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## Optimizing Eye Health with Citicoline

*Preliminary research indicates efficacy for glaucoma and amblyopia in particular*

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According to a 2016 online survey, people ranked losing vision equal to or worse than losing hearing, memory, speech or a limb. The fear of blindness is prevalent and for many people, protecting vision is paramount. Yet most patients have little understanding of the eye illnesses that can cause blindness. The eyes, and in particular vision, can be negatively impacted by many conditions including refractive errors (nearsightedness, etc), cataracts, macular degeneration, amblyopia (“lazy eye”), diabetic retinopathy, glaucoma, and other illnesses. All practitioners, not just eye doctors, should be interested in finding ways to protect vision and safely treat specific eye conditions that can lead to blindness. This paper describes the scientific research associated with citicoline and eye health with a special emphasis on glaucoma.

The eyes are complex specialized sensory organs that are directly connected to the brain and protected by the blood-brain barrier. There are seven parts of the eye—cornea, iris, pupil, lens, retina, tear ducts and optic nerve—that work together to create vision and protect the eyes from damage.

The optic nerve is what tethers the eye to the brain where it transmits information from the retina. The photoreceptors of the retina have the greatest density of mitochondria of all the neurons in the central nervous system (CNS). In the human body, the retina is one of the highest oxygen-consuming tissues, even more so than the brain.

Citicoline is a nutrient that is essential to the synthesis of membrane phospholipids and acetylcholine in the CNS. As a dietary supplement, it is primarily used to support brain function through phospholipid metabolism,

neurotransmitter synthesis, neuroplasticity, and mitochondrial function. Emerging research now indicates that citicoline can benefit eye health as well as brain health. Given the intimate connection between the eyes and the brain, this new application for citicoline makes sense.

The authors of the book *Glaucoma: A Neurodegenerative Disease* point out that glaucoma in particular is a neurodegenerative disease of the eye that has many similarities with neurodegenerative diseases of the brain. The authors predict that in the future neuroprotection will play a key role in the treatment of glaucoma.

### Mechanisms of Action

When citicoline is taken orally, it is absorbed rapidly and becomes a choline donor that can increase neurotransmitter levels and has a

neuroprotective effect. In the eyes, neurodegeneration occurs with the degeneration of retinal ganglion cells (RGC) and the fibers that form the optic nerve.

A key mechanism of action that citicoline has specific to eye health is what Parisi et al called “neurorescue,” which is the combination of neuroprotection and neuroenhancement. Their 2019 randomized pilot study featured in *PLoS ONE* demonstrated that RGC function significantly increased in the group taking citicoline orally while RGC function worsened in the group that did not take the citicoline. In that study, RGC fibers’ morphology stabilized or improved with the citicoline group, while it worsened in the non-citicoline group. In addition, visual acuity was improved in the citicoline group.

Dopamine is a major neurotransmitter in the retina and is expressed in post-retinal visual pathways. Citicoline has been shown to have a dopaminergic effect, which could explain in part its ability to positively influence RGC. Citicoline has also been shown to prevent the thinning of the retinal nerve fiber layer.

A 2018 review article by Parisi et al published in *Current Neuropharmacology* stated that “In rodent cultures and animal models, citicoline induces antiapoptotic effects, increases the dopamine retinal levels, and counteracts retinal nerve fibers layer thinning.”

Citicoline has also been shown to positively influence and protect mitochondria in the eyes. All of the mechanisms mentioned here are significant in many eye disorders but especially with glaucoma.

## Glaucoma

Worldwide, glaucoma is a leading cause of blindness. What’s worse, there may be no symptoms until after vision loss has already taken place, which is why glaucoma has been nicknamed “the sneak thief of sight.”

According to the Glaucoma Research Foundation, it’s estimated that more than 3 million Americans have glaucoma but only half of those know they have it. Presently there is no cure for glaucoma. Conventional treatment relies on eye drops, pills, surgery or a combination of these treatments to prevent vision loss. The primary goal of conventional treatment is to reduce intraocular

pressure. Any vision loss due to glaucoma is irreversible. That’s why a key clinical objective should be to protect the field of vision so patients can maintain the vision they still have. Citicoline has been shown to protect the field of vision in patients with glaucoma.

Glaucoma is a complex condition but it is known that high intraocular pressure causes RGC death and neurotoxicity. This leads to damage to the retinal nerve fiber layer, which results in a loss of peripheral vision and can ultimately lead to blindness. In addition to controlling intraocular pressure, a key therapeutic goal to halt the progression of this illness is to stop or delay RGC neurodegeneration and protect the optic nerve.

