SCIENCE SUMMARY

AMD & DIETARY MACULAR PIGMENTS (ZEAXANTHIN AND LUTEIN)

CATARACT & LENS (ZEAXANTHIN AND LUTEIN)

MACULAR PIGMENT OPTICAL DENSITY MEASUREMENT

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DRY EYE AND OCULAR NUTRITION

DIABETES VISUAL FUNCTION IMPROVEMENT

EyePromise®
Live in focus.

SCIENCE SUMMARY

AMD & DIETARY MACULAR PIGMENTS (ZEAXANTHIN AND LUTEIN)

AREDS 2 Clinical Research Study

(Emily Chew, et. al. – JAMA Ophthalmology, 2013)

- 4,203 subject multi-center study
- Intermediate to advanced AMD
- 50-85 years of age
- AREDS 1 formula along with lutein + zeaxanthin vs. no lutein and zeaxanthin
    - 10% incremental slowing of progression to advanced AMD
    - 26% incremental slowing of progression to advanced AMD in the lowest quintile of lutein and zeaxanthin intake, which is more representative of the general population

AREDS Report 22: The Relationship of Dietary Carotenoids and Vitamin A, E and C Intake with AMD

(Emily Chew, et. al. - Archives of Ophthalmology, 2007)

- 4,757 subjects
- Participants reporting highest intake of zeaxanthin & lutein less likely to have advanced AMD (NV & GA) and large or extensive intermediate drusen.

Improvement of Retinal Function in Early Age-Related Macular Degeneration after Lutein and Zeaxanthin Supplementation: A Randomized, Double-Masked, Placebo-Controlled Trial

(Le Ma, et. al. - American Journal of Ophthalmology October, 2012)

- Randomized, double masked, placebo controlled clinical research study
- 144 subjects (Early AMD)
- 4 study arms:
    - 10 mgs lutein
    - 10 mgs lutein & 10 mgs zeaxanthin
    - 20 mgs lutein
    - Placebo and age matched controls
- Pre and post supplementation multi-focal ERG was measured in 6 concentric annular zones around the macula.
- MPOD increase related positively to increases in N1P1 response in ring 1 and ring 2 with little effect in ring 3 through 6.
- Improvement of N1P1 response densities was positively associated with MPOD increase, suggesting a causative effect of MPOD on retinal function and health.
- Early functional abnormalities of the central retina in the early AMD patients may be improved by lutein and zeaxanthin supplementation.
- The 10 mgs lutein/10 mgs dietary zeaxanthin arm had the greatest ERG documented retinal function improvement in ring 1. (fovea)

SCIENCE SUMMARY

AMD & DIETARY MACULAR PIGMENTS (ZEAXANTHIN AND LUTEIN)

POLA Study: Plasma Lutein and Zeaxanthin and Other Carotenoids

(Delcourt, et. al. - Investigative Ophthalmology and Visual Science, 2006)

- 899 subjects
- Subjects with high plasma levels of zeaxanthin had a 93% reduction of AMD occurrence.
- Subjects with high plasma levels of lutein had a 79% reduction of AMD occurrence.
- These results are strongly suggestive of a protective role of the xanthophylls, in particular zeaxanthin, for the protection against AMD and cataract.

Serum Carotenoids and Risk of AMD

(Zhou, et. al. - Investigative Ophthalmology and Visual Science, 2011)

- 263 Chinese subjects
- Serum levels of carotenoids and retinol were significantly lower in subjects with exudative AMD than in controls.
    - Zeaxanthin (96% Relative Risk Reduction)
    - Lycopene (78% Relative Risk Reduction)
- The data suggests that higher levels of serum carotenoids, in particular zeaxanthin and lycopene, are associated with a lower likelihood of exudative AMD.

The Rotterdam Study: Reducing the Genetic Risk of AMD

(Lintje Ho, et. al - Archives of Ophthalmology, 2011)

- 2,167 subjects
- Subjects with genetic AMD risk factors in the highest tertile of dietary zinc, ß-carotene, lutein/zeaxanthin, and EPA/DHA intake achieved a significant early AMD hazard ratio risk reduction of approximately 40%.
- High dietary intake of nutrients with anti-oxidant properties reduces the risk of early AMD in those at high genetic risk.

