OXIDATIVE STRESS AND OPTIXCARE® EYE HEALTH

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Oxidative stress is a major area of research in aging and disease. The role of oxygen in both health and disease was first described by Dr. Denham Harmon in his "free radical" or oxidative damage theory of aging in 1955. Reactive oxygen species (ROS) are a by-product of normal cellular metabolism. Cells generate energy by reducing O_2 to H_2O. During this mitochondrial-mediated process small amounts of partially reduced reactive oxygen are produced. These free radicals or ROS may cause cell injury. Oxidative stress occurs because of an imbalance between the generation of ROS and ROS scavenging activity. This is not an all-or-none interaction because physiological levels of ROS are needed for cell signaling and regulation. The Fenton reaction is also a key player in the generation of damaging free radicals. This reaction occurs when free transition metals such as iron or copper interact with superoxide and hydrogen peroxide radicals to generate highly reactive hydroxyl radicals for which no natural antioxidant defenses are present. Oxidative stress and oxidative damage have been linked to many systemicand age related diseases, including ocular lesions. All tissues of the eye are susceptible to oxidative stress leading to impaired function.

The ocular surface is the most exposed mucosal surface of the body. "Dry eye" may develop associated with abnormalities of the outer lipid layer, the middle aqueous layer, and the inner mucin layer of the tear film. Oxidative stress may affect the Meibomian glands, lacrimal glands, and goblet cells, respectively contributing to the development of keratoconjunctivitis sicca (KCS). Keratitis, from chemical burn injury, was found to be associated with oxidative stress, showing increases in levels of IL-6, MMP-9, TGF-β1, and macrophage inhibitory factor. Anti-oxidants and immunosuppressive agents controlled inflammation and PBMC proliferation, however the effect was not uniform, suggesting different drugs may be needed at different stages of inflammation and healing.Uchino et. al. investigated mice with a deficient mitochondrial electron transport chain leading to excess O_2-. This produced lacrimal gland dysfunction resulting in "dry eye" disease. The increase in O- was associated with inflammation and fibrosis around the lacrimal gland.The use of Optixcare Eye Health has maintained tear volume in a scopolamine model of "dry eye" in rats. In clinical practice, it has also been effective in treating qualitative "dry eye", as well as quantitative KCS.

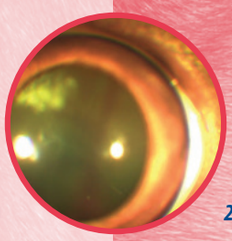
It is widely accepted that oxidative stress is a significant factor in cataract formation in both experimental animal models and in cultured lens systems.

Studies have shown that the concentration of proteins damaged by oxidative processes rises with age in the human lens and is significantly higher in cataractous compared with normal transparent lenses. Cataract formation is associated with the rapid reduction of reduced glutathione levels in the human lens. The veterinary literature on antioxidants also indicates that cataractous lenses have decreased levels of reduced glutathione than normal lenses. Moreover, McGahan's laboratory has reported that cataractous dog lenses have increased levels of free ironthat can participate in the Fenton reaction. Light-induced protein oxidation as well as photoperoxidation of lens lipidscan be prevented by antioxidants. Although diabetic cataracts are induced by osmotic stress associated with aldose reductase activity, oxidative stress is induced secondary to osmotic stress and cataract formation can be delayed by appropriate antioxidants. In a rat model of diabetic cataract formation Optixcare Eye Health delayed the development of cataract. In use in clinical practice, similar effects on stabilizing/preventing cataract have been noted in nondiabetic dogs as illustrated below.

A positive effect on oxidative stress with the use of anti-oxidants was also evaluated in glaucoma. Park et. al. showed improvement following anti-oxidant therapy in a senescent trabecular meshwork cell model. Moreno et. al. demonstrated aberrations in anti-oxidant enzymes, e.g., retinal superoxide dismutase and catalase in a rat model of glaucoma. An increase in retinal lipid peroxidation and a decrease in retinal melatoninwas also noted. Oxidative stress has been described in lamina cribosa cells in glaucomatous human eyes. Recently, Chen et. al. reported increased markers for oxidative stress in acutely glaucomatous canine eyes; glutamate concentrations may be affected by oxidative stress.

A July 2016 publication described the effect of anti-oxidants leading to neuroprotection in a rat model of induced retinal degeneration, mimicking macular degeneration. In 2014 Kador et. al. reported the anti-oxidant effects of Optixcare Eye Health on retinal oxidative stress in a rat model. Markers of oxidative stress were significantly decreased in Optixcare Eye Health treated rats compared to untreated light-exposed rats. It is clear that anti-oxidants play an important role in health and disease. Positive effects in vitro, as well as in vivo have been documented, however the challenge is delivering the anti-oxidants in the correct form and concentration for bioavailability.

Optixcare Eye Health incorporates 4 different anti-oxidant compounds, as well as cetrimide, a preservative that enhances corneal permeation. Based on studies by Kador et. al., Optixcare Eye Health has shown positive effects on "dry eye", preventing cataract progression and reducing retinal oxidative stress. It has been dispensed to many patients in my practice as part of the treatment planfor KCS, cataract formation, and retinal degeneration. One of the cataract patients has been followed for more than one year with positive results from Optixcare Eye Health administered B.I.D. The photographs demonstrate improvement in the cataract on macroscopic evaluation; Optixcare Eye Health is the only medication used. Other veterinary ophthalmologists have noted favorable results utilizing Optixcare Eye Health for prevention of cataract progression, tear staining, ocular surface disease, etc.



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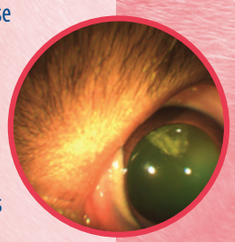

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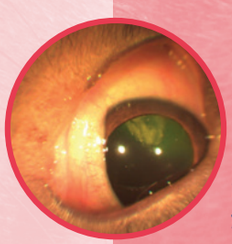

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Dr. Jennifer Hyman received her Bachelor of Arts from Towson University and attended graduate school at the College of William & Mary. After working in transplant rejection and immunological research at the Johns Hopkins University School of Medicine she entered the Veterinary School of the University of Pennsylvania and completed her Veterinary Medical Doctor degree. Prior to joining the residency program at Eye Care for Animals in 2002, Dr. Hyman worked as an emergency clinician at a veterinary referral and emergency center and completed an ophthalmology internship. Dr. Hyman is involved in the residency training program and is active in dinical research on eye diseases.

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