

Vista NeuroOAG Formula

A White Paper on Neuroprotection in Glaucoma

Prepared by: Vista Ophthalmic Research Team
in collaboration with leading Glaucoma Specialists

Abstract

Glaucoma is a multifactorial, neurodegenerative disease characterized by progressive optic neuropathy and visual field loss. While lowering intraocular pressure (IOP) remains the cornerstone of treatment, emerging evidence highlights the importance of addressing mitochondrial dysfunction, oxidative stress, and impaired cellular metabolism in disease progression. The **Vista NeuroOAG** Formula was developed in collaboration with leading glaucoma specialists to provide targeted neuroprotective support through four evidence-based ingredients: Nicotinamide riboside hydrogen malate (NRHM), Pyruvate, Grape Seed Extract, and Resveratrol. This white paper reviews the scientific rationale, mechanism of action, and supporting data underlying the **Vista NeuroOAG** formulation as an adjunctive approach to preserving optic nerve function in glaucoma.

Introduction: The Need for Neuroprotection in Glaucoma

Emerging evidence supports the hypothesis that aging and reduced ocular autoregulatory capacity play a critical role in optic nerve damage associated with glaucoma. The primary risk factor for glaucoma is increased intraocular pressure (IOP), and the most common treatment for patients with primary open-angle glaucoma focuses on decreasing IOP. While lowering the IOP is necessary, it is essential to add neuroprotective measures [1]. Clinicians should strive to maintain healthy cells and, where possible, reverse damage to wounded cells.

The Role of Mitochondrial Health in Glaucoma

The mitochondria—colloquially known as the powerhouse of the cell—plays a role in the development and progression of glaucoma.

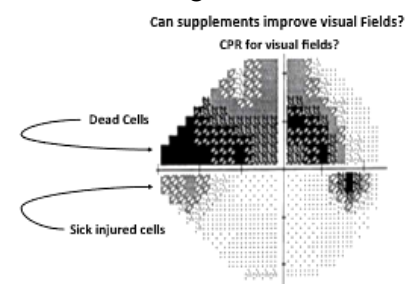
Notably, the optic nerve and ganglion cells of the retina are some of the most metabolically active cells in the human body. Accordingly, proper mitochondrial functioning is paramount to eye health. Studies have shown that impairments in mitochondrial function and mitophagy (the necessary removal of damaged mitochondria) contribute to glaucoma onset and advancement [2]. Indeed, dysfunctional mitochondria can:

1. Lead to an increased production of reactive oxygen species (ROS) and thus oxidative stress [3] and,
2. Result in the accumulation of metabolic waste.

Both processes, if left unchecked, can cause cellular damage and apoptosis in the optic nerve, which consequently, can lead to or worsen glaucoma prognosis [4].

Expert Collaboration and Clinical Vision

Vista has collaborated with a team of highly regarded glaucoma specialists and key opinion leaders to create science-driven formulations addressing the metabolic and neuroprotective needs of glaucoma patients. **Vista NeuroOAG** embodies this collaboration, offering evidence-based nutritional support designed to complement conventional therapies and revolutionize the standard of care for glaucoma patients worldwide.



Vista NeuroOAG Formula Overview

Supplement Facts

Serving Size: 4 capsules
Servings Per Container: 60

Amount Per Serving	% Daily Value
Pyruvate (from Calcium Pyruvate)	1000 mg*
Nicotinamide Riboside Hydrogen Malate (NAD ⁺ precursor)	500 mg*
Grape Seed Extract (<i>Vitis vinifera</i>) (standardized to 95% OPCs)	100 mg*
Resveratrol (from <i>Polygonum cuspidatum</i> root extract)	50 mg*

*Daily value not established.

No single nutrient can provide all the benefits patients need to promote eye health. That's why **Vista NeuroOAG** Formula incorporates four scientifically researched ingredients selected for their potential benefits, including reducing oxidative stress, supporting healthy blood circulation, promoting the survival of optic nerve cells, and maintaining mitochondrial health. **Vista NeuroOAG** Formula can complement standard methods of treatment for glaucoma by providing high-quality, evidence-based, and pharmacologically impactful ingredients.

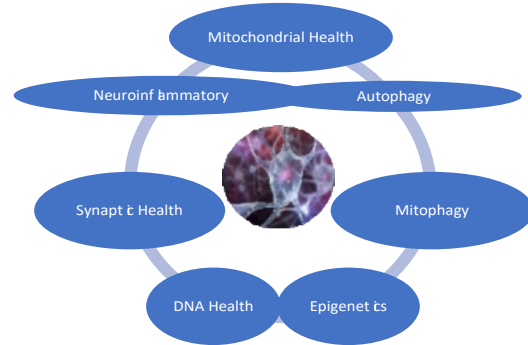
NAD⁺: Crucial for cellular energy production and a cofactor that inhibits axon degeneration

NAD⁺ (nicotinamide adenine dinucleotide) is a vital coenzyme involved in various cellular processes, including energy metabolism, DNA repair, and cellular signaling. As we age, the body tends to catabolize NAD⁺ faster than it can synthesize it. This decline in NAD⁺ is associated with several metabolic and age-related issues, including the neurodegenerative disease glaucoma [5], [6], [7]. Furthermore, the impact of low levels of niacinamide on neuronal energy metabolism may be worse when there is high pressure inside the eye [8].