It’s also important to note that even in patients with well-controlled intraocular pressure, disease progression can and often does still take place. That’s why the RGC connection is so important. Presently, the only treatment for glaucoma is to lower intraocular pressure. Other strategies are clearly needed if we are to reduce risk and improve clinical outcomes regarding the prevention and treatment of glaucoma.

Several studies have demonstrated efficacy of citicoline specifically for glaucoma. This includes cases where there is well-controlled or low intraocular pressure. Improved outcomes with citicoline are likely due to its multiple mechanisms of action.

In 2013 Ottobelli et al published results from their study in *Ophthalmologica* showing that citicoline taken orally significantly slowed the progression of vision loss in patients diagnosed with glaucoma. While this study was not a randomized trial, it did feature 41 patients who had progressing glaucoma for at least 3 years despite well-controlled intraocular pressure.

A few studies have also shown that citicoline in the form of eye drops can be effective at improving parameters associated with glaucoma.

Studies consistently show that citicoline is able to protect RGC from apoptosis. A 2015 review published in the *International Journal of Molecular Science* by Roberti et al concluded “...the available studies are consistent in indicating that the use of citicoline is associated with positive effects on the visual function” of patients with glaucoma.

## Other Clinical Considerations

Citicoline has been studied in patients with amblyopia, which is characterized by poorer vision in one eye due to a miscommunication between the eye and the brain. Amblyopia occurs when there is an interference of vision to 1 eye, which leads to lack of acuity development or the ability to focus clearly. The most common causes of poor vision development in 1 eye are either a misalignment of the eyes, called strabismus, and/or a large difference in refractive error between the eyes in which 1 eye cannot focus on objects as clearly as the unaffected eye. This condition is commonly referred to as “lazy eye.”

Specifically regarding the treatment of amblyopia, Chitu et al wrote in their 2017 review published in the *Romanian Journal of Ophthalmology* that “citicoline may improve the retinal and postretinal visual pathways by stimulating the dopaminergic system. It has been proven that it enhances contrast sensitivity, visual acuity, visual evoked responses and the effect of part-time occlusion.”

A 2008 open label parallel group study published in *Graefe’s Archive for Clinical and Experimental Ophthalmology* by Fresina et al found that 30 days of treatment with citicoline and patching helped children with amblyopia maintain the visual acuity gained by patching, while the children with patching only showed a decrease in visual acuity after patching was discontinued.

After 1 year of treatment, Pawar et al showed the same effect, that citicoline at an oral dose of 250 mg or 500 mg with patching was significantly more effective than patching alone. Their randomized controlled trial was published in the *Indian Journal of Ophthalmology*.

In addition to amblyopia and visual acuity, future research may demonstrate that citicoline can protect overall eye health given its neuroprotective effects. More research is needed to confirm the broad clinical applications of citicoline and eye health beyond glaucoma and amblyopia. While it’s use in primary prevention has not yet been studied, because of the multiple mechanisms of action, it is likely that citicoline can help protect vision in healthy individuals.

## Form and Safety

There are two forms of citicoline: citicoline free-base and citicoline sodium. Citicoline free-base is the form that is available as an ingredient in dietary supplements, foods and beverages in the United States. In Europe it is also available as a dietary supplement.

Citicoline free-base is manufactured and distributed by Kyowa Hakko USA, Inc., and its European sales divisions under the brand name Cognizin. Whereas most companies produce citicoline synthetically, Cognizin is produced using a patented, natural fermentation process. It is vegetarian, allergen-free, kosher, stable and pure. Cognizin achieved GRAS status and is considered safe for food and beverage applications. In Europe Cognizin has also been approved as a Novel Food ingredient in 2014.

Regarding safety, Roberti et al concluded in their 2015 review, “...all the studies mentioned have not reported any adverse effects among patients enrolled confirming that this molecule is safe and can be used for the long-term.”

## Conclusion

Given the research presently available specifically regarding glaucoma, citicoline should be considered an effective adjuvant therapy along with conventional treatment. Patients with a family history of glaucoma or those who are showing early signs will likely benefit from citicoline supplementation.

Nutrients and herbs often work synergistically. Because citicoline has several different key mechanisms of action, it can complement other ingredients designed to support eye health.

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