

Article

High-All-Trans Lutein Crystals for Macular Pigment and Visual Function: Formulation Characteristics and Human Intervention Evidence

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Abstract: Macular pigment optical density (MPOD) is a practical measure of lutein accumulation in the human macula. We examined the NVTIA® high-all-trans lutein crystalline material and then placed its analytical profile beside human intervention data on macular pigment and visual performance. Across five process conditions, total lutein was 81.7-82.8%, all-trans lutein 88.8-89.8%, recovery 79.5-80.6%, and cis isomers 10.2-11.2%. Process comparators produced larger changes: removal of MCT-assisted extraction reduced recovery, omission of low-oxygen/light control shifted all-trans lutein from 89.8% to 84.0% and cis isomers from 10.2% to 16.0%, and omission of pre-deoiling caused emulsification during saponification with greater resin-column resistance. Human evidence available through 18 August 2026 included randomized trials and meta-analyses of lutein-containing interventions. MPOD increased in several adult studies and in more recent pediatric and adolescent trials. Contrast sensitivity, glare, photostress recovery, visual acuity, and AMD progression were less uniform across populations and endpoints. The process data identify a chemically consistent starting material; the clinical literature identifies MPOD as a direct tissue-response measure, with visual-performance tests used as separate functional outcomes.

Keywords: lutein; all-trans lutein; macular pigment optical density; visual function; contrast sensitivity; age-related macular degeneration; crystalline formulation; NVTIA®.

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1. Introduction

Lutein, zeaxanthin, and meso-zeaxanthin form the principal carotenoid pigment of the human macula. The tissue filters short-wavelength visible light and sits in an environment with high oxygen use and abundant polyunsaturated lipids [1]. Because macular pigment can be measured non-invasively, MPOD has become a common exposure and tissue-response endpoint in lutein intervention studies.

The composition of the administered lutein matters before a visual outcome is measured. Extraction, saponification, concentration, and drying can expose carotenoids to oxygen, light, heat, and alkaline conditions. The NVTIA® process uses low-oxygen extraction, light protection, mild saponification, pre-deoiling, membrane clarification, resin enrichment, low-temperature crystallization, and vacuum drying to keep the crystalline profile within a narrow range.

Two sets of data were considered here. The first was the process profile of the NVTIA® high-all-trans crystals across five operating conditions and five process comparators. The second was the human intervention literature. MPOD was treated separately from contrast sensitivity, glare tolerance, photostress recovery, visual acuity, and AMD progression so that tissue enrichment was not conflated with every functional or disease-related endpoint.

2. Materials and Methods

2.1 NVTIA® lutein crystalline composition

Dried marigold flower granules were pretreated with vitamin E and ascorbyl palmitate and handled under light-shielded or yellow safe-light conditions. Cell walls were disrupted in citric acid-sodium citrate buffer containing cellulase, pectinase, and hemicellulase. Lutein esters were extracted under nitrogen-protected low-oxygen conditions with aqueous ethanol containing a low proportion of MCT oil. The free MCT phase was removed and washed with aqueous ethanol before saponification. Mild potassium-hydroxide saponification was followed by neutralization and soap removal, microfiltration, ethanol-resistant ultrafiltration, weak-polarity macroporous-resin enrichment, reduced-pressure concentration, low-temperature crystallization, washing, and vacuum drying.

2.2 Product characterization

Total lutein and isomer profiles were measured by C30 HPLC at 450 nm. Recovery was calculated from lutein equivalents in the marigold raw material. Saponification conversion was the molar proportion of free lutein relative to free lutein plus residual lutein esters after saponification. Five operating conditions were assessed descriptively. Five additional comparators removed MCT-assisted extraction, low-oxygen/light control, compound-enzyme disruption, pre-deoiling, or post-saponification neutralization/soap removal one at a time. No inferential statistics were applied to these process configurations.

2.3 Human evidence identification

PubMed and publisher-indexed databases were searched through 18 August 2026 using lutein, zeaxanthin, macular pigment, MPOD, contrast sensitivity, glare, photostress recovery, visual acuity, AMD, randomized trial, and meta-analysis. Randomized trials, longer-duration interventions, and systematic reviews or meta-analyses with clearly reported human outcomes were prioritized. Multi-ingredient interventions were interpreted according to the formulation actually used.

