



DOSSIER · SUBSTANCE

Lutein and Zeaxanthin

The combination of the two **carotenoids** lutein and zeaxanthin is among the most frequently studied micronutrients for eye health. The majority of studies focus on the **retina**, while other areas of application, such as cognition or skin, are still in their early stages.

238

STUDIES IN
TOTAL

105

IN HUMANS

41

OF WHICH
CONTROLLED

9

IN ANIMALS

18

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Lutein and Zeaxanthin (Combination) at a Glance

ORIGIN:

Lutein and zeaxanthin are oxygen-containing carotenoids (xanthophylls) that humans cannot synthesise themselves. They are derived from green leafy vegetables (spinach, kale), maize, eggs, and certain algae. In the retina, they selectively accumulate in the macula, where they act as macular pigment (MP), filtering blue light and exerting antioxidant effects. Measurement of macular pigment optical density (MPOD) serves as a biomarker for their availability in the eye.

STUDY LANDSCAPE:

238 evaluated studies · 41 controlled human trials · 64 observational studies · 21 review articles · 9 animal studies · 11 cell culture studies

STRONGEST EVIDENCE:

- **Age-Related Macular Degeneration (AMD)** The AREDS2 study (2014) with 4,203 participants showed no significant slowing of AMD progression but demonstrated a risk reduction for advanced AMD in a subgroup. A meta-analysis (1,176 patients) confirmed a dose-dependent improvement in visual acuity and contrast sensitivity through lutein/zeaxanthin supplementation.
- **Retinal Function** Preclinical studies in animals and cell cultures suggest that lutein/zeaxanthin may improve multifocal electroretinography (mfERG) responses and retinal sensitivity. A 2-year controlled human trial (112 patients) showed significant increases in macular pigment optical density (MPOD) and functional improvements in retinal performance.
- **Oxidative Stress** The Blue Mountains Eye Study (2,454 participants) found that high dietary intake of lutein/zeaxanthin reduced the risk of neovascular AMD by 65%. Controlled trials confirm an increase in antioxidant capacity and MPOD through supplementation.
- **Cognition** A controlled study with 51 young adults showed that 10 mg lutein + 2 mg zeaxanthin daily over 12 months improved MPOD and cognitive performance (attention, flexibility). Another controlled study (90 adults) demonstrated improvements in visual memory and learning.
- **Skin: Health** A controlled study with 46 participants showed that 10 mg lutein + 2 mg zeaxanthin daily over 12 weeks increased the minimal erythema dose (MED) and improved skin pigmentation, indicating antioxidant and anti-inflammatory effects.

LIMITATIONS:

- The causal role of lutein and zeaxanthin in AMD prevention is not fully elucidated. Observational studies show inverse correlations, but controlled trials do not yield consistent results.
- Applications such as cognition or skin ageing are significantly less researched. Systemic effects (e.g., anti-inflammatory actions) are still at an early stage of investigation.
- Bioavailability varies widely among individuals due to genetic differences (e.g., StARD3 protein), lipid metabolism, and gut microbiota. Standardised measurement methods are often lacking.

ASSESSMENT:

Controlled studies provide evidence for the protective and functional effects of lutein and zeaxanthin in AMD, particularly in subgroups. Other applications such as cognition or skin require further research to confirm effects in humans.

1. What Lutein and Zeaxanthin Are

Lutein and **zeaxanthin** are oxygen-containing carotenoids (**xanthophylls**) that humans cannot synthesise themselves. They are found in green leafy vegetables (spinach, kale), maize, eggs, and certain algae. In the **retina**, they selectively accumulate in the **macula**, where they reach the highest concentration in the body as **macular pigment** (MP). Chemically, they differ only in the position of a double bond: zeaxanthin is the symmetrical isomer, while lutein has an asymmetrical structure. Both absorb blue light (400–500 nm) and act as **physical filters** and **antioxidants**.

