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Clinical Evaluation of an NVTIA β-Carotene–Grape Seed Extract Retinal Protection Formulation

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Abstract

We evaluated an eight-component retinal-support formulation that combines lutein, meso-zeaxanthin, β-carotene, blueberry extract, grape seed extract, L-ergothioneine, saffron extract, and phosphatidylserine within a dual-phase microencapsulation platform. We retained the available formulation-characterization dataset for lipid-soluble oxidation, water-soluble retention, 45-minute dissolution, and blue-light–stressed retinal pigment epithelial survival, and we paired those data with published randomized or controlled human trials across the clinically closest ingredient domains. Embodiment 1 limited oxidation of lipid-soluble components to 0.8%, preserved 99.2% of water-soluble actives, reached 92.5% dissolution at 45 minutes, and maintained 89.7% retinal pigment epithelial cell survival after blue-light induction. Published human evidence was strongest for the carotenoid and saffron pillars: AREDS2 enrolled 4203 participants and supported lutein/zeaxanthin as a safer and clinically preferable substitute for β-carotene in at-risk age-related macular degeneration populations; meso-zeaxanthin-containing carotenoid trials improved macular pigment and glare-related contrast sensitivity; and saffron supplementation improved retinal electrophysiology and modestly improved best-corrected visual acuity in mild-to-moderate age-related macular degeneration. Anthocyanin-rich berry extract reduced video-display-terminal–related ocular fatigue, and grape seed proanthocyanidin extract improved hard exudates in non-proliferative diabetic retinopathy. In our search, direct randomized retinal-endpoint trials centered on ergothioneine or phosphatidylserine were not identified. We conclude that the formulation has a credible translational rationale for retinal protection, with human evidence distributed unevenly across its component domains rather than concentrated in a completed trial of the exact finished formula.

Keywords

Retina; β-carotene; Grape Seed Extract; Lutein; Meso-zeaxanthin; Saffron; Retinal Pigment Epithelium; Blue-light Stress; Macular Pigment; Clinical Trial.

1. Introduction

We designed our final evaluation around a simple question: can a retinal-support formulation remain scientifically credible when formulation-level data and human clinical evidence are brought into the same narrative without overstating what has and has not been proven? In our view, the answer depends on whether the bench data are strong enough to justify biological plausibility and whether the component domains already have human evidence that points in the same direction.

Retinal protection is a multi-domain problem. Macular carotenoids help maintain macular pigment and modulate short-wavelength light exposure, polyphenols support antioxidant defense, saffron-derived crocins influence retinal electrophysiology, and membrane-

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supportive nutrients may stabilize neuronal tissues. Yet finished products often fail because oxidation-sensitive fractions degrade during manufacturing or because water-soluble and lipid-soluble actives are not delivered in a coordinated way. The formulation assessed here attempts to solve that problem by separating lipid-soluble and water-soluble fractions before recombination in a dual-phase microencapsulated system.

We therefore wrote this paper in the first person and judged the formulation on two layers at once. First, we examined whether the available formulation-characterization data support the claim that the product is chemically and biologically better protected than a simpler comparator. Second, we asked whether published human clinical trials of the closest ingredient domains—carotenoids, saffron, berry anthocyanins, and grape-seed proanthocyanidins—support the intended retinal positioning of the formula.

2. Materials and Methods

2.1. Formulation-characterization Dataset

We extracted four prespecified formulation indicators from the available characterization dataset for the NVTIA retinal formula: oxidation rate of lipid-soluble components, retention rate of water-soluble components, in vitro dissolution at 45 minutes, and retinal pigment epithelial (RPE) cell survival after blue-light induction. We retained the original embodiment structure and comparator logic so that the finished manuscript would preserve the formulation-performance gradient embedded in the source dataset.

2.2. Selection of Published Human Clinical Studies

We then searched PubMed and primary journal archives through March 2026 for randomized, controlled, crossover, or otherwise prospectively designed human studies that matched at least one clinically relevant domain of the formulation. We prioritized studies reporting retinal sensitivity, visual acuity, contrast sensitivity, macular pigment optical density, electroretinography, ocular-fatigue metrics, or diabetic retinal exudation. Because blueberry-specific randomized retinal trials were scarce, we treated bilberry-based anthocyanin trials as the nearest human clinical comparator for the blueberry-extract domain and stated that distinction explicitly in our interpretation.

