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Review Article

## A REVIEW OF CHOLINERGIC ACID'S ANTIOXIDANT POTENTIAL IN AGE-RELATED EYE DISORDERS

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Article History	Abstract
Received: 19-07-2024 Revised: 08-08-2024 Accepted: 18-08-2024	Sepsis is a disordered host response to an infection, and one of its hallmarks is organ failure. Mitochondria appear to be a key actor in the chain of events that results in multiple organ failure and potentially death, despite the pathophysiology being complex and little understood. Apart from supplying energy and metabolic intermediates required for immune cell activation and function, mitochondria also impact inflammation and cell death pathways. These two functions of mitochondria influence immunological responses. Crucially, the stability of end organ metabolism and the efficacy of the immune system are both compromised by mitochondrial dysfunction. A hyperinflammatory state and a lack of cellular homeostasis are further consequences of malfunctioning mitochondria, which also contribute to poor clinical outcomes. Hence, strategies to maximize mitochondrial efficiency are necessary since signs of mitochondrial malfunction are evident even in early stages of sepsis. Replacing or repairing damaged mitochondria may therefore aid in the recovery of organ function in sepsis. Toward the conclusion.
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<b>Keywords:</b> ageing, antioxidants, cholinergic acid (CGA), ocular disease, oxidative stress.	

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### Introduction

Age-related eye conditions continue to have an ocular impact on a person's physical, emotional, and overall quality of life. As life expectancy increases and the population ages, age-related eye disorders pose significant financial burdens to society. The precise underlying mechanism of ageing remains unclear to this day. The most widely accepted and well-supported hypothesis of ageing is the free radical theory. According to the idea, oxidative stress is a key ageing mechanism. NADPH oxidase, xanthine oxidase, cytochrome P450 enzymes, and inflammatory responses. This build-up results in cellular damage to proteins, lipids, and DNA, which triggers apoptosis and inflammation in the cells. This can then lead to physical dysfunction and organismal ageing, which can ultimately result in a number of age-related ocular illnesses. Oxidative stress is also increased by ageing itself at the same time. On the one hand, age-related declines in endogenous antioxidants are accompanied by the production of lipid peroxide and radicals (1).

ANTIOXIDATIVE ACTIVITY CGA: The levels of Oxidation-

related Proteins, which include antioxidants and oxidative stress markers (ROS, NO, etc.), are often used indicators of the body's redox state. Exogenous and endogenous antioxidants make up the antioxidant system. The Lipid oxidation level is another significant indicator of the body's oxidation state. Lipid peroxidation can be triggered by ROS, which leads to the build-up of lipid peroxidation products such as malonic aldehyde (MDA) and hydroperoxides. Oxidative stress and antioxidant activity are in a state of dynamic balance under normal circumstances. Cell homeostasis, on the other hand, can become disturbed when the equilibrium between the production of ROS and natural anti-oxidative processes falters. Free radicals cause damage to mitochondrial DNA, and reactive oxygen species (ROS) function as secondary messengers to intensify the inflammatory response, which in turn causes early cell death and speeds up the ageing and disease progression processes in the body. Natural food is another important source of antioxidants, in addition to endogenous cellular antioxidant species. There is a lot of CGA in fruits and vegetables. And plants, making it one among the strongest polyphenols found in food for humans (2).

This mechanism prevents lipid oxidation and helps shield tissues from oxidative damage in general. Numerous investigations have demonstrated CGA's potential as an antioxidant.

A marker of lipid peroxidation, thus inhibiting inflammatory apoptosis and fibrosis and playing a protective Role in liver injuries. Anodyne Veneto tea extracts can ameliorate Hepatocyte deem, reduce the concentration of pro inflammatory Factors, and increase the expression of anti-inflammatory factors, of Which CGA has been identified and reported as the main active component. It can also reduce the production of two key , which inhibit inflammatory apoptosis and fibrosis and play a protective role in liver injuries. The principal active component of Anodynes venetum tea extracts, CGA, has been found and reported to be able to alleviate hepatocyte edema, decrease pro-inflammatory factor concentrations, and raise the expression of anti-inflammatory factors. This allows NRF2 to promote the transcription of several antioxidant genes. Modes: Standard Under Physiological conditions, NRF2 is present at low concentrations in The cytoplasm. Under oxidative stress conditions, NRF2 translocates into the cell nucleus to maintain redox homeostasis.(3)