The critical factor for all studies is the **measurement of macular pigment optical density (MPOD)**. It is considered a biomarker for the availability of these carotenoids in the eye and correlates with dietary or supplemental intake. However, MPOD varies widely among individuals—even with identical intake. Reasons for this include genetic differences in the **StARD3 protein** (a lutein transporter), **lipid metabolism** (carotenoids are fat-soluble), and the **gut microbiota**, which influences bioavailability. While standardised measurement methods such as **heterochromatic flicker photometry** or **fundus reflectometry** enable comparable data, interpretation remains complex: an increased MPOD does not necessarily correspond to a clinical effect.

2. What the Studies Show in Detail

The foundational human studies and key reviews—by application, including population, duration, preparation, measurement, and results, as reported in the original works. Numbers are included only where the study provides them.

Distribution of **controlled human trials** by application—numbers are not additive, as one study may be assigned to multiple categories:

APPLICATION	CONTROLLED STUDIES
Oxidative Stress	11
Safety and Tolerability	9
Metabolism	7

APPLICATION	CONTROLLED STUDIES
Uptake and Availability	7
Cognition and Mental Health	6
Fatigue and Stress	5
Inflammatory Processes	4
Cardiovascular Health	3

Age-Related Macular Degeneration (AMD) – Progression and Functional Parameters

Confirmed: The controlled, multicentre AREDS2 study examined 4,203 participants (aged 50–85) at high risk for late AMD over a median follow-up of 5 years. Participants received either placebo, 10 mg lutein + 2 mg zeaxanthin combined with other antioxidants, 1 g omega-3 fatty acids, or a combination daily. The primary endpoint was progression to late AMD. The study thus showed the benefit of the *combination* as an adjunct to the AREDS formulation, particularly in existing AMD, but did not isolate the effect of lutein and zeaxanthin alone.

The primary endpoint was macular pigment optical density (MPOD). After 48 weeks, MPOD increased by 0.076 ± 0.022 density units in the 20 mg lutein group and by 0.058 ± 0.027 in the *lutein-containing combination* group. Secondary endpoints such as best-corrected visual acuity (BCVA) and contrast sensitivity (CS) improved in a dose-dependent manner, with the 20 mg lutein group showing the strongest effects. The results confirm a dose-dependent increase in macular pigment for lutein and suggest functional improvement in retinal performance in early AMD.

PLAUSIBLE A meta-analysis of eight randomised controlled trials (RCTs) involving 1,176 patients with AMD ⁽³⁾ demonstrated that lutein/zeaxanthin supplementation in the included studies *was associated with* a significant improvement in logMAR visual acuity (weighted mean difference -0.04 ; 95% CI -0.06 to -0.03) and contrast sensitivity (WMD 0.08 – 0.18 ; $p < 0.05$). Each additional mg/day of the carotenoids reduced the logMAR value by 0.003. The study *supports the hypothesis* of consistent improvement in *these functional parameters* through supplementation in the analysed RCTs, with the increase in MPOD directly correlating with enhanced retinal function. A limitation is the heterogeneity of study populations and dosages.

PROVEN A 2-year study involving 112 patients with early AMD ⁽⁷⁾ compared placebo with 10 mg lutein, 20 mg lutein, or 10 mg lutein + 10 mg zeaxanthin daily. After 24 months, MPOD increased significantly in all active groups, with 20 mg lutein producing the strongest rise in the first 48 weeks. Contrast sensitivity at 3 cycles/degree improved in parallel with MPOD, while visual acuity and glare sensitivity remained unchanged. The study shows that 10 mg lutein daily can sustainably increase MPOD and *suggests a potential link* to improved visual function without higher doses being superior in the long term.

AMD – Observational Studies and Epidemiological Data

Over 24 years ⁽³⁸⁾, lutein/zeaxanthin intake was assessed via validated dietary questionnaires and converted into predicted plasma concentrations. The results suggest a protective effect in advanced AMD, while the impact on early stages is less clear.

PROVEN The CAREDS study ⁽³⁷⁾ analysed 1,787 women (aged 50–79) from the Women's Health Initiative. The findings indicate that the benefits of lutein/zeaxanthin are age- and health-dependent, with the strongest effects observed in younger, healthy women.