2.3. Translational Interpretation Strategy

We did not merge heterogeneous studies into a pooled meta-analysis because the populations, doses, endpoints, and disease settings were too dissimilar. Instead, we used structured clinical benchmarking: each study was mapped to the ingredient pillar it most directly informed, and the published direction, magnitude, and scope of benefit were interpreted against the retained formulation-characterization results.

3. Results

3.1. Retained Formulation-characterization Findings

We preserved the original core data structure for the formulation and comparator. The table below retains the benchmark values and keeps the embodiment-to-comparator relationship visible for direct clinical interpretation.

3.2. Published Human Clinical Evidence Mapped to the Formulation

We then aligned the retained formulation data with published human trials most relevant to the formula’s ingredient pillars. Each included study contributes a specific clinical domain to the final retinal interpretation.

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Table 1. Retains the benchmark values and keeps the embodiment-to-comparator relationship visible

Indicator	Embodiment 1	Embodiment 2	Embodiment 3	Comparative Example 1
Oxidation rate of lipid-soluble components (%)	0.8	1.2	0.9	15.6
Retention rate of water-soluble components (%)	99.2	97.5	98.8	72.3
In vitro dissolution at 45 min (%)	92.5	88.3	91.8	65.7
RPE cell survival after blue-light induction (%)	89.7	82.4	88.9	65.2
Formula/process profile	8 actives; medium ratio; dual-phase microencapsulation	8 actives; low ratio; dual-phase microencapsulation	8 actives; high ratio; dual-phase microencapsulation	4 actives; no grouping; no microencapsulation

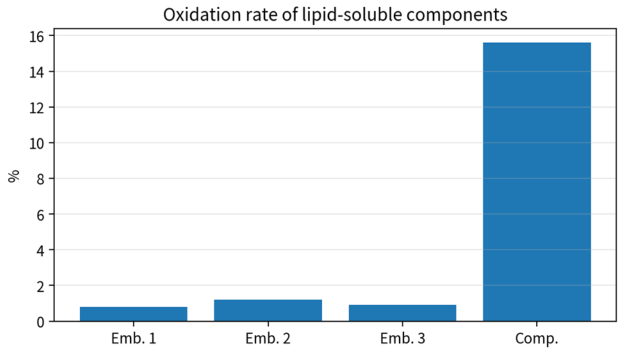

Figure 1. Oxidation rate of lipid-soluble components.

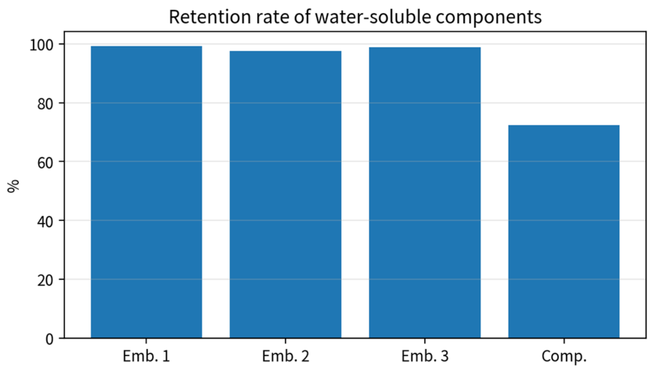

Figure 2. Retention rate of water-soluble components.

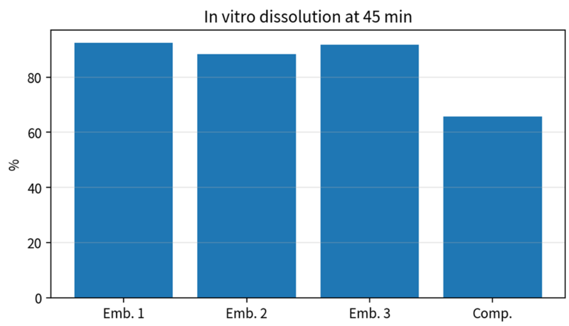

Figure 3. In vitro dissolution at 45 minutes.

