

Evaluating the Lubricating Effect of Semifluorinated Alkanes on the Ocular Surface

P. Agarwal¹, Darina Khun¹, Sonja Krösser², Kirsten Eickhoff², Frederick S. Wells³, Geoff R. Willmott³, Jennifer P. Craig⁴, Ilva D. Rupenthal¹

¹Buchanan Ocular Therapeutics Unit, Department of Ophthalmology, New Zealand National Eye Centre, The University of Auckland, Auckland, New Zealand; ²Novaliq GmbH, Heidelberg, Germany;

³Department of Physics, Faculty of Sciences, The University of Auckland, New Zealand; ⁴Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

Purpose

Dry eye disease (DED) is one of the most prevalent ocular surface disorders causing significant pain and discomfort to patients. Recently, the semifluorinated alkane (SFA), perfluorohexyloctane (NovaTears®; EvoTears®), was introduced as a preservative-free, non-aqueous eye drop for the treatment of DED symptoms. This study evaluated the mechanisms by which perfluorohexyloctane exerts its effect on the ocular surface in comparison to a shorter chain SFA (perfluorobutylpentane) and saline.

OBJECTIVES

- a) To evaluate the spreading behaviour of semifluorinated alkanes on the corneal surface *ex vivo*; and
- b) To study their effects on tear fluid dynamics *in vivo*.

Methods

Spreading of both SFAs on the ocular surface was evaluated *ex vivo* using high speed photography.

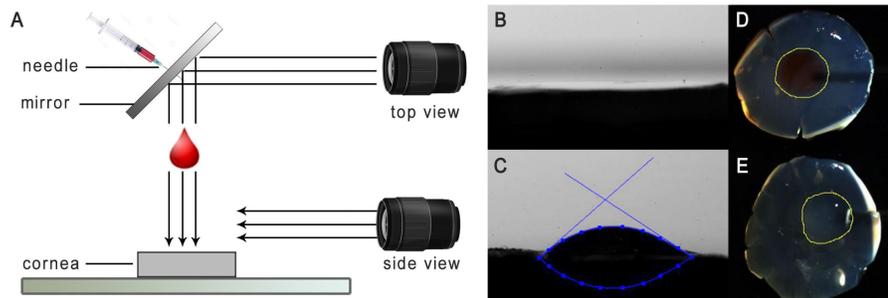


Figure 1. High speed photography set up and analysis. A. Schematic diagram of the experimental set-up with side view images of B. perfluorohexyloctane and C. saline used to measure the contact angle and top view images of D. perfluorohexyloctane and E. saline used to measure the spread area.

Additionally, the influence of SFAs on tear fluid dynamics in comparison to saline was evaluated *in vivo* after instillation of the test eye drops twice a day (b.i.d.) into healthy rabbit eyes for seven days. Lipid layer grade, tear evaporation rate and tear volume were observed daily during the course of treatment, while tear osmolarity was observed before commencing the study and after the final instillation. Safety and tolerability of SFAs were also assessed by clinical scoring and sodium fluorescein staining.

Results

High speed photography studies showed that aqueous saline droplets underwent partial restitution immediately after contact with the cornea resulting in a contact angle of $40.0 \pm 3.2^\circ$. SFAs, on the other hand, rapidly spread on the corneal surface to form thin films with their contact angle being practically zero.

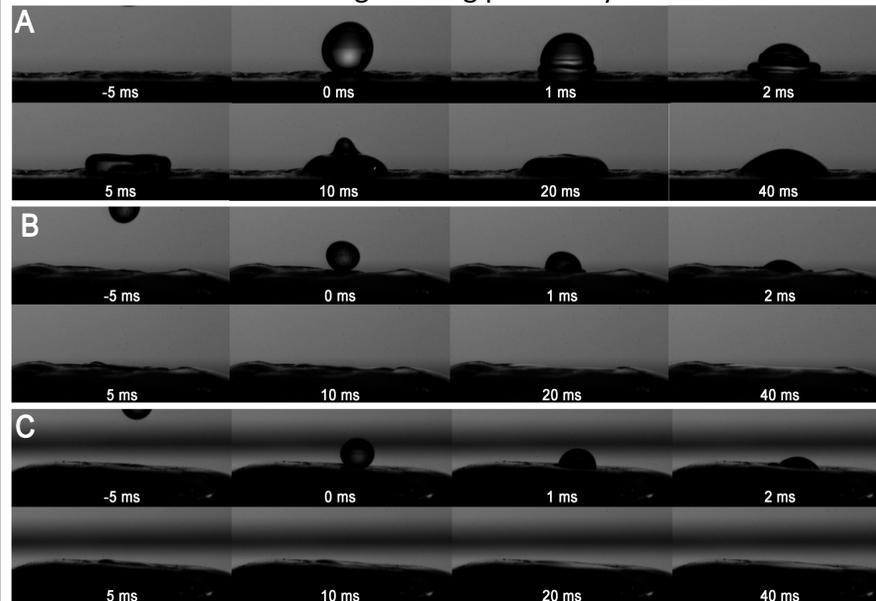


Figure 2. Representative images showing interaction of A. saline, B. perfluorobutylpentane and C. perfluorohexyloctane on the ocular surface