HYPOTHESIS The genetic CAREDS study ⁽³⁹⁾ identified 24 gene variants across five genes (BCMO1, BCO2, NPCL1L1, ABCG8, FADS2) independently associated with AMD while simultaneously influencing lutein/zeaxanthin concentrations in serum or macula. A genetic risk model incorporating nine variants discriminated AMD cases more effectively than established risk factors such as smoking or CFH/ARMS2 gene variants ($p = 0.002$). This suggests that individual genetic predisposition may modulate the efficacy of lutein/zeaxanthin—a question open for future personalised prevention strategies.

Retinal Function and Electrophysiological Parameters

The primary endpoint was multifocal electroretinography (mfERG). After 48 weeks, N1P1 response densities in Ring 1 (central macula) increased significantly in the 20 mg lutein group and the combination group, while in Ring 2, only the 20 mg lutein group showed a significant rise. The increase in MPOD correlated positively with improved mfERG responses. The study confirms that lutein/zeaxanthin can enhance central retinal function in early AMD.

PROVEN A 2-year study with 112 patients ⁽⁹⁾ compared the effects of 10 mg lutein, 20 mg lutein, or 10 mg lutein + 10 mg zeaxanthin daily on MPOD and retinal sensitivity. After 48 weeks, N1P1 response densities in Rings 1 and 2 increased significantly, while mean retinal sensitivity (MRS) in microperimetry improved after 24 months in the 10 mg and 20 mg lutein groups ($p < 0.05$). The study demonstrates that supplementation not only increases MPOD but also enhances long-term functional retinal performance—an indication of neuroprotective effects.

PROVEN A study involving 100 healthy participants ⁽¹⁴⁾ examined the effects of lutein- or zeaxanthin-enriched eggs or a lutein-containing buttermilk drink over 90 days. Serum lutein concentrations rose by 76–77% in the lutein-egg and buttermilk groups ($p < 0.001$), while zeaxanthin increased by 430% in the zeaxanthin-egg group ($p < 0.001$). However, MPOD increased significantly only in the lutein-egg group ($p < 0.05$). The study confirms that the bioavailability of lutein/zeaxanthin depends strongly on the matrix and that eggs are an effective source for increasing MPOD.

Oxidative Stress and Antioxidant Mechanisms

PLAUSIBLE A randomised study with 172 patients with non-exudative AMD ⁽⁸⁾ investigated the effects of 10 mg lutein + 1 mg zeaxanthin combined with 100 mg DHA + 30 mg EPA daily over 12 months. Primary endpoints were plasma concentrations of xanthophylls and antioxidant capacity. Supplementation significantly increased lutein and zeaxanthin levels in plasma ($p < 0.001$) and improved antioxidant capacity (TEAC value) by 12% ($p < 0.05$). MPOD increased in a dose-dependent manner, with the group receiving double the dose showing the strongest effects. The study suggests that the combination may act synergistically to strengthen antioxidant defences in AMD, though the specific contribution of lutein and zeaxanthin alone remains to be clarified.

PLAUSIBLE A randomised study with 79 AMD patients ⁽¹⁰⁾ compared the effects of 10 mg lutein combined with antioxidants with or without additional omega-3 fatty acids over 6 months. MPOD increased significantly in the lutein group ($p < 0.005$), while the combination with omega-3 fatty acids showed no additional benefit ($p = 0.059$). Contrast sensitivity improved only in the lutein-containing group. The study provides a hypothesis that omega-3 fatty acids may impair lutein bioavailability, though the effect of lutein alone in this context requires further investigation.

PROVEN The Blue Mountains Eye Study ⁽³⁶⁾ followed 2,454 participants over 10 years. High dietary intake of lutein/zeaxanthin reduced the risk of neovascular AMD by 65% (RR 0.35; 95% CI 0.13–0.92) and the risk of indistinct soft drusen by 34% (RR 0.66; 95% CI 0.48–0.92). The study highlights the role of carotenoids as protective factors against oxidative stress in the retina, with the strongest effect observed in neovascular AMD.

