*Review*

**Use of nutraceuticals in the management of cataracts**

Dr+Vet by Böthmen Pharma

## Introduction and Objectives

The lens is biconvex, lenticular, flexible and avascular, and his main function is to focus on objects at different distances correctly.

The structures that make up the lens are:

1. The capsule, which completely surrounds it.
2. The anterior epithelium, which is located under the anterior capsule.
3. The fibers of the lens (cortical and nuclear). They divide it into a surrounding crust and a central core. These fibers are formed throughout life, constituting layers that form from the outside to the inside.

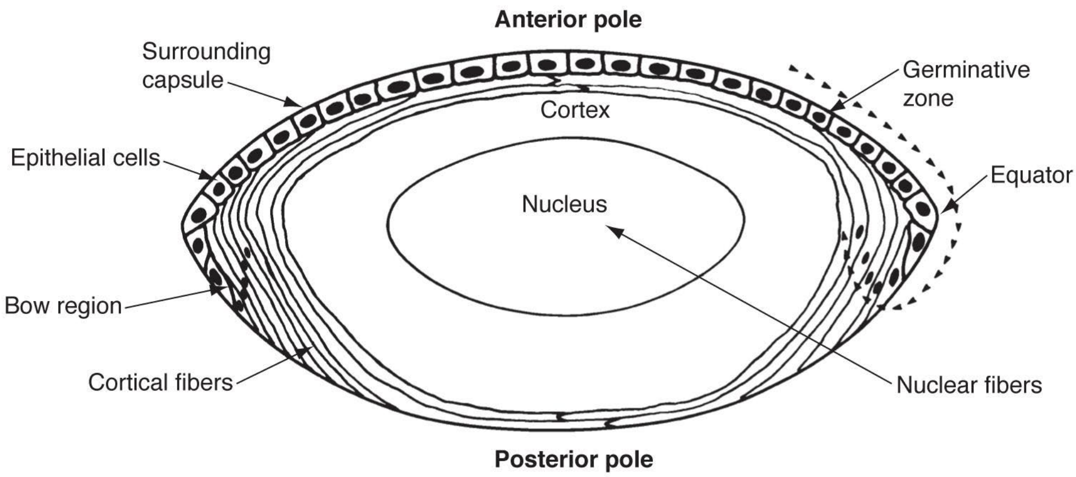


**Figure 1.** Structure of the lens

The avascular nature of the lens means that its metabolic needs depends on the substances that diffuse from the aqueous humor. Glucose is the main source of energy for the lens (1,2).

Knowing that cataract is a chronic progressive disease and that the only curative solution consists of surgery, at Dr+Vet we want to offer nutritional support to animals that may suffer or already suffer from this disease as a way of trying to delay its appearance or slow down its evolution through diet. In this *review* we want to summarize a series of studies and articles on which we have based the design of our product Occulus+.

## Geriatric cataract

Cataract is a clouding of the lens that causes a decrease in vision. Aging is its main cause, but also obesity, diabetes and diet.

Inflammation, oxidation, osmotic balance, and protein metabolism of the lens are important factors in cataract formation (3).

Since diet modulates these processes, the relationship between specific foods or dietary components and cataract development has been prospectively evaluated (3–5).

Specifically, cataracts are associated with a loss of low molecular weight (soluble) proteins, an increase in hydrolytic and proteolytic enzymatic activity, as well as a higher proportion of the water content in the lens (1,6). The consequence of all this is the breakage of the lens fibers, cell death and the formation of cracks (1,2).

As the lens ages, it reduces its ability to neutralize free radicals and minimize oxidative damage, as well as the effectiveness of protective enzymes such as superoxide dismutase (7). The levels of components with antioxidant capacity such as glutathione or ascorbic acid also decrease with age. Oxygen free radicals also increase due to exposure to ultraviolet light, due to the formation of cholesterol oxide derivatives and mitochondrial dysfunction (8).

The accumulation of reactive oxygen species (ROS) causes lipid peroxidation, protein denaturation and cross-linking that aggregate within the lens and lead to cataract formation (7).

**Diabetic cataract**

The development of lens opacification is a major problem in diabetic dogs (9). The opacity appears rapidly as glucose in the lens is metabolized to sorbitol, the sugar alcohol of glucose (10). Normal lenticular metabolism of glucose to carbon dioxide and water occurs primarily through anaerobic metabolism, due to the avascular nature of the lens and its widespread lack of mitochondria (only in the lens epithelium). The enzyme hexokinase metabolizes glucose into glucose-6-phosphate, but when this enzyme is saturated, aldose reductase is activated, converting glucose into sorbitol, with a higher osmotic potential than glucose. This osmotic gradient attracts water to the lens and is a cause of cataract development. (11).

**Alpha lipoic acid**

Alpha lipoic acid is a potent antioxidant and aldose reductase inhibitor. Alpha lipoic acid also regenerates glutathione, coenzyme q10 and vitamins C and E to their reduced forms, acting as an inhibitor of lipid oxidation (12). Topical administration of an aldose reductase inhibitor has been shown to slow the onset of cataract in diabetic dogs (13,14). Similar effects on the lens have been observed with the oral administration of alpha lipoic acid together with other antioxidants in dogs, delaying the appearance of cataracts compared to the placebo group, even showing some improvement in dogs with already developed cataracts (15). Alpha lipoic acid has also shown benefits in studies in mice with induced diabetes, showing protection of retinal ganglion cells (16).