Blue Mountains Eye Study: Dietary Antioxidants and the Long-term Incidence of AMD

(Tan, et. al. - American Academy of Ophthalmology, 2008)

- 2,454 subjects
- Higher dietary intake of zeaxanthin and lutein reduced risk of AMD by 65%.
- Confirmed protective influence of zinc
- Higher beta-carotene was associated with increased risk of AMD.

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AMD & DIETARY MACULAR PIGMENTS (ZEAXANTHIN AND LUTEIN)

Lutein and Zeaxanthin Status and Risk of AMD

(Gale, et. al. - Ophthalmology and Visual Science, 2003)

- 380 subjects
- Risk (early or late) was significantly higher in people with lower plasma concentrations of zeaxanthin.
- These findings provide support for the view that zeaxanthin may protect against AMD.

Bone & Landrum: Macular Pigment in Donor Eyes

(Bone, et. al. - Investigative Ophthalmology and Visual Science, 2001)

- 112 cadaver donors (56 with AMD and 56 controls), a total of 224 eyes.
- Lutein and zeaxanthin levels in all three concentric regions of the retina were less, on average, for AMD donors than controls.
- Donor eyes in the highest quartile of lutein and zeaxanthin per unit area had an 82% lower prevalence of AMD compared with those in the lowest quartile.

Sunlight Exposure, Antioxidants and Age-Related Macular Degeneration (EurEye)

(Astrid E. Fletcher, et. al. – Archives of Ophthalmology, 2008)

- 4,753 subjects
- 65 years or older
- Subjects were questioned for adult lifetime sunlight exposure throughout their working life and retirement up to current age.
- Fundus photography conducted and evaluated
- Blood analysis of antioxidant levels
- Blue light exposure was estimated by combining meteorological and questionnaire data.
- The combination of blue light exposure in the presence of low levels of zeaxanthin, alpha-tocopherol and vitamin C was associated with a nearly four fold risk of neovascular AMD.
- EurEye is the first clinical study to report an adverse association of blue light exposure with neovascular AMD in humans with low levels of antioxidants including zeaxanthin.

SCIENCE SUMMARY

CATARACT & LENS (ZEAXANTHIN AND LUTEIN)

AREDS 2 Clinical Research Study

(Emily Chew, et. al. – JAMA Ophthalmology, 2013)

- Results showed subjects in the lowest quintile of dietary lutein and zeaxanthin intake had a 30% reduction in cataract development post supplementation.

POLA Study: Plasma Lutein, Zeaxanthin, and Other Carotenoids

(Delcourt, et. al. - Investigative Ophthalmology and Visual Science, 2006)

- 899 subjects
- Subjects with high plasma levels of zeaxanthin had a 77% reduction of nuclear cataract occurrence.

Women's Health Initiative Study

(Moeller, et. al. - Archives of Ophthalmology, 2008)

- 1,802 female subjects
- Women with highest quantity of lutein and zeaxanthin intake had 32% lower incidence of nuclear cataract.

Blue Mountains Eye Study: Dietary Antioxidants and the Long-term Incidence of AMD

(Tan, et. al. - American Journal of Clinical Nutrition, 2008)

- 2,454 elderly subjects
- Vitamin C and combined dietary antioxidants intake reduced nuclear cataract occurrence by 50%.

SCIENCE SUMMARY

MACULAR PIGMENT OPTICAL DENSITY MEASUREMENT

A New Desktop Instrument for Measuring Macular Pigment Optical Density

(Van Der Veen, et. al. - Ophthalmology and Physiological Optics, 2009)

- MPOD was measured with the QuantifEye instrument and the method demonstrated good repeatability of 97%.

Desktop Macular Pigment Optical Density Measurement: A New Approach Based On Heterochromatic Flicker Photometry

(Berendschot, et. al. – E, volume 25,)

- We found high agreement between test and retest measurements of QuantifEye (0.02 ± 0.18 density units) and the fundus reflectance method.