Cognition and Mental Health

PLAUSIBLE A randomised, placebo-controlled study with 51 young adults (aged 18–30) examined the effects of 10 mg lutein + 2 mg zeaxanthin daily over 12 months ⁽⁴⁾. The primary endpoint was MPOD, with secondary endpoints including cognitive performance tests (CNS Vital Signs). MPOD increased significantly in the supplementation group ($p < 0.001$), while test scores improved in the domains of complex attention, cognitive flexibility, and psychomotor speed ($p < 0.05$). The study suggests a potential link between lutein/zeaxanthin and cognitive performance in young adults, though the clinical relevance of these findings remains to be established.

PROVEN A randomised, placebo-controlled study with 90 adults (aged 40–75) with subjective cognitive complaints investigated the effects of 10 mg lutein + 2 mg zeaxanthin daily over 6 months ⁽¹¹⁾. Supplementation significantly improved visual episodic memory ($p = 0.005$) and visual learning ($p = 0.001$), while other cognitive tests or self-reported questionnaires showed no significant changes. The study suggests that lutein/zeaxanthin may enhance specific cognitive domains in individuals with mild cognitive impairment—a finding requiring further validation.

Anti-Inflammatory Effects and Skin Health

Primary endpoints were minimal erythema dose (MED) and skin lightness (L^*). Supplementation significantly increased MED ($p < 0.05$) and improved skin tone ($p < 0.0237$), while L^* values rose in the active group. The study showed preclinical evidence that lutein/zeaxanthin may protect the skin from UV-induced inflammation and influence skin pigmentation—findings indicating systemic antioxidant and anti-inflammatory effects that require further clinical investigation in human trials.

PLAUSIBLE A review ⁽¹³⁾ discusses the role of lutein/zeaxanthin in preventing retinopathy of prematurity (ROP) and diabetic retinopathy (DR). Both conditions are characterised by hypoxia-induced inflammation and oxidative damage. Observational studies show that preterm infants with higher lutein intake are less likely to develop severe ROP, while patients with non-proliferative DR exhibit lower serum levels. The authors suggest that carotenoids may slow microvascular degeneration through their antioxidant and anti-inflammatory properties—a hypothesis requiring clinical validation.

Bioavailability and Absorption

Both formulations significantly increased serum lutein concentrations, while MPOD rose only in a subgroup of “responders.” The study demonstrates that lutein bioavailability depends on particle size and matrix, and that individual factors (e.g., genetics, baseline levels) influence response rates.

PROVEN A study involving 12 AMD patients and controls ⁽⁴⁰⁾ examined the effects of a 4-week high-lutein/zeaxanthin diet (11 mg/day). Plasma concentrations increased 2- to 3-fold, with 52% of lutein and 44% of zeaxanthin transported via HDL. The study confirms that AMD patients and healthy individuals respond similarly to increased intake and that HDL plays a central role in transporting carotenoids to the retina. The findings underscore the importance of lipoprotein-mediated uptake for bioavailability.

Overall Picture

The body of evidence on lutein and zeaxanthin consistently supports their protective and functional role in age-related macular degeneration (AMD). Controlled studies demonstrate that supplementation increases macular pigment optical density (MPOD) and slows progression to late-stage AMD, particularly in individuals with low baseline levels. Functional parameters such as visual acuity, contrast sensitivity, and electrophysiological retinal responses improve in a dose-dependent manner, with daily doses of 10–20 mg lutein proving most effective. Epidemiological data corroborate these findings, showing an inverse association between dietary intake and the risk of late AMD—though evidence for early stages is less robust.

Beyond AMD, initial studies suggest neuroprotective and cognitive effects, particularly in young adults and individuals with mild cognitive impairment. The antioxidant and anti-inflammatory properties of carotenoids may also exert systemic effects, such as in the skin or in microvascular retinal diseases. However, bioavailability varies significantly depending on the matrix (e.g., eggs vs. dietary supplements) and individual factors. Open questions concern long-term efficacy, optimal dosing for different target groups, and interactions with other nutrients such as omega-3 fatty acids.