Another preliminary study in diabetic dogs found that those taking an oral alpha lipoic acid supplement took an average of 80 days longer to develop a cataract than the placebo group (over the course of a year). Those dogs who did not develop cataract continue taking the product (17).

**Carotenoids - Lutein and Zeaxanthin**

Carotenoids are fat-soluble plant pigments found in some fruits and vegetables. The carotenoid group substances act as antioxidants. They contain several double bonds, which react with reactive oxygen species (ROS) to scavenge radicals (18).

Lutein is a xanthophyll type of carotenoid. Lutein is not synthesized in mammals and must be obtained from the diet. It is absorbed from the intestinal epithelium into the blood, and circulates systemically to reach the liver, lung, and the eye. The administration of oral supplements with lutein and zeaxanthin improves serum concentration of those products (19).

Some observational studies suggest that the carotenoids lutein and zeaxanthin may play a role in preventing cataracts. These two pigments are the only ones present in the human lens (20). They have the ability to filter and absorb potentially harmful short wavelength light and therefore reduce oxidative stress (21).

In vitro studies with human lens epithelial cells incubated with lutein and zeaxanthin before exposure to hydrogen peroxide or ultraviolet-B light radiation show that carotenoids protect lens cells from protein oxidation, lipids and DNA damage, and also results in increased glutathione levels in response to oxidative stress (22,23).

Some clinical studies have observed that high dietary intake of lutein/zeaxanthin protects against the development and progression of nuclear cataract (3,24,25). On the other hand, other studies did not find a relationship between carotenoid intake and cataracts, such as the AREDS2 study (7).

**Minerals (Zinc)**

Zinc is a trace element that influences cellular metabolism through a variety of mechanisms and appears to play an important role in maintaining normal ocular function. The eye has an unusually high zinc content, with the highest amount of zinc concentrated in the retina. Zinc exists in the other ocular tissues, in the following (descending) order of content: the ciliary body, iris, optic nerve, sclera, cornea, and the lens (26).

Zinc has an antioxidant effect on tissues (27). Zinc deficiency has been related to aging and geriatric diseases that cause an increase in the copper/zinc ratio and systemic oxidative stress in general. (27).

Diabetes and zinc are related: diabetes disrupts zinc homeostasis and zinc deficiency increases diabetes complications. Zinc supplementation helps reduce oxidative stress caused by diabetes and may help reduce hyperglycemia (28). Excessive zinc supplementation can cause a copper deficiency due to the interaction/regulation mechanism between these two elements. (27).

In in vivo studies with mice with induced diabetic cataract, it was observed that zinc supplementation helped preventing lens thickening and reduce reactive oxygen species in the lens. Those animals with zinc supplementation had reduced activity of the enzymes aldose reductase and sorbitol dehydrogenase and accumulated 25% less sorbitol (28).

**Minerals (Calcium)**

Calcium is an important component of the aqueous humor, hypocalcemia is a predisposing factor for cataract formation. Vitamin D alters calcium metabolism with mechanisms related to parathyroid hormone. From this interaction it is concluded that low levels of vitamin D contribute to lens degeneration (29).

**Vitamins A, C and E**

The beneficial properties of multivitamin complexes have been studied, demonstrating the beneficial effects in reducing the risk of developing nuclear and cortical cataract, although not the posterior capsular cataract (29).

Vitamin C, also known as L-ascorbic acid, is a water-soluble nutrient known to have antioxidant properties (30).

Multivitamin complexes also slow the progression of cataracts once they appear (3). Low levels of vitamins A, C and E may predispose to cataract formation (29).

## Vitamins D3, K

Vitamin K has anti-inflammatory and antioxidant properties and is related to glucose and insulin metabolism (5).

In observational studies, a high intake of vitamin K1 has been correlated with a reduced risk of developing cataracts and subsequent surgery in humans. It has also been associated with lower circulating blood glucose levels and a lower risk of type 2 diabetes (5).

Vitamin D is a steroid prohormone, present in the body in the form D2 and D3. It is an antioxidant vitamin and helps reduce oxidative stress. It also has anti-inflammatory properties (inhibiting release of proinflammatory cytokines and increasing release of anti-inflammatory cytokines) and prevents excessive stimulation of cytotoxic T cells (31). Vitamin D levels in patients with cataracts are usually low (29,31). It has been shown that deficient levels of vitamin D cause cataracts in children and, together with observational studies in older adults, it has been related to senile cataracts (31).

## Vitamins B (B1, B2, B3, B6, B7, B9, B12)

In humans, it has been observed that oral intake of vitamins B2, B3, B6 and B12 reduces the development of nuclear and cortical opacities in the lens (3,7).

B vitamins can help maintain the cellular response to oxidative stress by acting as cofactors in the enzymatic activation of antioxidants. The role of vitamins B6 and B12 in preventing oxidative damage can be attributed to their role in the metabolic pathway that eliminates homocysteine, in which B12 and B6 act as enzymatic cofactors (7).

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Riboflavin (B2) and niacin (B3), once converted to their biologically active forms as flavin adenine dinucleotide (FAD) and nicotinamide adenine dinucleotide phosphate (NADPH), contribute to the reduction of glutathione by acting as a cofactor and reductant, to the enzyme glutathione reductase (32).

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A study in human medicine in a malnourished population comparing a placebo group with a group supplemented with B vitamins showed that in the group with vitamin supplements there was a reduction in the appearance and progression of nuclear opacities of the lens (33).

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