The Value of Measurement of Macular Carotenoid Pigment Optical Densities and Distributions in Age-Related Macular Degeneration

(Bernstein, et. al. – Vision Research, 2010)

- The antioxidant and blue light filtering functions of lutein and zeaxanthin have an impact upon eye health beyond just decreasing the risk of age-related eye disease. Macular pigment has also been shown to influence visual function and comfort.
- The panel concluded it might be possible to identify individuals at reduced, medium, and elevated risk for age-related eye disease based on high, medium, and low central MPOD levels.
- The panel members agreed a central MPOD below 0.2 density units (du) should be considered low, between 0.2 du and 0.5 du mid-range, and levels above 0.5 du high MPOD.
- Approximately 78% of the US population has a central MPOD below 0.5 du.

SCIENCE SUMMARY

MACULAR PIGMENT OPTICAL DENSITY MEASUREMENT

Macular Pigment Optical Density Associated With and Without Zeaxanthin and Lutein Supplementation

(Davis – Advances in Ophthalmology & Visual System 2015)

- 198 healthy subjects
- Twelve-month study
- Objective: To determine the change in macular pigment optical density (MPOD) after subjects with low macular pigment (<0.30 density units) elect to supplement with EyePromise Restore or forgo supplementation.
- 2 study arms:
    - Group 1 supplemented 1 EyePromise Restore softgel per day
    - Group 2 did not consume supplements
- Subjects supplementing with Restore achieved an increase of density units. Subjects not supplementing experienced an MPOD decrease.
- Nutritional counseling alone did not increase MPOD scores.

Women's Health Initiative: Diet Intervention Did Not Increase Macular Pigment Optical Density in an Ancillary Study of a Subsample of the Women's Health Initiative

(Moeller, et. al. – The Journal of Nutrition, 2009)

- Macular pigment density was compared in women 60-87
- 394 subjects
- The study examined the impact of long-term (>8 y), low-fat, high-fruit and vegetable diets on levels of lutein and zeaxanthin in the macula.
- 2 study arms
    - 158 received dietary and behavioral modification counseling and intervention
    - 236 did not receive dietary and behavioral modification counseling
- The intervention group participated in 18 dietary and behavioral counseling sessions in year 1 and quarterly sessions thereafter.
- Macular pigment density did not differ between the intervention (0.36 ± 0.02 density units) and comparison (0.35 ± 0.01 density units) groups.
- Macular pigment tended to be higher in women consuming lutein and zeaxanthin in the highest amount compared with the lowest however the difference was not statistically significant.
- The increase in fruit and vegetable intake among dietary modification participants of this WHI subsample was not of sufficient magnitude to alter the mean density of retinal carotenoids.
- Intensive dietary and behavioral counseling did not result in a significant macular pigment density increase in the intervention group, suggesting that supplementation may be necessary to achieve a significant macular pigment increase.

SCIENCE SUMMARY

BENEFITS OF ZEAXANTHIN & LUTEIN IN VISUAL PERFORMANCE

Zeaxanthin and Visual Function (ZVF) Clinical Research Study

(Richer, et. al. - Journal of Optometry, 2011)

- 60 elderly subjects with early to moderate AMD were supplemented
- 12 month study period
- 3 study arms: (1) Patients were supplemented with 8 mg of dietary zeaxanthin per day or (2) 9 mg of lutein, or (3) a combination of the 2 carotenoids. (17 mg total)
- Results: Subjects supplementing high dose (8mg) dietary zeaxanthin daily achieved
    - Improved high contrast near visual acuity of 8.5 letters or 1.5 lines
    - Clearing of central scotomas
    - Improved foveal shape discrimination
    - Improved night driving skills
- Only EyePromise brands contain 8 mg or more dietary zeaxanthin

Macular Re-pigmentation Enhances Driving Vision in Elderly Adult Males with Macular Degeneration

(Richer, et. al. - Clinical & Experimental Ophthalmology, 2012)

- 60 elderly subjects with early to moderate AMD
- Supplemented 8 mgs of dietary zeaxanthin per day for 12 months.
- Self-described improvement of driving skills was strongly associated with macular re-pigmentation via high dose dietary zeaxanthin supplementation.

The Influence of Dietary Lutein and Zeaxanthin on Visual Performance

(Stringham, Hammond, et. al. - Journal of Food Science, 2009)

- Retinal increase of zeaxanthin and lutein (MPOD) reduced glare disability and improved photo- stress recovery time.
- Contrast sensitivity improvement was achieved in supplemented subjects.
- Glare induced photostress recovery times can be reduced by 5 seconds by increasing macular pigment via supplementation. This equates to 440 ft. of improved reaction time at 60 MPH while driving at night.