Methodology of the evidence base

Typical endpoints include MPOD (measured via heterochromatic flicker photometry or Raman spectroscopy), functional parameters (visual acuity, contrast sensitivity, mfERG), and clinical progression (AMD stages). Systematic gaps exist in the standardisation of measurement methods (e.g., MPOD determination), long-term follow-up (> 2 years), and the investigation of specific subgroups (e.g., genetic predisposition, early AMD stages). Furthermore, direct comparisons of different formulations and dose-response studies for non-ocular effects are lacking. Most studies focus on AMD; for other applications (cognition, inflammation), the evidence is still in its early stages.

Are lutein and zeaxanthin only relevant for the eyes?

The overwhelming majority of studies examine lutein and zeaxanthin in the context of

OCULAR HEALTH

. This leads to the assumption that their effects are limited to the retina. However, the **molecular mechanisms**—antioxidant, anti-inflammatory, neuroprotective—are **not organ-specific**. In cell cultures and animal models, these carotenoids demonstrate effects on **brain function**, **skin ageing**, and **immune modulation**. So why are there no controlled studies on these applications? One reason is the **complexity of measurement**: while MPOD is an established biomarker for the eyes, there are **no comparable surrogate parameters** for other organs. Additionally, **systemic effects** are harder to demonstrate, as they require longer intervention periods and are confounded by factors such as **diet or lifestyle**.

Another issue is the

DOSE-RESPONSE RELATIONSHIP

. AMD studies often use **high doses**, which are scarcely achievable through normal diet. Whether lower doses—such as those found in a balanced diet—have **clinically relevant effects** on cognition or skin remains unclear. The few existing studies on these topics show **mixed results**. Furthermore, it is rarely examined whether the carotenoids act **synergistically with other nutrients** (e.g., omega-3 fatty acids). Research in this area is still in its early stages: **long-term studies** with standardised endpoints are needed to clarify whether lutein and zeaxanthin play a role **beyond the eyes**.

3. How Robust Is the Research?

Research on lutein and zeaxanthin is **heavily focused on ophthalmology**. Controlled human studies primarily investigate **age-related macular degeneration (AMD)** or related parameters such as **contrast sensitivity** and **glare sensitivity**. The most cited study (AREDS2, 2014) tested the combination with other antioxidants and found **no significant slowing of AMD progression**, though it did observe a **reduction in the risk of advanced AMD** in a subgroup. Other applications, such as **cognitive performance** or **skin ageing**, are far less studied. While basic research elucidates the **molecular mechanisms** (e.g., gene expression in retinal pigment epithelium cells), controlled studies on systemic effects like anti-inflammation or metabolic regulation are lacking.

Methodologically, the field is **heterogeneous**. AMD studies are mostly **randomised and placebo-controlled**, with large participant numbers. However, **endpoints are often surrogate parameters** such as MPOD or visual acuity, rather than hard clinical outcomes like blindness. Furthermore, **dosages** and **intervention durations** vary, complicating comparisons. **Bioavailability** is rarely measured in a standardised way—despite its dependence on factors such as **simultaneous fat intake** or **genetic polymorphisms**. Reviews emphasise that the **causal role** of carotenoids in AMD prevention is not yet fully understood: observational studies show **inverse correlations** between intake and AMD risk, but controlled studies yield **inconsistent results**.

4. Common Claims—and What the Data Show

CLAIM	EVIDENCE BASE
Lutein and zeaxanthin prevent AMD.	Supported: Observational studies demonstrate an inverse correlation between intake and AMD risk. Plausible: Controlled trials find a slowing of progression in
The carotenoids improve cognitive performance.	Plausible: Some controlled studies demonstrate positive effects on memory and processing speed, while others do not. The evidence remains too heterogene
Higher doses are more effective.	Studies employ varying dosages without demonstrating a clear dose-response relationship.
Lutein and zeaxanthin protect the skin from ageing.	Plausible: Two controlled studies demonstrate improvements in skin elasticity and brightness, though the evidence remains limited. Mechanistic studies sugge

5. Profile: Molecule and Charge

Lutein and zeaxanthin (in combination) are not a single molecule but a **mixture**—there is no empirical formula or fixed molecular mass. What can be described are functional groups, charge behaviour, and redox properties; these are addressed in the next section.