By regulating the NRF2Pathway, increasing SOD activity and the level of GSH, reducing theAccumulation of MDA, and inhibiting the expression of apoptosisrelated proteins (cleaved caspase 3 and caspase 9), exerting overprotective effect in rats with cerebral ischemia- reperfusionInjury. Another study also demonstrated that CGA, through activating the NRF2 pathway, enhances the expression of the downstream antioxidant effectors HO1, NQO1, and GPX1, amelioratingEndothelial dysfunction in diabetic mice. Additionally, CGA canAlleviate intestinal barrier disruption in weaned piglets by activating The NRF2/HO1 pathway. In rats with cerebral ischemia-reperfusion injury, a study revealed that CGA can inhibit the expression of apoptosis-related proteins (cleaved caspase 3 and caspase 9), increase SOD activity and the level of GSH, decrease the accumulation of MDA, Another study also showed that CGA improves the production of the downstream antioxidant effectors HO1, NQO1, and GPX1 by activating the NRF2 pathway, hence reducing endothelial dysfunction in diabetic mice. Furthermore, through stimulating the NRF2/HO1 pathway, CGA can lessen intestinal barrier disruption in weaned piglets. Furthermore, CGA can lessen intestinal epithelial damage and inflammation. (20)Growing data points to CGA's ability to mitigate oxidative damage, and it has a solid scientific foundation. By lowering oxidative stress and mitigating lipid peroxidation and DNA damage, CGA prevents the death of inflammatory cells.(4)

Depolarizing the mitochondrial membrane and releasing proapoptotic proteins, oxidative stress can cause apoptosis and tissue damage. Furthermore, mitochondria can sustain damage to their DNA. Because of this, mitochondria are important in aging-related processes.The eye is a

sensory organ that is comparatively independent, possessing a sophisticated anatomical structure and unique physiological attributes.Direct exposure tosunlight, air pollution, and other ROS sources occurs in the eye.Through intricate biological processes, it transforms external light impulses into visual information. Illnesses of the surface (such as malfunctioning of the Miamian gland, cornea, conjunctiva, and lacrimal gland), and lens opacity. (18)A substantial body of research indicates that CGA may have a negative regulatory effect on oxidative stress and theinflammatory response. Currently understood to be absorbed, used, and metaboliseddifferently in each individual, CGA is distributed throughout the systemic circulation and metabolised to differing degrees in the gastrointestinal tract, liver, and kidneys.Numerous investigations, both in vitro and in vivo, have shown its wide severaladvantages for the cardiovascular, neurological, gastrointestinal, urinary, and even muscular systems.Numerous fields, including ophthalmology, have examined andapplied itsantioxidantandanti-inflammatoryproperties.(19)

#### Cataract

The most important risk factor for the development of cataracts is becoming older. External and internal factors can interact in a complex way to cause cataracts.Global visual impairment is primarily caused by senile cataract. Forty The fundamental processes of this age-related eye disorder, which includes degenerative changes in lenscells, include the aggregation and modification of lens proteins brought on by lipid peroxidation, cumulative oxidative stress, and DNA damage. The function of lens epithelial cells is responsible for lens transparency. Oxidative stress affects these cells' ability to survive, differentiate, and proliferate in both direct and indirect ways.

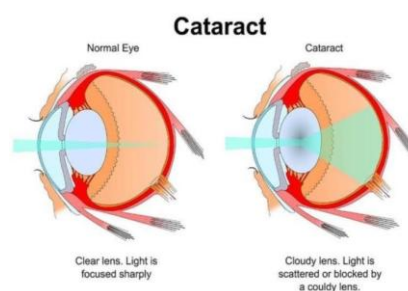
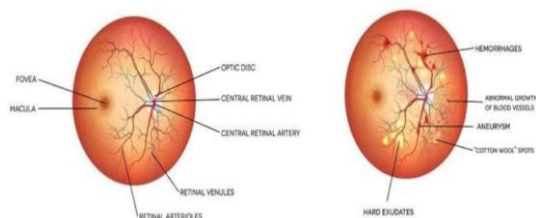


Figure 1 cataract

Retinal degeneration and the thickness of the outer nuclear layer (ONL) in animal models are therefore successfully restrained by signalling, PR inflammatory gene transcription (CXCL8 and IL1B), and decreased apoptosis brought on by blue light.VEGF-mediated retinal neovascularization was validated in a study employing a rodent model of wet AMD.(16)The main substance thought to be in charge of this activity is CGA. According to a different study, CGA can inhibit laser-induced choroidal neovascularization in rat models, suggesting that it could be helpful as an inhibitor for endovascular AMD treatment or prevention.(17) When considered collectively, these



findings suggest that CGA may be a viable option for treating AMD. It is possible to produce the therapeutic effect by reducing retinal neoangiogenesis, attenuating inflammatory cell death, and preventing the production of lipofuscin. (5)

### Diabetic retinopathy (DR)

Figure 2 Diabetic retinopathy.