As mentioned previously, the cells of the retina and optic nerve are especially vulnerable to mitochondrial dysfunction and energy deficits [9]. Intriguingly, a laboratory study using animal subjects found that administering niacinamide boosted the metabolic reliability (regular cell activity and functioning) of aging retinal ganglion cells, keeping these cells healthier for longer [10], [11].

Nicotinamide riboside hydrogen malate (NRHM): A highly bio-available precursor that increases the body's NAD⁺ levels

A convenient way to boost brain NAD⁺ levels is by supplementing with NAD⁺ precursors such as Nicotinamide riboside hydrogen malate (NRHM), which directly increases the levels of



NAD⁺ in the bloodstream. Nicotinamide riboside hydrogen malate (NRHM) is a stable, bioavailable dietary supplement that acts as a precursor to Nicotinamide Adenine Dinucleotide (NAD⁺), a crucial coenzyme for cellular energy and function. NAD⁺ itself is not frequently supplemented directly due to its low bioavailability and stability, therefore supplements like NRHM are used to increase the body's natural NAD⁺ levels. As a precursor to NAD⁺, NRHM helps restore NAD⁺ levels, which are depleted in glaucoma. NAD⁺ is crucial for cellular energy production and is also a cofactor that inhibits SARM1, a protein that drives axon degeneration [12].

Studies suggest that NAD⁺ (nicotinamide riboside) supplementation can improve mitochondrial function and cellular energy levels in various tissues, including the optic nerve [13]. A more recent small study investigated the effects of NAD⁺ supplementation in human glaucoma patients and found that it improved visual function and decreased optic nerve damage progression [14] [29].

There are two prospective trials [15] on NAD⁺ supplementation currently underway:

1. The Glaucoma Nicotinamide Trial, which is a randomized, placebo-controlled double-masked clinical trial. Change in visual field progression over 2 years is the primary outcome measure.

2. The NR as a Neuroprotective Therapy for Glaucoma Trial is also a prospective, randomized, placebo-controlled study on open-angle glaucoma patients. The primary outcome measures are the rates of progressive retinal nerve fiber layer thinning and changes in visual field sensitivity.

Nicotinamide riboside hydrogen malate (NRHM): Liver safety & Metabolic Rationale

The formulation uses **nicotinamide riboside hydrogen malate (NRHM) (500 mg)** as the NAD⁺ precursor. Compared with older vitamin B₃ derivatives like **nicotinamide (NAM)** or **niacin (nicotinic acid)**, NRHM bypasses the hepatic methylation bottleneck responsible for most NAD-related hepatotoxicity.

- **NRHM** is metabolized through the **NRK/NMNAT salvage pathway**, leading directly to NAD⁺ synthesis without generating **N-methyl-nicotinamide** or depleting methyl donors (S_{AMe}).
- Clinical trials have shown **no meaningful increases in ALT/AST** even at doses up to 2,000 mg/day for 8–12 weeks.
- In contrast, **NAM at ≥3 g/day** has been linked to hepatic enzyme elevations, steatosis, and in rare cases, cholestatic injury.
- The malate salt form improves **bioavailability and mitochondrial uptake**, supporting cleaner NAD⁺ regeneration.

Summary

This combination offers **high mitochondrial and retinal neuroprotection** with **minimal hepatic risk**. The chosen NAD precursor, NRHM, avoids the methylation stress and enzyme elevation risk associated with **NAM** or **niacin**, making it a **clinically safe and mechanistically elegant** choice for chronic use in neuro-ophthalmic applications.

Pyruvate: Boosting Visual Function in Glaucoma Treatment

The body naturally produces Pyruvate during glycolysis—the metabolic pathway that generates cellular energy [16]. Intriguingly, Pyruvate has shown promising benefits in boosting visual function in glaucoma treatment [17]. A study published in the journal *Neurobiology of Disease* investigated the effects of pyruvate supplementation on retinal ganglion cells in a glaucoma rat model [18]. The study results showed that pyruvate treatment improved visual function, preserved retinal ganglion cells, and increased the activity of mitochondria in the optic nerve. These findings suggest that pyruvate may have neuroprotective effects on the optic nerve and enhance visual function in those with glaucoma.