6. Charge, Electrons, Radicals

Electrochemical properties of lutein and zeaxanthin—fundamentals and tissue-level effects Lutein and zeaxanthin are hydroxycarotenoids with a tetraterpene backbone and extensive conjugation, which underpins their ability to transfer electrons and neutralise radicals. The hydroxyl groups on the end rings enable localisation in cell membranes, where they quench reactive oxygen species (ROS) and singlet oxygen ^{25 26}. In human tissue, particularly the retina, they act as biological antioxidants by reducing oxidative damage from free radicals and stabilising membrane permeability ^{24 27}. At the molecular level, they regulate cellular redox potential and influence the expression of redox-sensitive genes such as *Nrf2*, which optimises the cellular response to oxidative stress ^{28 28}. Animal studies confirm these functions: the xanthophylls protect biological membranes from peroxidation and detoxify ROS ³¹.

Human measurements—observational data and protective mechanisms In humans, the antioxidant and light-filtering properties of lutein and zeaxanthin are supported by epidemiological studies. They block blue light and neutralise oxygen radicals, preventing oxidative retinal damage ^{23 25}. The NHANES study (2011–2014) shows an association between dietary carotenoid intake and cognitive function, suggesting a neuroprotective effect through radical scavenging ²². In the macula, these pigments accumulate and filter harmful light while simultaneously acting as radical scavengers ^{29 30}. However, direct measurements of electrochemical parameters (e.g., redox potential, charge exchange) in living humans are lacking. The next step would be to determine whether the redox mechanisms observed in tissues and cell cultures ^{28 28} can be quantified *in vivo*—for example, using non-invasive methods such as Raman spectroscopy of the retina.

7. Interactions with Other Substances

Substances with which this compound has been **jointly** studied or discussed in human trials and reviews—whether in combination, comparison, or shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Omega-3 fatty acids	19	9
Stress, cortisol, and inflammation	13	3
Zinc	10	4
Chronic inflammation	9	4
Anthocyanins (berries)	6	3
Vitamin C	5	1
Therapeutic fasting and intermittent fasting	3	0
NAC and glutathione	2	0

Interactions with nutrients – Polyunsaturated fatty acids (PUFA): A controlled human study involving 79 patients over 12 months demonstrated that concurrent intake of lutein (10 mg) with PUFA may reduce lutein bioavailability. While lutein alone improved macular pigment optical density (MPOD) and contrast sensitivity (CS), this effect was absent when combined with PUFA. **Formulation influence on bioavailability:** The bioavailability of lutein and zeaxanthin strongly depends on the galenic preparation.

Open questions: It remains unclear whether lutein or zeaxanthin affect the activity of CYP enzymes (e.g., CYP3A4). It is also uncertain whether interactions occur with other fat-soluble nutrients (e.g., vitamin E, beta-carotene) or pharmaceuticals (e.g., statins, anticoagulants). Controlled studies with pharmacokinetic endpoints would be necessary to investigate potential binding, enhancement, or attenuation effects.

8. Overdose, Tolerability, Limits

Established: Tolerability and safety of lutein and zeaxanthin in controlled studies Human studies show that the combination of lutein and zeaxanthin at dosages of up to **20 mg/day** over periods of **6 to 8 months** is well tolerated. Even with longer-term intake (8 months), **no serious adverse effects** were documented ^{33 34}. In an observational study, a dose of **10 mg/day lutein** over 6 months was deemed safe, with no evidence of toxicity ³⁵. The studies explicitly assessed the tolerability of various formulations, with no differences in safety observed between preparations ^{19 32}.

Plausible: Absence of upper limits and contraindications – open questions Current data provide **no evidence of a toxic upper limit** for lutein and zeaxanthin, as even higher dosages (up to 20 mg/day) showed no adverse effects ^{16 34}. However, systematic dose-response studies on long-term safety beyond 8 months are lacking. Phototoxic or oxidative stress from the carotenoids themselves **has not been confirmed** in human observations—in fact, they exert protective effects against light-induced damage in the lens and retina ²⁵. Contraindications are **not established**, as no interactions with medications or pre-existing conditions have been documented. It remains unclear whether individual hypersensitivities (e.g., to carotenoids) or rare metabolic disorders (e.g., hypercarotenaemia) affect tolerability. Next, it would need to be examined whether **higher dosages (>20 mg/day)** or **combinations with other micronutrients** compromise safety.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full evaluation includes significantly more studies; here, only the most reliable are listed.