SCIENCE SUMMARY

BENEFITS OF ZEAXANTHIN & LUTEIN IN VISUAL PERFORMANCE

A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency

(Bovier, Renzi, Hammond, et al. – Public Library of Science (PLOS), 2014)

- 64 subjects (young healthy adults)
- 18-32 years of age
- 4 month study
- 3 study arms
    - EyePromise Zeaxanthin (20 mgs of dietary zeaxanthin)
    - EyePromise vizual EDGE PRO™ supplement (26 mgs dietary zeaxanthin, 8 mgs lutein)
    - Placebo
- Subjects in the EyePromise Zeaxanthin and EyePromise vizual EDGE PRO arms experienced significant improvements in visual processing speed and reaction time, each P= <0.005:
- A 14% improvement in Temporal Contrast Sensitivity Function
- A 12% improvement in Critical Flicker Fusion Threshold
- A 10% improvement in Visual Motor Reaction Time
- A 20% increase in Macular Pigment Optimal Density (MPOD)
- High dose zeaxanthin and lutein supplementation improved visual processing speed, even among young healthy adults.
- Supplemented subjects achieved improved ability to process information and react faster.

A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Photostress Recovery, Glare Disability, and Chromatic Contrast

(Hammond, Fletcher, Roos, et. al. – Investigative Ophthalmology and Visual Science, 2014)

- 115 subjects (young healthy adults)
- Average age of 22 years
- Macular pigment optical density increased significantly in the zeaxanthin and lutein arm versus placebo at all eccentricities (10, 30, 60, and 105 minutes from the center of the macula).
- Serum zeaxanthin and lutein increased significantly at first follow-up visit (3 months), and remained elevated throughout the 1 year intervention period.
- Chromatic contrast and photostress recovery time improved significantly versus placebo.
- Glare disability was correlated with increased macular pigment density during the study period.
- Daily supplementation with zeaxanthin and lutein resulted in significant serum increase, MPOD score, improved chromatic contrast, and photostress recovery.

SCIENCE SUMMARY

BENEFITS OF ZEAXANTHIN & LUTEIN IN VISUAL PERFORMANCE

A Randomized Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Visual Processing Speed in Young Healthy Subjects

(Bovier, Hammond, et. al. – Archives of Biochemistry and Biophysics, 2014)

- 69 subjects (young healthy adults)
- 18-32 years of age
- 4 month study
- 3 study arms
  - EyePromise vizual EDGE PRO supplement (26 mgs dietary zeaxanthin, 8 mgs lutein)
  - EyePromise Zeaxanthin (20 mgs of dietary zeaxanthin)
  - Placebo
- Neither MPOD nor temporal contrast sensitivity function changed in the placebo arm.
- Both improved significantly with high dose dietary zeaxanthin supplementation.

A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency

(Bovier, Renzi, Hammond, et al. – Public Library of Science (PLOS), 2014)

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- 18-32 years of age
- 4 month study
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- Glare disability was correlated with increased macular pigment density during the study period.
- Daily supplementation with zeaxanthin and lutein resulted in significant serum increase, MPOD score, improved chromatic contrast, and photostress recovery.

Macular Pigment and Visual Performance in Glare: Benefits for Photostress Recovery, Disability Glare, and Visual Discomfort

(Stringham, Garcia, Smith, et. al. – IOVS, 2011)

- 26 healthy subjects
- Average age of 31 years
- Higher macular pigment levels correlated with all outcome measures
    - Improved photostress recovery time
    - Reduced glare
    - Diminished visual discomfort
- Higher macular pigment levels resulted in faster photostress recovery, lower disability glare contrast thresholds, and lower visual discomfort.

SCIENCE SUMMARY

BENEFITS OF ZEAXANTHIN & LUTEIN IN VISUAL PERFORMANCE

The Influence of Dietary Lutein and Zeaxanthin on Visual Performance

(Stringham, Bovier, Wong, Hammond, et. al. – Concise Reviews in Food Science, 2009)

- High-intensity lamps (such as stadium lights) often cause visual discomfort.
- Macular Pigment Optical Density (MPOD) filters high energy visible blue light .
- Visual discomfort was strongly attenuated for much of the blue region of the visible light spectrum, suggesting the filtering properties of macular pigment serve to reduce visual discomfort associated with central viewing of any light containing short wavelengths.
- Findings suggest small increases in MPOD could contribute to visual comfort benefits.
- There was a significant inverse relationship between photostress recovery and MPOD.
- Higher MPOD values resulted in shorter photostress recovery time.

