The HydroEye Clinical Trial Lead Investigators

John D. Sheppard, MD, MMSc

- Professor of Ophthalmology, Microbiology & Molecular Biology, Eastern Virginia Medical School
- President and Senior Partner, Virginia Eye Consultants
- Ophthalmology Residency Research Program Director, and Clinical Director, Thomas R. Lee Center for Ocular Pharmacology, Eastern Virginia Medical School; Associate and Mentor Examiner, American Board of Ophthalmology since 2002
- Principal investigator in over 70 clinical research trials for major pharmaceutical companies and the FDA
- Author of over 100 peer review abstracts, journal articles, and chapters; serves on editorial board, EyeNet Magazine and as an editor for eMedicine online; reviewer for 9 major peer-reviewed ophthalmic journals, advisory board member for 17 pharmaceutical and device companies
- Included in "Best Doctors in America"; received the American Academy of Ophthalmology Honor Award in 1995

Stephen C. Pflugfelder, MD

- Director, Ocular Surface Center, Cullen Eye Inst., Baylor Coll. of Med.
- James and Margaret Elkins Chair and Professor of Ophthalmology, Baylor College of Medicine
- Published over 220 peer-reviewed articles, over 45 book chapters and monographs; co-edited the textbook: "Dry Eye and Ocular Surface Disorders"; serves on editorial boards of the journals: American Journal of Ophthalmology, Eye & Contact Lens, The Ocular Surface, and Investigative Ophthalmology and Visual Science
- Included in "Best Doctors in America"; received the 2000 American Academy of Ophthalmology Senior Achievement Award and 2002 Research to Prevent Blindness Senior Investigator Award
- Jackson Memorial Lecturer, Tear Dysfunction and the Cornea, American Academy of Ophthalmology Meeting, 2011
- Served as chairman of the American Academy of Ophthalmology's Lifelong Education for Ophthalmologists Committee and Preferred Practice Pattern Committee on Corneal & Ocular Surface diseases

"Statistical significance in any dry eye study is a remarkable achievement, especially considering the exceptional difficulty experienced by numerous pharmaceutical companies attempting to bring a new dry eye therapeutic to the marketplace over the past decade. Thus, our data becomes even more remarkable."

- John D. Sheppard, MD, MMSc

"These are impressive results, since reaching significance for multiple study endpoints typically requires far more clinical trial participants."

- Stephen C. Pflugfelder, MD

HydroEye - Powerful Dry Eye Relief:

HydroEye is a patented nutritional formula that works from the inside out to provide continuous dry eye relief. HydroEye delivers a proprietary blend of omega fatty acids, antioxidants and other key nutrients that work together to support a healthy tear film and dampen inflammation.

Suggested Use:

Take a total of four softgels daily (two in the morning, two in the evening), with meals.

Note:

Using HydroEye with anticoagulants, such as Coumadin®, may increase their effect. Prothrombin time (bleeding time) can be assessed by the primary care physician to ensure the safe addition of HydroEye to an anticoagulant regimen. Sufficient scientific evidence for safe use of GLA during pregnancy and while breast feeding is not available. Individuals with medical conditions should consult a physician before using. Keep out of the reach of children.

Supplement Facts

Serving Size: 4 softgels
Servings Per Container: 30

	Amount Per Serving	% Daily Value*
Calories	30	
Total Fat	2.5 g	3%
Vitamin A (from retinyl palmitate and cod liver oil)	625 mcg RAE	69%
Vitamin C (as ascorbic acid)	240 mg	267%
Vitamin E (d-alpha tocopherol)	8 mg	53%
Vitamin B6 (from pyridoxal 5-phosphate)	12.6 mg	741%
Magnesium (from magnesium sulfate)	40 mg	10%
Black Currant Seed Oil [15% gamma linolenic acid (GLA); also contains 12-15% alpha linolenic acid (ALA)]	1570 mg	†
Omega-3 Fatty Acids (100 mg EPA, 70 mg DHA from USP®-Verified fish oil)	170 mg	†

*Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Other Ingredients: Bovine Gelatin, Glycerin, Beeswax, Water, Mucin Complex, Sunflower Lecithin, Caramel Color, Titanium Dioxide and Lemon Oil.

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The HydroEye® Clinical Trial ▸Fact Sheet

Participants receiving HydroEye® had significant improvements in irritation symptoms, a smoother corneal surface, and lower levels of inflammation compared to placebo after 6 months of study.