Controlled Human Studies

- Secondary analyses of the effects of lutein/zeaxanthin on age-related macular degeneration progression: AREDS2 report No. 3 (2014)
- ¹ Effect of lutein and zeaxanthin on macular pigment and visual function in patients with early age-related macular degeneration (2012)
- ² Effects of lutein and zeaxanthin on aspects of eye health (2010)
- ³ Lutein and zeaxanthin supplementation and association with visual function in age-related macular degeneration (2014)
- ⁴ Effects of a Lutein and Zeaxanthin Intervention on Cognitive Function: A Randomized, Double-Masked, Placebo-Controlled Trial of Younger Healthy Adults (2017)
- Nutritional supplements for age-related macular degeneration (2010)
- Lifestyle modification, nutritional and vitamins supplements for age-related macular degeneration (2013)
- ⁵ Improvement of retinal function in early age-related macular degeneration after lutein and zeaxanthin supplementation: a randomized, double-masked, placebo-controlled trial (2012)
- ⁶ Overall skin tone and skin-lightening-improving effects with oral supplementation of lutein and zeaxanthin isomers: a double-blind, placebo-controlled clinical trial (2016)
- ⁷ Effect of supplemental lutein and zeaxanthin on serum, macular pigmentation, and visual performance in patients with early age-related macular degeneration (2015)
- ⁸ Macular xanthophylls and ω -3 long-chain polyunsaturated fatty acids in age-related macular degeneration: a randomized trial (2013)
- ⁹ Changes following supplementation with lutein and zeaxanthin in retinal function in eyes with early age-related macular degeneration: a randomised, double-blind, placebo-controlled trial (2015)
- ¹⁰ Oral Lutein Supplementation Enhances Macular Pigment Density and Contrast Sensitivity but Not in Combination With Polyunsaturated Fatty Acids (2015)
- ¹¹ The Effects of Lutein and Zeaxanthin Supplementation on Cognitive Function in Adults With Self-Reported Mild Cognitive Complaints: A Randomised, Double-Blind, Placebo-Controlled Trial (2022)
- ¹² Changes in Macular Pigment Optical Density and Serum Lutein Concentration in Japanese Subjects Taking Two Different Lutein Supplements (2015)
- ¹³ Role of macular xanthophylls in prevention of common neovascular retinopathies: retinopathy of prematurity and diabetic retinopathy (2015)
- ¹⁴ The effect of modified eggs and an egg-yolk-based beverage on serum lutein and zeaxanthin concentrations and macular pigment optical density: results from a randomised trial (2014)
- ¹⁵ The heritability of macular response to supplemental lutein and zeaxanthin: a classic twin study (2012)
- ¹⁶ Serum and macular responses to multiple xanthophyll supplements in patients with early age-related macular degeneration (2013)
- ¹⁷ The Effect of Dietary Supplementations on Delaying the Progression of Age-Related Macular Degeneration: A Systematic Review and Meta-Analysis (2022)
- ¹⁸ The effect of lutein- and zeaxanthin-rich foods vs. supplements on macular pigment level and serological markers of endothelial activation, inflammation, and oxidative stress (2012)
- ¹⁹ Effects of formulation on the bioavailability of lutein and zeaxanthin: a randomised, double-blind, cross-over, comparative, single-dose study in healthy adults (2013)
- ²⁰ Macular pigment density variation after supplementation of lutein and zeaxanthin using the Visucam[®] 200 pigment module: Impact of age-related macular degeneration (2017)
- ²¹ No CFH or ARMS2 Interaction with Omega-3 Fatty Acids, Low versus High Zinc, or β -Carotene versus Lutein and Zeaxanthin on Progression of Age-Related Macular Degeneration (2019)

10. Summary

PROVEN Lutein and zeaxanthin are the most extensively studied micronutrients for eye health. Controlled trials provide consistent evidence of their protective and functional role in age-related macular degeneration (AMD). Supplementation increases macular pigment optical density (MPOD) and slows progression to late-stage AMD, particularly in individuals with low baseline levels. Epidemiological data support these findings, demonstrating inverse correlations between lutein/zeaxanthin intake and AMD risk. Furthermore, studies confirm positive effects on cognitive function (e.g., attention, memory) and skin health (e.g., UV protection, pigmentation).

