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Department of Ophthalmology
University Hospital of Cologne

Omega-3 Fatty Acids Using F6H8-Carrier as Topical Therapy in Experimental Dry-Eye Disease

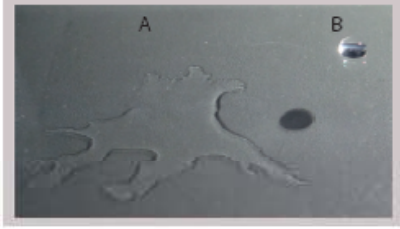
U. Gehlsen[1,2], T. Braun[1,2], P. Steven[1,2]

[1] Department of Ophthalmology, University of Cologne, Cologne, Germany, [2] Cluster of Excellence: Cellular Stress Responses in Aging-associated Diseases (CECAD), University of Cologne, Germany

Background/ Purpose: Dry eye disease is a frequent inflammatory disorder of the lacrimal functional unit including disturbances of the tearfilm. Oral as well as topical treatment with omega-3 fatty acids (O3F) has shown positive effects on dry eye (1,2) . However, O3F are water insoluble, therefore have to be formulated using emulsifiers and surfactants, which might have strong ocular side effects.

Semifluorinated alkanes (SFA) have the ability to serve as drug delivery platform for lipophilic substances. Furthermore, a SFA, F6H8, was just introduced as medical device in EU as NovaTears/Evotears®. It improved signs and symptoms (corneal staining, Schirmer test, TFBUT) in dry eye disease. OSDI dropped also significantly (3).

This experimental study was designed to test the efficacy of topical application of O3F using a semifluorinated alkane (F6H8) as preservative-free lipophilic carrier.



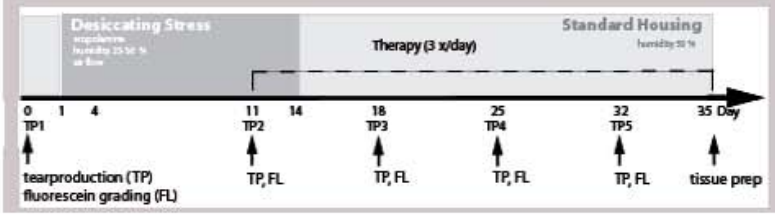
SFAs

- Thermally, chemically, biologically inert
- Amphiphilic compounds
- Low surface tension

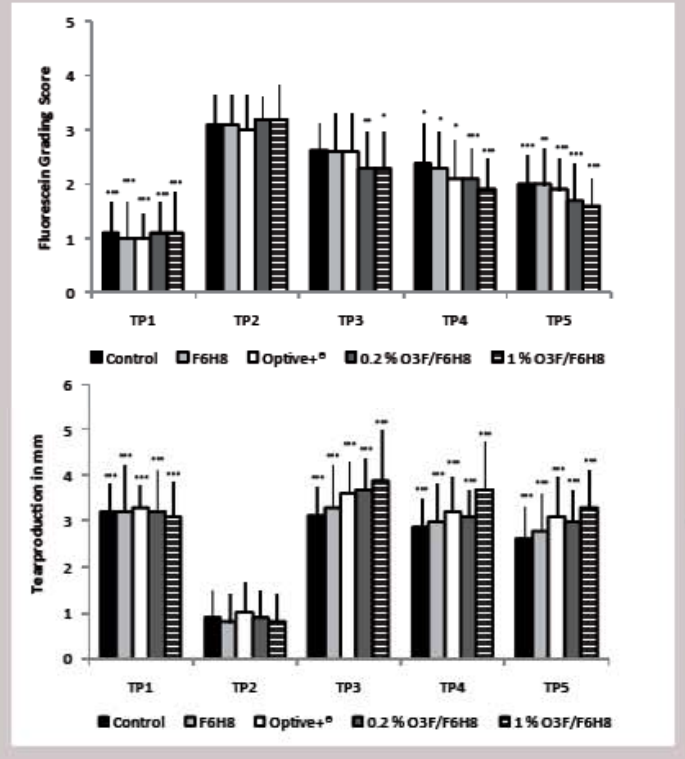
Droplets on glass surface: (A) F6H8 (NovaTears/Evotears®, Novaliq GmbH, Germany), (B) artificial tear containing 0.24% hyaluronic acid