Design

- In this multi-center, randomized, controlled trial, 38 postmenopausal women with dry eye (moderate to severe KCS) received 4 softgels daily of HydroEye® or placebo, and were evaluated at 0, 4, 12, 24 weeks for a number of efficacy outcomes.

Dry Eye Symptoms

- ***Measure:*** validated questionnaire, the Ocular Surface Disease Index (OSDI) was used to assess severity of symptoms.
- ***Results:*** OSDI scores progressively improved in the HydroEye group, reaching significance at 12 and 24 wks *(p=0.004)*. OSDI scores were significantly improved over placebo at the trial's end *(p=0.05)*.

Ocular Surface Inflammation

- ***Measures:*** Inflammation was measured by two biomarkers – HLA-DR, a dendritic cell activation marker that increases when exposed to inflammatory cytokines; and CD11c, a molecule on certain dendritic cells that regulates their migration. Conjunctival impression cytologies were obtained (pressing a membrane to the conjunctiva to collect cell samples) and immunostained.
- ***Results:*** HydroEye® prevented increases of HLA-DR (Class II antigen) positive dendritic conjunctival cells, plus CD11c positive cells over time.
- In contrast, these cells significantly increased in placebo takers *(p=0.03 & 0.004, respectively for biomarkers)*. CD11c levels were significantly increased starting at 12 weeks.
- At the trial's end, both biomarkers were significantly lower in the HydroEye® group than in placebo *(p=0.001)*. CD11c levels were significantly different between groups starting at 12 weeks.

Corneal Surface Smoothness

- ***Measure:*** Topographic corneal regularity indexes (SAI & SRI) – reported to increase in dry eye, contribute to irritation symptoms, and correlate with quality of vision – were assessed as measures of corneal smoothness.
- ***Results:*** SAI values were maintained in the HydroEye group over time. SAI values increased in placebo group, indicating decreased corneal surface smoothness. SAI was significantly lower in supplement-treated subjects than placebo at the study's end *(p=0.005)*.

Summary of Findings

- HydroEye® improved dry eye symptoms over time, and compared to placebo. Ocular surface inflammation was suppressed and corneal surface smoothness maintained in the HydroEye group, while the placebo group worsened over the 6-mo testing period.

Conclusion

- HydroEye® presents a safe, effective and affordable option for managing dry eye in this patient population.

In the Words of the Investigators:

"This is the most meaningful study to date on a nutritional supplement's role in dry eye."

- Stephen C. Pflugfelder, MD

"This is a prospective, masked, randomized, placebo controlled, multi-center study conducted as would be any FDA registration trial, and monitored under the most stringent standards."

- John D. Sheppard, MD, MMSc

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Study Abstract | *From: Sheppard JD, et al. Long-term supplementation with n-6 and n-3 PUFAs improves moderate-to-severe Keratoconjunctivitis Sicca: A randomized double-blind clinical trial. Cornea 32:1297-1304, 2013.*

Purpose:

Supplementation with gamma-linolenic acid (GLA) and omega-3 (n-3) polyunsaturated fatty acids (PUFAs) has been found to decrease the production of disease-relevant inflammatory mediators that are implicated in the pathogenesis of chronic dry eye. This study evaluated the effect of a supplement containing both GLA and n-3 PUFAs on signs and symptoms of moderate-to-severe keratoconjunctivitis sicca in postmenopausal patients.

Methods:

This multicenter, double-masked placebo-controlled clinical trial enrolled 38 patients (both eyes) with tear dysfunction who were randomized to supplemental GLA + n-3 PUFAs or placebo for 6 months. Disease parameters, including Ocular Surface Disease Index, Schirmer test, tear breakup time, conjunctival fluorescein and lissamine green staining, and topographic corneal smoothness indexes (surface asymmetry index and surface regularity index), were assessed at baseline and at 4, 12, and 24 weeks. The intensity of dendritic cell CD11c integrin and HLA-DR expression was measured in conjunctival impression cytologies.

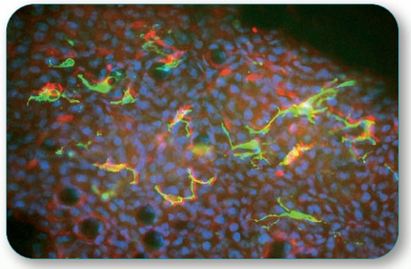

FIGURE 1. Representative picture of impression cytology membrane. Dendritic cells in a baseline conjunctival impression cytology immunostained for HLA-DR (green) and CD11c (red) antigens.

Results:

The Ocular Surface Disease Index score improved with supplementation and was significantly lower than placebo (21 ± 4 vs. 34 ± 5) after 24 weeks *(P = 0.05, see Figure 2)*.