The Effects of Macular Carotenoid Zeaxanthin on Visual Performance and Neural Efficiency in Young, Healthy Subjects and College Athletes

(Renzi, Bovier, Shon, et. al. – Macular carotenoids & AMD conference poster 2011)

- 7 college baseball players (male)
- Average age of 20.3 years
- Subjects supplemented with 20 mgs of dietary zeaxanthin per day experienced:
  - MPOD increase
  - Reduced glare and improved photostress recovery time
  - Improved contrast enhancement
  - Improved fixed and variable reaction times
  - Improved coincidence anticipation timing accuracy at the highest frequency
  - Improved temporal processing speed

SCIENCE SUMMARY

DRY EYE AND OCULAR NUTRITION

Report of the International Dry Eye Workshop (DEWS)

(Foulks, et. al. - The Ocular Surface, 2007)

- Level 2 dry eye patient care recommendations: If Level 1 treatments are inadequate, add: Anti-inflammatories (Omega-3 fatty acids, topical CsA and corticosteroids), Tetracyclines (for meibomianitis, rosacea), Punctal plugs, Secretogogues, Moisture chamber spectacles.
- Omega-3 fatty acid supplementation beginning at level 2 dry eye is standard of care.

The International Workshop on Meibomian Gland Dysfunction

(Nichols, et. al. Investigative Ophthalmology and Visual Science, 2011)

- Level 2 MGD Workshop patient care recommendation: Advise patient on improving ambient humidity; optimizing workstations and increasing dietary omega-3 fatty acid intake.
- Omega-3 fatty acid supplementation beginning at level 2 dry eye is standard of care.

Ocular Nutrition Impact on Tear Film Study (ONIT)

(Mulqueeny, Townsend, Davis, Koffler, et. al. – Advances in Ophthalmology and Visual System, 2015)

- Multi-center, clinic-based dry eye study
- 67 subjects
- Eight week study duration
- Objective: To determine if subjects presenting with dry eye, confirmed by diagnostic markers and symptoms (Ocular Surface Disease Index or OSDI), responded to a multi-component, Omega-3 based anti-inflammatory nutritional oral supplement (EyePromise EZ Tears).
- Protocol required patients to meet minimum of 4 dry eye diagnostic inclusion criteria.
- Study Results:
    - OSDI Improved 38%
    - TBUT Improved 45%
    - Conjunctival Staining Improved 50%
    - Corneal Staining Improved 33%
    - Tear meniscus height Improved 50%
    - Lid Inflammation Improved 40%
    - Phenol Red Thread Improved
    - Osmolarity scores Variable and inconclusive
- Rapid Onset of relief: Patients began demonstrating symptom improvement (OSDI) after one week of EyePromise EZ Tears supplementation.
- Improvements continued over the course of the study. (Rationale to keep supplementing beyond 8 weeks.)

SCIENCE SUMMARY

DIABETES VISUAL FUNCTION IMPROVEMENT

Diabetes Visual Function Supplement Study (DiVFuSS)

(Chous, Richer, Kowluru, Gerson, et. al. – British Journal of Ophthalmology, 2015)

- Six-month clinical research study
- Randomized, placebo controlled
- Subjects with type 1 or type 2 diabetes > 5 years duration
- 67 subjects
    - No significant inter-group differences at baseline.
    - Some with no retinopathy or mild to moderate non-proliferative retinopathy.
- Objective: Determine if patients benefit from a novel, multi-component oral supplement (DiVFuSS Formula = EyePromise DVS)
- Supplement results;
    - MPOD Increase of 31%
    - Color vision improvement of 21%*
    - Contrast sensitivity increase of 19%*
    - Macular visual field (5-2) improvement of 12%*
    - All P values were highly statistically significant
- The supplement achieved the aforementioned results without significantly affecting blood sugar control (A1c)

**Averaged between the two eyes*

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