2.4 Translational interpretation

The process experiments were used to describe material identity and consistency. Human studies were used to describe tissue and visual responses after lutein-containing supplementation. Keeping those roles separate allows the NVTIA® material to be positioned against the clinical exposure literature without assigning a published effect size from another formulation to this crystalline ingredient.

Table 1. Performance profile of the NVTIA® lutein crystalline composition across five process conditions.

Condition	Total lutein (%)	All-trans (%)	Recovery (%)	Saponification (%)	Cis (%)	Operation
C1	82.8	89.8	80.6	86.9	10.2	Stable
C2	82.2	89.2	80.1	86.4	10.8	Stable
C3	81.7	88.8	79.5	86.0	11.2	Stable
C4	82.5	89.5	80.3	86.7	10.5	Stable
C5	82.4	89.3	80.2	86.5	10.7	Stable

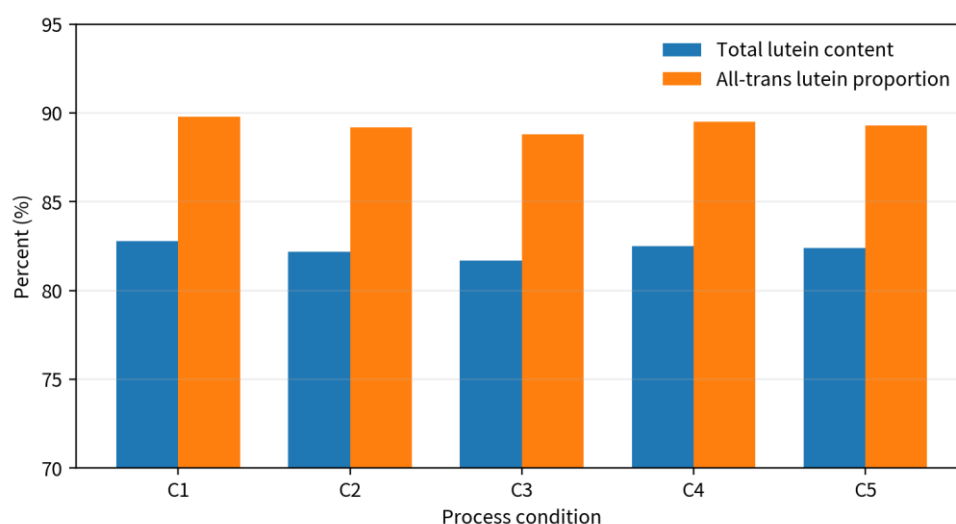


Figure 1. Total lutein content and all-trans lutein proportion across the five evaluated process conditions. Values are direct condition-level measurements; no inferential error bars are added.

Table 2. Directional effects of selectively removing key process controls.

Comparator	Total (%)	All-trans (%)	Recovery (%)	Sapon. (%)	Cis (%)	Observed state
No MCT-assisted extraction	78.2	85.8	75.8	86.2	14.2	Stable
No low-oxygen/light control	78.9	84.0	78.6	85.8	16.0	Stable
No enzyme-assisted disruption	78.5	86.5	74.9	86.1	13.5	Stable
No pre-deoiling	79.4	87.5	77.2	83.6	12.5	Emulsification ; resin pressure rise
No neutralization/s oap removal	79.8	87.8	77.8	86.3	12.2	Resin pressure rise; turbid eluate

3. Results

3.1 Reproducible high-lutein, high-all-trans product profile

The five operating conditions produced similar analytical values. Total lutein was 81.7-82.8%, all-trans lutein 88.8-89.8%, recovery 79.5-80.6%, and saponification conversion 86.0-86.9%. Cis isomers remained between 10.2% and 11.2%. Ethanol residue met the specified limit in every condition, and no downstream-operability problem was recorded.