Synergy: Integrated NAD⁺ and Pyruvate Metabolic Coupling

Oral supplementation with Nicotinamide and Pyruvate shows promise for improving visual function in glaucoma patients, as seen in a Phase II clinical trial, and may be a safe, adjunctive treatment for neuroprotection by boosting energy metabolism in retinal ganglion cells [19]. Glaucoma is linked to declining NAD⁺ levels and impaired glycolytic capacity, which this combination therapy addresses by supplying necessary components to improve cellular bioenergetics and function [20]. While early results are encouraging, larger-scale clinical trials are needed to establish long-term efficacy and safety.

Mechanism of Action:

- **Nicotinamide (NRHM):** As a precursor to NAD⁺, NRHM helps restore NAD⁺ levels, which are depleted in glaucoma. NAD⁺ is crucial for cellular energy production and is also a cofactor that inhibits SARM1, a protein that drives axon degeneration.
- **Pyruvate:** Pyruvate is the final product of glycolysis and helps to replenish NAD⁺. It also enhances glucose metabolism and provides bioenergetic support to the cells of the optic nerve.
- **Synergistic Effect:** Targeting both declining NAD⁺ and pyruvate levels with

this combination may provide additive neuroprotection by supporting the metabolic function of retinal ganglion cells (RGCs), which are vital for vision and are vulnerable in glaucoma [21].

Clinical Evidence:

- **Phase II Trial:** A randomized, Phase II clinical trial demonstrated that a combination of oral nicotinamide and pyruvate was safe and resulted in more improving visual field test locations in glaucoma patients compared to a placebo [19].
- **Improved Visual Fields:** The treatment group showed an improvement in visual field results, particularly at the edges of existing defects where cells are injured but not yet dead.
- **Safety and Tolerance:** The combination therapy was well-tolerated, with no significant adverse events reported.

Grape Seed Extract: Rich in antioxidants – Protection against oxidative stress

Grape seed extract—which is derived from wine grapes—is rich in antioxidants, including phenolic acids, anthocyanins, flavonoids, and oligomeric proanthocyanidin complexes (OPCs). Due to its high antioxidant content, GSE can help prevent disease and protect against oxidative stress, tissue damage, and inflammation [22].

Via antioxidant action, the compounds in grape seed extract can protect retinal cells from oxidative stress and damage and thus may reduce the risk of age-related macular degeneration and other retinal degenerative diseases [23]. This conclusion is consistent with the results reported by Yang et al., who found that grape seed extract aids in protecting against oxidative-induced retinal ganglion cell damage [24].

Resveratrol: Enhances bioavailability of nutrients and may modulate the RhoA/ROCK pathway

Resveratrol is a polyphenol with antioxidant, anti-inflammatory, mitochondria-supportive, and vasomodulatory actions that are mechanistically relevant to glaucomatous optic neuropathy [25]. It is often combined with other phytochemicals

that can increase the permeability and absorption of other nutrients within the supplement. Resveratrol can influence the composition of gut microbiota, which plays a critical role in metabolizing various nutrients and phytochemicals [26]. Some studies have suggested that by altering the microbial environment, resveratrol may indirectly affect nutrient metabolism and absorption [27], [28].

Preclinical and mechanistic studies indicate that resveratrol can activate SIRT1, reduce oxidative stress, attenuate pro-apoptotic signaling in retinal neurons, and improve endothelial function (e.g., nitric-oxide-mediated vasodilation). There is emerging, context-dependent evidence that resveratrol may indirectly modulate the **RhoA/ROCK pathway** (e.g., via upstream regulators such as SIRT1), which is implicated in trabecular meshwork contractility and retinal ganglion cell survival. While resveratrol is not a selective **ROCK inhibitor**, its potential to temper ROCK activity further **synergizing** the IOP-independent, neuroprotective aims of **Vista NeuroOAG**.

Conclusion: Vista NeuroOAG Formula a new standard of care for glaucoma patients

Vista NeuroOAG Formula provides a comprehensive blend of evidence-based ingredients that supports optic nerve health and visual function in individuals with glaucoma. It combines NAD⁺ precursor Nicotinamide riboside hydrogen malate (NRHM), Pyruvate, Grape Seed Extract and Resveratrol to address various aspects of glaucoma management, including the protection of retinal cells from oxidative stress, improvement in visual field performance, decrease in intraocular pressure, support for mitochondrial health, and enhancement of overall visual function. Alongside standard methods, such as reducing intraocular pressure, **Vista NeuroOAG** Formula can be a valuable addition to glaucoma management.

As the AREDS has become synonymous and the standard of care for ARMD patients, we are striving to make **Vista NeuroOAG** Formula a standard of care for glaucoma patients, offering a comprehensive approach to support optic nerve health and improve visual function.

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