Insulin resistance can be accelerated and pancreatic islet  $\beta$ -cell death or damage can result from oxidative stress and inflammation. Chronic exposure to hyperglycemia can also result in mild inflammation, raise ROS generation, upset the equilibrium of oxidation-reduction, and induce diabetes. Complexities. (15) The retina becomes more vulnerable to oxidative stress as we age due to mitochondrial malfunction and Müller cell injury, which increases the occurrence of DR in elderly people. RI is a common consequence of diabetes that is characterized by progressive optic nerve injury and retinal microvascular degeneration, which can result in an irreversible loss of visual ability. In order to prevent and treat the complications associated with diabetes, CGA has been shown to either postpone or prevent the onset of diabetes itself. Research indicates that CGA can lessen insulin resistance and increase insulin sensitivity. (6)

### Dry eye

The ageing process can lead to acinus atrophy of lacrimal and maiming glands and inflammatory cell infiltration. Furthermore, aging can also lead to corneal and conjunctival degeneration, thereby Disrupting the integrity of the tear film. These changes make the Ocular surface microenvironment more irritable, with increases in A series of oxidative stress markers, such as 8-OHdG, nitrotyrosine, 4-HNE and lipofuscin-like inclusions. The data showed that The accumulation of lipofuscin-like Material in lacrimal acini and Corneal epithelial metaplasia are higher among aged rats, accompanied by a decrease in the level of the antioxidant marker vitamin. (7)

One of the main risk factors for dry eye is ageing. Acara atrophy of the mamboing and lacrimal glands, as well as infiltration of inflammatory cells, might result from ageing. Moreover, ageing can cause corneal and conjunctival degradation, which might compromise the tear film's integrity. An rise in a number of oxidative stress indicators, including 8-OHdG, nitrotyrosine, 4-HNE, and lipofuscin-like inclusions, results in an irritable ocular surface microenvironment. The results demonstrated that elderly rats had increased levels of lipofuscin-like material deposition in the lacrimal acini and corneal epithelial metaplasia, along with decreased levels of the antioxidant marker vitamin E. (13,14) When there is desiccating stress, more oxidative stress is created. One potential strategic approach to the prevention and treatment of dry eye disease is to examine the cellular redox balance on the ocular surface. An investigation on a rat model of corneal

abrasion exposed to urban particulate matter found increased levels of oxidative stress, inflammation, and apoptosis. (8)

### CURRENT AND EMERGING CGA DELIVERY METHODS:

Researchers have been investigating ways to optimize the administration of CGA, including liposomal, micelle, and nanoparticle delivery, in recent years. Due to its superior encapsulating ability, biocompatibility, and biosafety, liposomes are frequently used to increase CGA's stability in vivo and extend its Blood circulation duration, and hence lower the frequency of dosage. Furthermore additionally, self+micro emulsifying drug delivery systems, or SMEDDS, Demonstrated to be highly effective in a variety of CGA delivery scenarios. Medication penetration of intestinal epithelial cells and support Drug build-up via the lymphatic system in the mesenteric lymph nodes Transportation route.

Long wave UV radiation. Furthermore, a lot of research has looked into the possible applications of nanocarriers Bioavailability as well. In general, scientists have long been interested in improving CG Abioavailability (9, 10,11,12)

### Conclusion

Continued improvement in understanding the underlying genetic, Cellular and molecular pathways of mitochondrial dysfunction, as well As the interplay between ageing, disease-specific genes and oxidative Stress will help uncover viable therapeutic targets for glaucoma. In particular, restoring the feedback systems maybe An important holistic approach. To this end therapeutic strategies Against oxidative stress in glaucoma are currently under active investigation, included identification of promising sustainable antioxidant Compounds from native fruits, herbs and spices and complementary nanocarriers to delivery enough to the back Of the eye. The reviewed dietary plant natural products (DPNPs) in this study have demonstrated strong preventive and therapeutic effects on age-related eye diseases such as age-related macular degeneration (AMD), cataract, diabetic retinopathy and glaucoma in both animal and human model experiments. The positive effects observed in DPNPs are due to their antioxidant, anti-inflammatory, and anti-angiogenic properties as well as their capacity to improve the antioxidant defence systems.

### Author contributions

All authors are contributed equally.

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### Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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