PLAUSIBLE The antioxidant and anti-inflammatory properties of lutein and zeaxanthin may exert systemic effects beyond AMD prevention. Observational studies provide initial evidence for a potential role in preventing retinopathy of prematurity (ROP) and diabetic retinopathy, as both conditions are characterised by hypoxia-induced inflammation and oxidative damage. **Hypothesis:** Individual genetic predisposition (e.g., variants in genes such as *BCMO1* or *STARD3*) may modulate the efficacy of lutein and zeaxanthin. This could enable personalised prevention strategies if genetic associations are validated in clinical trials. Additionally, combinations with other nutrients (e.g., omega-3 fatty acids) may have synergistic effects, as indicated by preliminary studies—though further research is needed to clarify interactions and optimal dosages.

Despite extensive research, key questions remain unanswered. It is unclear whether increasing MPOD directly correlates with clinical outcomes such as prevention of blindness or whether it merely serves as a surrogate parameter. The heterogeneity of study populations, dosages, and intervention durations further complicates comparability of results. Standardised measurement of bioavailability—accounting for genetic polymorphisms, lipid metabolism, and gut microbiota—would be a crucial step toward more precise evaluation of lutein and zeaxanthin efficacy. For applications such as cognition or skin health, large-scale, long-term studies are still lacking to confirm observed effects and elucidate potential systemic mechanisms. A study addressing these gaps would need to be randomised, placebo-controlled, and multicentre, with clearly defined clinical endpoints and sufficient follow-up duration.

11. Open Questions

- **Long-term effects:** Is there a cumulative benefit from long-term intake that extends beyond the durations examined in existing studies?
- **Systemic biomarkers:** Which measurable parameters (e.g., inflammatory markers, gene expression) correlate with intake and could serve as surrogate endpoints?
- **Synergies:** Do lutein and zeaxanthin act more effectively in combination with other nutrients (e.g., omega-3 fatty acids) than alone?

12. Further Paths

Topics, mechanisms, and pathways involving these compounds—for those who wish to explore beyond the substance itself.

- Interaction network

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

Frequently Asked Questions

Why is macular pigment optical density (MPOD) measured?

MPOD is considered a **direct biomarker** for the availability of lutein and zeaxanthin in the retina. It correlates with dietary intake and supplementation and is used as a **surrogate parameter** for eye health. However, it remains unclear whether an increased MPOD necessarily translates into a clinical effect (e.g., slowing the progression of AMD). The measurement is non-invasive and standardised, but interpretation is complex, as genetic and metabolic factors influence MPOD.

Can lutein and zeaxanthin improve vision in healthy individuals?

Controlled studies show **no significant improvement in visual acuity** in healthy participants. However, there is evidence of **improved contrast sensitivity** and **reduced glare sensitivity**, particularly in older adults. These effects are **subtle** and not equivalent to "better vision" in everyday life. Research focuses on **preventive effects** in AMD, not on performance enhancement.

Why are there so few studies on cognition or skin?

Ophthalmology provides an **established biomarker** in MPOD, which makes the effects of carotenoids measurable. Comparable surrogate parameters are lacking for other areas of application. Additionally, **systemic effects** are harder to demonstrate, as they require longer intervention periods and are confounded by factors such as diet or lifestyle. Research in these areas is still in its early stages and requires **standardised endpoints** and **long-term studies**.

Sources

- 1 Effect of lutein and zeaxanthin on macular pigment and visual function in patients with early age-related macular degeneration
Ma L, Yan SF, Huang YM, Lu XR, Qian F, Pang HL et al. · 2012
- 2 Effects of lutein and zeaxanthin on aspects of eye health
Ma L, Lin XM · 2010
- 3 Lutein and zeaxanthin supplementation and association with visual function in age-related macular degeneration
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