Materials/ Methods: EDE was induced in adult 10-12 week old female C57BL/6 mice using a controlled environmental chamber for 14 days and treatment with scopolamine (Desiccating Stress Model) (4) and subsequent transfer to standard housing conditions until day 35. Topical therapy was performed 3 x 5µl/day starting from day 11. Mice were distributed in four groups: (1) 0.2 % O3F/F6H8 (Novaliq GmbH, Germany), (2) 1% O3F/F6H8 (Novaliq GmbH, Germany), (3) carrier only F6H8 and (4) artificial tears containing castor oil (Optive plus®, Allergan, USA). A control group (5) received no eye drops, but was kept under the same conditions as the therapy groups. Clinical readouts were undertaken weekly (amount of tear fluid, corneal epithelial staining) in combination with a final preparation of conjunctival tissue for counting goblet cell density at day 35. Experiments were performed two times with comparable results.

Experimental Set-Up:



1. O3F/F6H8 is effective in treating EDE
O3F/F6H8 shows faster response than F6H8



2. Goblet cell numbers following topical therapy with O3F/F6H8

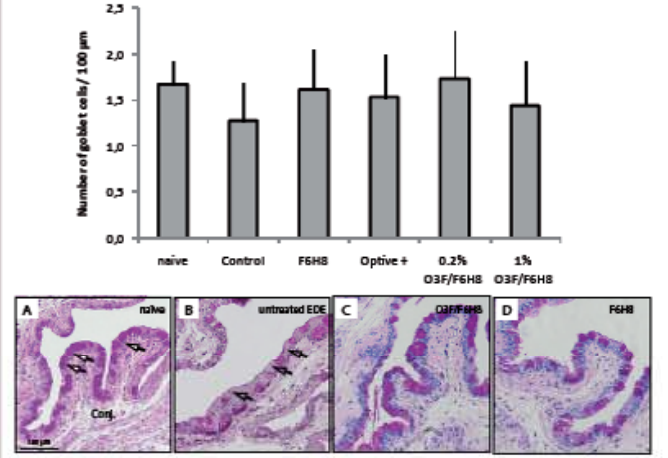


Fig. 1: Topical therapy with 0.2% and 1% O3F/F6H8 resulted in significant earlier decrease of epithelial staining compared to control, F6H8 and Optive+ ° in 12 week old mice.
Amount of tear fluid tended to be increased in O3F/F6H8 group compared to control group. (n=5 mice/group, experiment was repeated twice with comparable results. (* indicating statistical differences compared to TP2 (end of EDE). Statistical analysis was performed using ANOVA, post hoc LSD. * p<0.05, ** p< 0.001, *** p<0.0001).

Fig. 2: EDE resulted in a significant loss of goblet cells (open arrows) at day 35 in untreated control mice (B). Following therapy with F6H8 and O3F/F6H8 goblet cell numbers tended to be increased compared to untreated control (C+D). Numbers of goblet cells were calculated from the lower cul-de-sac until the lid margin and presented per 100 µm (E). (PAS-staining. Conj.- conjunctiva).

Conclusion:

- O3F/F6H8 is moderately effective in treating experimental dry-eye disease by reducing corneal staining
- Compared to a treatment with an artificial tear containing castor oil O3F/F6H8 showed a faster response in this study
- Based on these results first clinical applications in dry eye patients are planned. O3F formulated in SFA may present an improved treatment of dry eye delivering O3F directly to the lipid layer of the ocular surface

Literature:
1 Rashid et al.(2008) Arch. Ophthalmol. 126(2).
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3 Steven et al. (2015) J. Ocular Pharma. Therap. 31(8).
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uta.gehlsen@uk-koeln.d