3.2 Process features associated with structural preservation

The comparator runs separated the contribution of individual process steps. Removing MCT-assisted extraction reduced recovery from 80.6% to 75.8% and lowered all-trans lutein from 89.8% to 85.8%. Loss of low-oxygen/light control produced the largest isomer shift: all-trans lutein was 84.0% and cis isomers 16.0%. Recovery was 74.9% without enzyme-assisted cell-wall disruption. Direct saponification of the MCT-containing extract

gave 83.6% conversion and was accompanied by emulsification and greater resin-column resistance.

3.3 Human macular-pigment response is the most consistent clinical signal

Macular pigment changed more consistently than the functional outcomes. Richer et al., Weigert et al., Ma et al., Murray et al., Huang et al., and Machida et al. each reported increases in MPOD or macular pigmentation after lutein-containing supplementation, with intervention periods ranging from 16 weeks to 2 years [2]-[7]. In a 2021 systematic review and meta-analysis of 46 studies involving 3189 participants, Wilson et al. reported MPOD increases of 0.04 units at total lutein/zeaxanthin intakes of 5 to <20 mg/day and 0.11 units at ≥ 20 mg/day; below 5 mg/day, the pooled estimate was 0.02 units (95% CI, -0.01 to 0.05) and included the null [8].

3.4 Visual-function outcomes vary by endpoint and population

Functional outcomes did not move as uniformly as MPOD. In Veterans LAST, 10 mg/day lutein was associated with improved visual acuity and contrast sensitivity [2]. Weigert et al. recorded a marked MPOD increase over six months without statistically significant changes in visual acuity or mean differential light threshold [3]. Hammond et al. reported improvements in photostress recovery, glare disability, and chromatic contrast after one year of 10 mg lutein plus 2 mg zeaxanthin [9]. Machida et al. found higher MPOD, contrast sensitivity, and glare sensitivity after 16 weeks with a 12-mg crystalline lutein formulation [7]. MPOD also increased in recent pediatric and adolescent trials using 10 mg lutein plus 2 mg zeaxanthin [10], [11]. Liu et al. likewise reported visual-function associations in AMD supplementation studies, adding to the evidence that functional response depends on the specific test and population [12].

3.5 Disease-progression evidence illustrates a different clinical question

AREDS2 addressed a different question. The trial enrolled 4203 adults at high risk of advanced AMD and evaluated 10 mg lutein plus 2 mg zeaxanthin in a factorial design. In the primary comparison, adding lutein/zeaxanthin to the original AREDS formulation did not significantly change progression to advanced AMD [13]. A disease-progression endpoint therefore should not be read as equivalent to MPOD, glare, or contrast-sensitivity response.

Table 3. Selected human intervention evidence relevant to macular pigment and visual function.

Study	Population	Intervention	Duration	Main finding
Richer et al. [2]	90 adults with atrophic AMD	Lutein 10 mg/d; lutein 10 mg/d + antioxidant formula; placebo	12 mo	Both active arms increased MPOD by about 0.09 log units; the lutein-alone arm improved visual acuity by 5.4 letters and contrast sensitivity.
Weigert et al. [3]	126 adults with AMD	Lutein 20 mg/d for 3 mo, then 10 mg/d for 3 mo; placebo	6 mo	MPOD increased 27.9% versus placebo; visual-acuity and microperimetry changes showed trends without conventional statistical significance.