The drop volume of both SFAs was one-third that of saline; nevertheless, their spread area on the ocular surface was significantly greater than that of saline. Perfluorobutylpentane appeared to spread slightly more rapid on the corneal surface than perfluorohexyloctane, possibly due to the comparatively lower viscosity.

Table 1. Spreading dynamics of the test eye drops (n = 3; mean ± SEM).

	Drop volume (mm ³)	Contact angle (θ°)	Spread area (mm ²)	Volume adjusted area [#]
Saline	11.0 ± 0.1	40.0 ± 3.2	18.5 ± 1.2	3.7 ± 0.2
Perfluorobutylpentane	3.1 ± 0.2	n/a*	28.2 ± 0.4	13.3 ± 0.3
Perfluorohexyloctane	3.0 ± 0.1	n/a*	20.1 ± 1.1	9.6 ± 0.4

* contact angle too low to be measured given the image contrast

[#] volume adjusted area calculated as spread area (mm²) divided by drop volume (mm³)^{2/3}

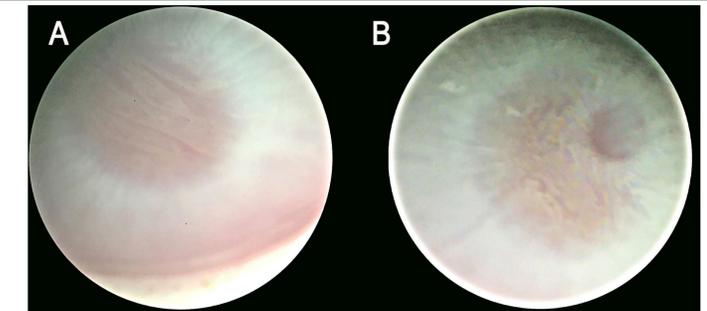


Figure 3. Representative images showing the improvement in lipid layer grade from A. Grade 3 (waves) at baseline to B. Grade 5 (coloured fringes) post-instillation of perfluorohexyloctane

A significant improvement in lipid layer grade was observed immediately post-instillation of both SFAs. However, this effect was more pronounced and long-lasting in perfluorohexyloctane treated eyes which showed a statistically significant improvement from baseline from day-5 onwards.

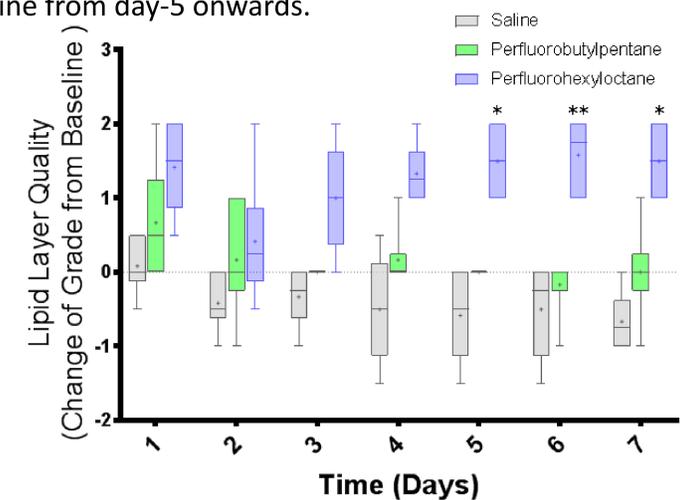


Figure 4. LLG observed after b.i.d. instillation of the test eye drops over seven days (n=6; 12 eyes)

No perceptible change in tear evaporation rate, tear volume or tear osmolarity was evident upon b.i.d. instillation of either SFA. Moreover, both SFAs appeared to be well-tolerated on the ocular surface with no corneal or conjunctival adverse effects being observed during the course of the study.

Conclusion

Both SFAs showed excellent corneal wetting and tended to rapidly spread on the ocular surface. Perfluorohexyloctane was also found to progressively improve the lipid layer grade after topical application supporting its lubricating effect to provide symptomatic relief in DED patients.