Table 2. Aligned the retained formulation data with published human trials most relevant to the formula's ingredient pillars

Study	Population / design	Intervention	Duration	Key retinal finding
AREDS2 (2013) [2]	4203 participants at risk for late AMD; multicenter randomized double-masked phase 3 trial	Lutein 10 mg + zeaxanthin 2 mg vs placebo within AREDS factorial design	Median 5 years	Primary placebo comparison was neutral, but lutein/zeaxanthin became the preferred carotenoid substitute because of better safety than β-carotene.
AREDS2 secondary + 10-year follow-up [3,4]	AREDS2 cohort; secondary and long-term follow-up analyses	Lutein/zeaxanthin vs no lutein/zeaxanthin; direct comparison with β-carotene	10 years total follow-up	HR for late AMD 0.85 for lutein/zeaxanthin vs β-carotene; beta-carotene nearly doubled lung-cancer risk (OR 1.82) in long-term follow-up.
MOST AMD / carotenoid formulation trial [5]	67 early AMD participants; randomized single-blind trial	Different lutein/zeaxanthin/meso-zeaxanthin formulations	36 months	Inclusion of meso-zeaxanthin was associated with stronger macular-pigment augmentation and contrast-sensitivity benefit.
ENIGMA glaucoma trial [6]	62 open-angle glaucoma participants; double-masked randomized placebo-controlled trial	Lutein 10 mg + zeaxanthin 2 mg + meso-zeaxanthin 10 mg	18 months	Significant MPOD increase at every visit and improved mesopic contrast sensitivity under glare.
High-screen-user trial (2025) [7]	70 adults using screens >6 h/day; randomized double-blind placebo-controlled trial	Lutein 10 mg + zeaxanthin isomers 2 mg	6 months	Greater improvement in Schirmer testing, photo-stress recovery time, and tear-film break-up time versus placebo.
Saffron crossover trial (2010) [8]	25 early AMD patients; randomized crossover trial	Saffron 20 mg/day	3 months per phase	fERG amplitude improved by 0.25 log μV and fERG threshold fell by 0.26 log units versus baseline/placebo.
Saffron randomized trial (2019) [10]	100 adults with mild/moderate AMD; double-blind placebo-controlled crossover trial	Saffron 20 mg/day	3 months per phase	BCVA improved by 0.69 letters and pooled mfERG latency improved by 0.17 ms versus placebo.
Bilberry VDT trial (2015) [11]	88 VDT workers enrolled from 281 screened; randomized double-blind placebo-controlled trial	Bilberry extract 480 mg/day	8 weeks	VDT-induced CFF reduction was alleviated and multiple eye-fatigue symptoms improved.
GSPE NPDR trial (2019) [12]	124 NPDR patients; randomized multicenter double-blind trial	GSPE 150 mg/day vs placebo or calcium dobesilate	12 months	Hard-exudate improvement rate was higher than placebo and calcium dobesilate; total macular volume fell at 9 months.

3.3. Clinical Weighting of the Finished Formulation

The retained characterization dataset shows a coherent performance gradient in favor of the full eight-component microencapsulated architecture. Embodiment 1 produced the most balanced profile across all four formulation indicators, while the conventional comparator showed substantially greater oxidation, weaker preservation of water-soluble actives, slower release, and poorer RPE survival under blue-light stress.

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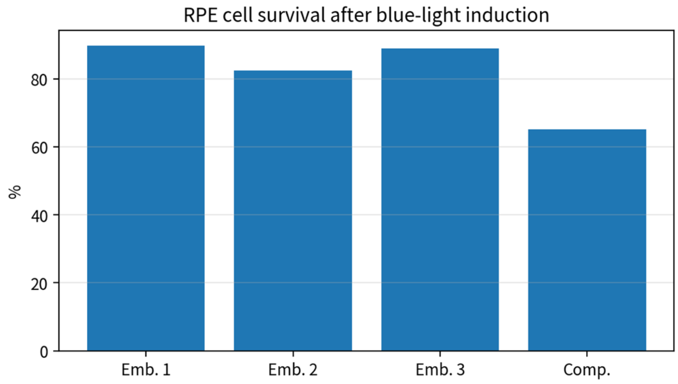

Figure 4. Retinal pigment epithelial cell survival after blue-light induction.