Study	Population	Intervention	Duration	Main finding
Ma et al. [4]	108 adults with early AMD	Lutein 10 mg/d; lutein 20 mg/d; lutein 10 mg + zeaxanthin 10 mg/d; placebo	48 wk	Macular pigment increased, with a clear response in the 20-mg lutein and combined groups; visual-function outcomes varied by endpoint.
Murray et al. [5]	72 adults with early AMD	Lutein ester providing 10 mg/d; placebo	12 mo	MPOD increased during supplementation and visual acuity showed a mild favorable signal.
Hammond et al. [9]	Healthy adults	Lutein 10 mg + zeaxanthin 2 mg/d; placebo	12 mo	Macular pigment enrichment was accompanied by improvements in glare-related and photostress-related visual performance.
AREDS2 [13]	4203 adults at high risk of advanced AMD	Lutein 10 mg + zeaxanthin 2 mg/d in factorial design	Median ~5 y	The primary comparison was statistically neutral for overall progression to advanced AMD, illustrating endpoint- and population-dependent effects.
Huang et al. [6]	112 adults with early AMD	Lutein 10 or 20 mg/d; lutein 10 mg + zeaxanthin 10 mg/d; placebo	2 y	Serum carotenoid status and macular pigmentation increased; selected retinal-sensitivity and contrast-sensitivity measures improved.
Machida et al. [7]	60 healthy adults randomized	Crystalline lutein formulation, 12 mg/d; placebo	16 wk	MPOD, contrast sensitivity and glare sensitivity improved at week 16; serum lutein rose by weeks 8 and 16.
Parekh et al. [10]	60 children aged 5-12 y	Lutein 10 mg + zeaxanthin 2 mg/d; placebo	180 d	MPOD increased from early follow-up; eye-strain/fatigue and several visual-cognitive outcomes favored supplementation.
Lopresti & Smith [11]	82 teenagers aged 13-18 y	Lutein 10 mg + zeaxanthin 2 mg/d; placebo	6 mo	MPOD increased in both eyes; attention and processing speed improved, while several other cognitive outcomes remained similar between groups.

4. Discussion

4.1 Why all-trans preservation matters

The process data are easiest to interpret at the material level. All-trans lutein remained within 88.8-89.8% across the five operating conditions, whereas removing low-oxygen/light protection shifted the product toward cis isomers. Pre-deoiling also affected saponification behavior and downstream handling. These are direct manufacturing observations and can be documented independently of any biological response.

4.2 Crystalline material quality and human exposure

Systemic exposure, not the label amount alone, determines how much lutein is available to the macula. Food matrix, co-ingested lipid, particle characteristics, esterification state, and formulation can change carotenoid bioaccessibility. Machida et al. are useful in this respect: their crystalline lutein formulation increased serum lutein, MPOD, contrast sensitivity, and glare sensitivity after 16 weeks [7]. That study gives a concrete clinical comparison for future work with another crystalline lutein source.

4.3 A hierarchical view of ocular outcomes

Ocular endpoints are better read as a sequence than as one combined efficacy measure. Serum lutein and MPOD sit closest to exposure and tissue enrichment. Contrast sensitivity, glare, and photostress recovery add functional information. Visual acuity and progression to advanced AMD are influenced by more variables. Reviews of lutein and zeaxanthin across the lifespan make the same distinction between tissue status and functional outcomes [14], while broader carotenoid literature emphasizes that absorption and tissue delivery depend on the nutritional and formulation context [15].

4.4 Relevance of the NVTIA® composition

The NVTIA® high-all-trans material showed little analytical spread across the tested process window. For a human study, that chemical definition is useful because it removes one avoidable source of exposure variability. The strongest recurring clinical endpoint in the reviewed literature is MPOD; contrast sensitivity, glare, photostress recovery, or visual acuity can then be selected according to the population and study question.

4.5 Current Scope and Future Directions

A controlled NVTIA® study could measure plasma lutein and MPOD at predefined exposure levels, then add a small set of functional tests such as contrast sensitivity and glare recovery. Baseline macular pigment, dietary carotenoid intake, age, and ocular status should be recorded before randomization or used for stratification. A comparator lutein delivery form could also be included if the aim is to test whether the controlled crystalline profile is associated with different systemic exposure or macular enrichment.

5. Conclusion

Across five process conditions, the NVTIA® crystals contained 81.7-82.8% total lutein and 88.8-89.8% all-trans lutein; cis isomers were 10.2-11.2% and downstream operation remained stable. The process comparators showed measurable contributions from MCT-assisted extraction, low-oxygen/light control, enzyme-assisted tissue disruption, pre-deoiling, and soap removal. In human intervention studies, MPOD was the most repeatable lutein-related response. Contrast sensitivity, glare-related measures, visual acuity, and AMD progression varied more by test and population. MPOD is therefore a practical primary tissue-response endpoint for direct NVTIA® evaluation, with selected visual-performance outcomes added separately.

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