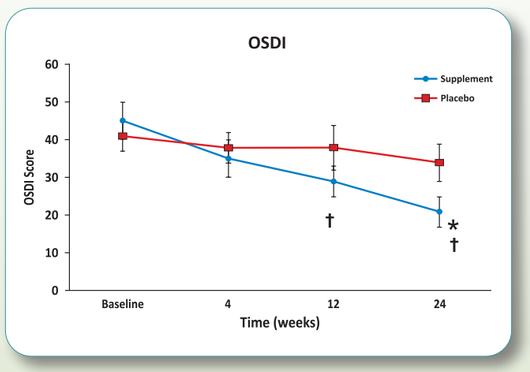

FIGURE 2. OSDI scores (mean ± SEM) decreased consistently over the 24-week treatment period after supplement treatment. †Significant improvement when compared to baseline, P = 0.004. *Significant improvement compared to placebo, P = 0.05.

The surface asymmetry index was significantly lower in supplement-treated subjects *(0.37 ± 0.03)* than placebo *(0.51 ± 0.03)* at 24 weeks *(P = 0.005, see Table 2)*.

Table 2. Comparison of Corneal Topographical Indexes in a Subset of the Patient Population

Topography	Baseline	4 Week	12 Week	24 Week	N	*P*
SRI						
Supplement	0.24 ± 0.03	0.34 ± 0.04	0.39 ± 0.05	0.29 ± 0.03	15	0.1
Placebo	0.30 ± 0.04	0.46 ± 0.05	0.33 ± 0.02	0.37 ± 0.04	16	
SAI						
Supplement	0.39 ± 0.03	0.47 ± 0.04	0.44 ± 0.05	0.37 ± 0.03*	15	0.005*
Placebo	0.43 ± 0.03	0.49 ±0.03	0.37 ± 0.02	0.51 ± 0.03	16	

Data are represented as mean 6 SEM.
*Comparison with placebo at 24 weeks.

Placebo treatment also significantly increased HLA-DR intensity by 36% ± 9% and CD11c by 34% ± 7% when compared with supplement treatment *(P = 0.001, 24 weeks, See Figures 3 & 4)*.

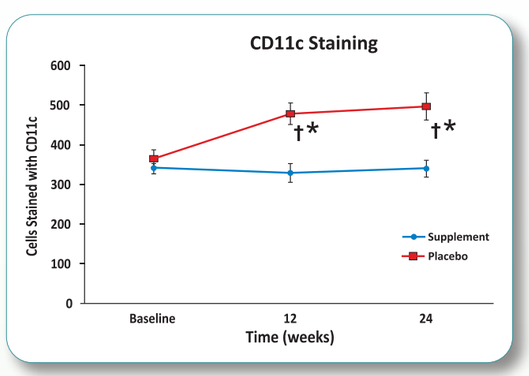

FIGURE 3. Fluorescence intensity (mean ± SEM) of CD11c-positive dendritic cells in conjunctival impression cytology. †Significant increase in CD11c-positive cell staining compared to baseline, P = 0.004. *Significantly greater staining intensity compared to supplement, P = 0.001.

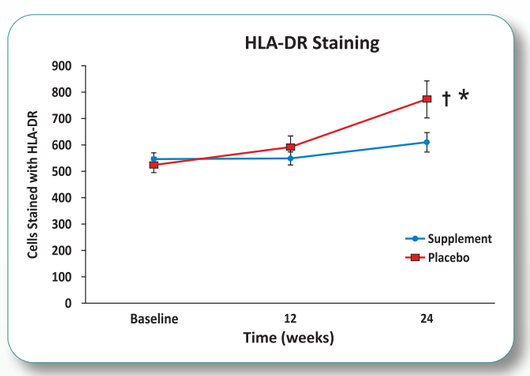

FIGURE 4. Fluorescence intensity (mean ± SEM) of HLA-DR-positive dendritic cells in conjunctival impression cytology. †Significant increase in HLA-DR-positive cell staining compared to baseline, P = 0.03. *Significantly greater staining intensity compared to supplement, P = 0.001.

Neither treatment had any effect on tear production, tear breakup time, or corneal or conjunctival staining.

Conclusions:

Supplemental GLA and n-3 PUFAs for 6 months improved ocular irritation symptoms, maintained corneal surface smoothness, and inhibited conjunctival dendritic cell maturation in patients with postmenopausal keratoconjunctivitis sicca.

Text and graphs on this page, courtesy of Cornea Journal