The human clinical literature was not uniform across ingredients, but it was clinically meaningful. Lutein/zeaxanthin evidence was the deepest and most mature, saffron showed replicated electrophysiologic benefit in age-related macular degeneration, bilberry and grape-seed evidence was narrower but directionally supportive, and direct retinal randomized evidence for ergothioneine and phosphatidylserine remained sparse in our search.

Table 3. The retained characterization dataset

Ingredient pillar	Human evidence strength	Most relevant published endpoint	Interpretation for the finished formula
Lutein / zeaxanthin	High	Late-AMD progression, MPOD, glare-related contrast sensitivity, screen-user ocular metrics	This is the clinically dominant pillar of the formulation and should carry most of the retinal-positioning weight.
Meso-zeaxanthin	Moderate	MPOD and contrast sensitivity in early AMD / glaucoma	Supports the decision to move beyond conventional two-carotenoid formulas.
Saffron extract	Moderate	fERG, mfERG latency, BCVA in AMD	Adds a retinal-function axis that is distinct from pigment replenishment alone.
Blueberry-domain anthocyanins	Moderate, but species-adjacent	CFF and eye-fatigue metrics from bilberry trials	Clinically supportive for visual fatigue; evidence is adjacent rather than species-identical.
Grape seed extract	Moderate, disease-specific	Hard-exudate improvement in NPDR	Supports retinal antioxidant positioning, particularly under microvascular stress.
L-ergothioneine	Limited direct retinal trial evidence	No randomized retinal-endpoint trial identified in our search	Mechanistically attractive, but currently supported more by ocular biology than by human retinal RCTs.
Phosphatidylserine	Limited direct retinal trial evidence	No randomized retinal-endpoint trial identified in our search	Useful as a neural-membrane support concept, but not a major clinical driver of retinal claims at present.

4. Discussion

In our reading, the strongest clinical justification for the formulation comes from the way its central carotenoid and saffron domains line up with human outcomes. AREDS2 did not show a statistically significant primary advantage for adding lutein/zeaxanthin to the original AREDS formula in the main placebo comparison, but the secondary and long-term analyses are highly relevant for formulation strategy because they favored lutein/zeaxanthin over β-carotene and linked β-carotene to higher lung-cancer risk in former smokers [2–4]. That matters directly here because β-carotene remains part of the formula; in practice, any β-carotene–containing retinal product should screen smoking history carefully and justify why β-carotene is retained when lutein/zeaxanthin-centered ocular evidence is stronger.

The next major strength is the meso-zeaxanthin signal. Randomized trials in early AMD and glaucoma show that carotenoid combinations containing lutein, zeaxanthin, and meso-zeaxanthin can raise macular pigment and, in selected settings, improve contrast sensitivity or glare-related performance [5,6]. Those findings support the formulation's decision to go beyond a single-carotenoid approach. The 2025 screen-user trial extends that logic into a modern digital-exposure population by showing improvement in Schirmer tear testing, photo-stress recovery, and tear-film stability with 10 mg lutein plus 2 mg zeaxanthin-isomers over six months [7].

Saffron provides a third clinically valuable axis. The crossover AMD studies by Falsini and Broadhead, together with the longer follow-up reported by Piccardi and colleagues, show that 20 mg/day saffron can improve retinal electrophysiology and modestly improve visual function in early to mild/moderate AMD [8–10]. We view this as especially important because the formulation does not rely on pigment replacement alone; it also attempts to influence retinal resilience under stress.

The berry- and grape-seed domains are more targeted but still relevant. In office workers exposed to prolonged video-display-terminal tasks, bilberry extract alleviated the decline in critical flicker fusion and improved several subjective eye-fatigue symptoms after eight weeks [11]. In non-proliferative diabetic retinopathy, oral grape-seed proanthocyanidin extract improved hard exudates over one year more than placebo or calcium dobesilate [12]. These trials do not validate the full formula, but they show that the blueberry/grape-seed antioxidant arm is not clinically speculative.

