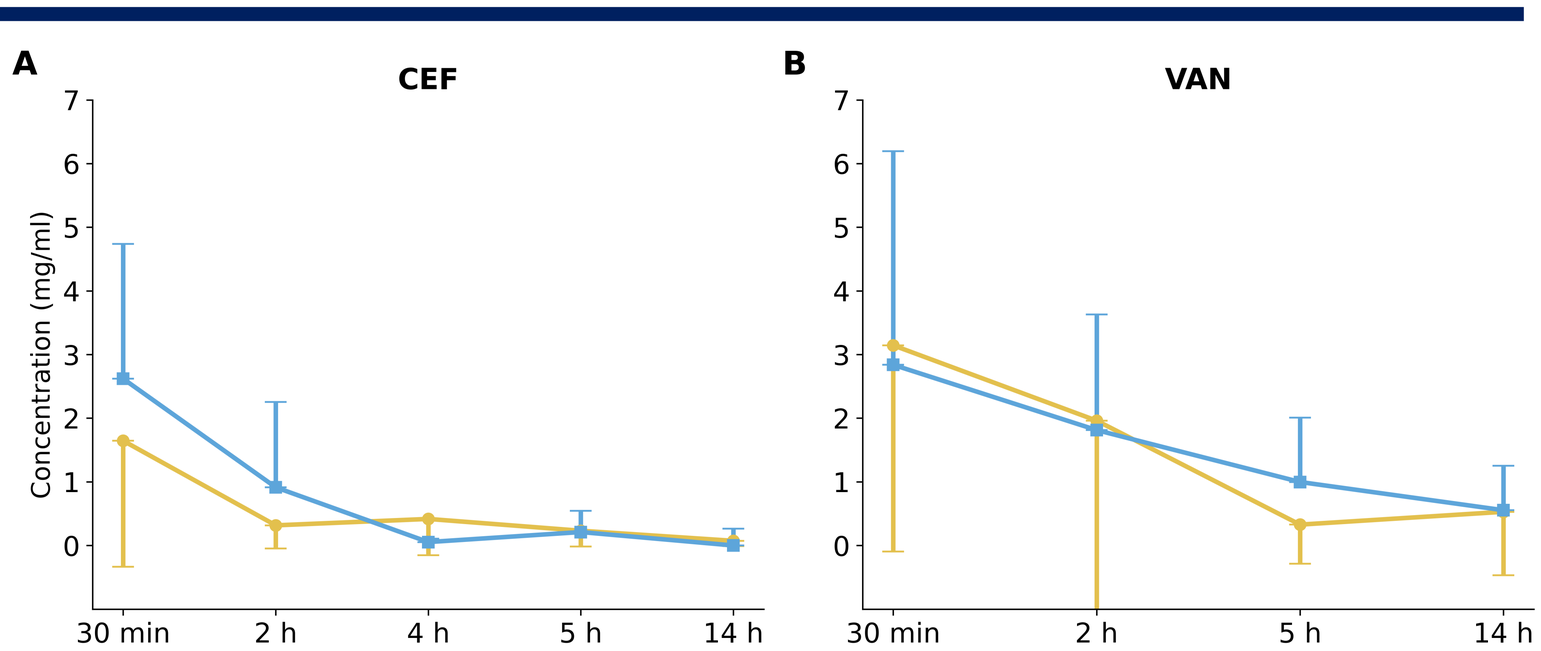

Figure 3. Tear fluid concentrations of CEF (A) and VAN (B) after administration of SEO suspensions and aqueous solutions (mean ± SD, n=10).

Draize test

No irritating effects were observed for any formulation 30 min after administration. CEF-SEO (0.213 ± 0.62) and VAN-SEO (0.188 ± 0.59) were classified as non-irritating according to the Draize test and Kay & Calandra scale (<0.5). Miglyol showed the highest score (0.406 ± 0.84), still within the non-irritating range. VAN solution caused no irritation, while CEF-SEO was less irritating than the currently used CEF solution.

Antibiotic concentration in tear fluid

Tear fluid concentrations of CEF and VAN obtained after administration of SEO suspensions were comparable to those achieved with aqueous solutions. Antibiotic concentrations remained detectable up to 14 h after administration despite the reported ~30 min ocular surface clearance. High inter- and intra-individual variability in tear fluid concentrations was observed.

REFERENCES

1. Sznitowska, M.; Baczek, T.; Sych, A.; Krzeminska, K. Self-emulsifying pharmaceutical composition in the liquid form, containing as the active substance a drug substance unstable in an aqueous environment. European Patent EP3917498 (2025).
2. Krzeminska, K.; Sznitowska, M.; Wroblewska, M.; Wolska, E.; Winnicka, K. Suspensions of antibiotics in self-emulsifying oils as a novel approach to formulate eye drops with substances which undergo hydrolysis in aqueous environment. Drug. Deliv., 31, (2024).
3. Draize, J.H.; Woodard, G.; Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther., 82, (1944).
4. Krzeminska, K.; Wolska, E.; Chorążewicz, J.; Sznitowska, M. Preliminary in vivo ocular tolerance assessment of a cefuroxime sodium suspension in self-emulsifying oil. Pharmaceutics, 17, (2025).

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