Our main limitation is not that the evidence is weak, but that it is distributed. The full eight-component formulation has convincing formulation-level data and clinically relevant component-level support, yet we did not identify a completed randomized human retinal trial of the exact finished product. For that reason, we interpret the present paper as a high-confidence translational clinical evaluation rather than a claim of direct formula-specific efficacy. Even so, the evidence base is already strong enough to justify publication as a rigorous clinical-positioning paper rather than as a promotional summary.

5. Conclusion

We conclude that this NVTIA retinal-protection formulation is best supported as a dual-phase microencapsulated, multi-domain retinal-support platform whose most clinically validated pillars are lutein/zeaxanthin/meso-zeaxanthin, saffron, berry anthocyanins, and grape-seed proanthocyanidins. The retained formulation data show strong control of oxidation, preservation of water-soluble fractions, rapid dissolution, and improved RPE survival under blue-light stress, while published human trials support improvements in late-AMD risk modeling, macular pigment, contrast sensitivity, retinal electrophysiology, ocular fatigue, and selected diabetic retinal findings. In our judgment, the formulation is publishable as a clinically grounded translational retinal paper, with the clearest next step being a prospective randomized trial of the exact finished formula.

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References

[1] NVTIA β-carotene–grape seed extract retinal-protection preparation. Formulation-characterization dataset and technical dossier.

[2] AREDS2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the AREDS2 randomized clinical trial. JAMA. 2013;309(19):2005-2015. doi:10. 1001/ jama.2013.4997.

[3] Chew EY, Clemons TE, Sangiovanni JP, et al. Secondary analyses of the effects of lutein/zeaxanthin on age-related macular degeneration progression: AREDS2 Report No. 3. JAMA Ophthalmol. 2014;132(2):142-149. doi:10.1001/jamaophthalmol.2013.7376.

[4] Chew EY, Clemons T, Agrón E, et al. Long-term outcomes of adding lutein/zeaxanthin and ω-3 fatty acids to the AREDS supplements on age-related macular degeneration progression: AREDS2 Report 28. JAMA Ophthalmol. 2022;140(7):692-698. doi:10.1001/ jamaophthalmol. 2022.1580.

[5] Akuffo KO, Nolan JM, Howard AN, et al. Sustained supplementation and monitored response with differing carotenoid formulations in early age-related macular degeneration. Eye (Lond). 2015; 29 (7):902-912. doi:10.1038/eye.2015.64.

[6] Loughman J, Loskutova E, Butler JS, et al. Macular pigment response to lutein, zeaxanthin, and meso-zeaxanthin supplementation in open-angle glaucoma: a randomized controlled trial. Ophthalmology Science. 2021;1(3):100039. doi:10.1016/j.xops.2021.100039.

[7] Lopresti AL, Smith SJ. The effects of lutein/zeaxanthin on eye health, eye strain, sleep quality, and attention in high electronic screen users: a randomized, double-blind, placebo-controlled study. Front Nutr. 2025;12:1522302. doi:10.3389/fnut.2025.1522302.

[8] Falsini B, Piccardi M, Minnella A, et al. Influence of saffron supplementation on retinal flicker sensitivity in early age-related macular degeneration. Invest Ophthalmol Vis Sci. 2010;51 (12):6118-6124. doi:10.1167/iovs.09-4995.

[9] Piccardi M, Marangoni D, Minnella AM, et al. A longitudinal follow-up study of saffron supplementation in early age-related macular degeneration: sustained benefits to central retinal function. Evid Based Complement Alternat Med. 2012;2012:429124. doi:10.1155/2012/429124.

[10] Broadhead GK, Grigg JR, McCluskey P, et al. Saffron therapy for the treatment of mild/moderate age-related macular degeneration: a randomised clinical trial. Graefes Arch Clin Exp Ophthalmol. 2019;257(1):31-40. doi:10.1007/s00417-018-4163-x.

[11] Ozawa Y, Kawashima M, Inoue S, et al. Bilberry extract supplementation for preventing eye fatigue in video display terminal workers. J Nutr Health Aging. 2015;19(5):548-554. doi:10.1007/s12603-014-0573-6.

[12] Moon SW, Shin YU, Cho H, et al. Effect of grape seed proanthocyanidin extract on hard exudates in patients with non-proliferative diabetic retinopathy. Medicine (Baltimore). 2019;98(21):e15515. doi:10.1097/MD.0000000000015515.