

## For Better or Worse...Natural Supplements and the Eye

Whether an animal is receiving natural supplements for an ophthalmologic condition or for some other problem, herbs and nutraceuticals can affect eye health. This has not escaped the notice of ophthalmologists, as several publications have recently surfaced in the ophthalmology literature, exposing these possibilities and raising concern.<sup>1 2 3 4</sup>

Certain natural products confer clear benefits, with little to no toxic outcome. For example, daily oral administration of 400 mg of L-lysine reduced viral shedding from the conjunctival fornix following rehousing in cats latently infected with feline herpesvirus type-1 (FHV-1).<sup>5 6</sup> Usually, a physiologic stressor such as rehousing would stimulate viral reactivation.<sup>7</sup> The successful control of herpes simplex virus type 1 (HSV-1) in humans with L-lysine had suggested that it might benefit cats afflicted with FHV-1. High intracellular concentrations of lysine and low levels of L-arginine inhibit herpes simplex virus growth in tissue culture.<sup>8 9</sup> However, the sensitivity of cats to L-arginine deficiency required assessment of the effectiveness of L-lysine supplementation alone, i.e., *sans* concurrent L-arginine restriction. L-lysine poses few safety concerns. Two potential contraindications include renal and hepatic disease in which patients may have difficulty eliminating the large amounts of nitrogen generated from L-lysine metabolism.<sup>10</sup> Potential drug interactions include 1) increased absorption and decreased elimination of calcium when the two compounds are co-administered and 2) enhanced toxicity of aminoglycoside medications if given along with large amounts of L-lysine.

Animals may benefit from certain other natural approaches, though these have mainly been evaluated in humans. Long-term supplementation with antioxidants

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<sup>1</sup> Fraunfelder FW. Ocular side effects associated with dietary supplements and herbal medicines. *Drugs of Today*. 2005;41(8):537-545.

<sup>2</sup> West AL, Oren GA, and Moroi SE. Evidence for the use of nutritional supplements and herbal medicines in common eye diseases. *American Journal of Ophthalmology*. 2006;141(1):157-166.

<sup>3</sup> Bartlett H and Eperjesi F. Possible contraindications and adverse reactions associated with the use of ocular nutritional supplements. *Ophthal Physiol Opt*. 2005;25:179-194.

<sup>4</sup> Schwartz SG and Chavis PS. Dietary supplements and the ophthalmologist. *Comp Ophthalmol Update*. 2005;6(3):153-159.

<sup>5</sup> Maggs DJ, Collins BK, Thorne JG, and Nasisse MP. Effects of L-lysine and L-arginine on in vitro replication of feline herpesvirus type-1. *AJVR*. 2000;61(12):1474-1478.

<sup>6</sup> Maggs DJ, Nasisse MP, and Kass PH. Efficacy of oral supplementation with L-lysine in cats latently infected with feline herpesvirus. *AJVR*. 2003;64(1):37-42,

<sup>7</sup> Maggs DJ, Nasisse MP, and Kass PH. Efficacy of oral supplementation with L-lysine in cats latently infected with feline herpesvirus. *AJVR*. 2003;64(1):37-42,

<sup>8</sup> Griffith RS, DeLong DC, and Nelson JD. Relation of arginine-lysine antagonism to herpes simplex growth in tissue culture. *Chemotherapy*. 1981;27:209-213.

<sup>9</sup> Elish D, Singh F, and Weinberg JM. Therapeutic options for herpes labialis: experimental and natural therapies. *Cutis*. 2005;76:38-40.

<sup>10</sup> Tomblin FA and Lucas KH. Lysine for management of herpes labialis. *Am J Health-Syst Pharm*. 2001;58:298-304.

appears to protect the lens and may improve marginal dry eye conditions.<sup>11 12 13</sup>  
<sup>14 15 16</sup> The antioxidant compounds most noteworthy for supporting eye health include the xanthophyllic carotenoids “zeaxanthin” and “lutein”, another dietary carotenoid called “lycopene”, and vitamin E.

Lutein, as well as its stereoisomer, zeaxanthin, occurs in the lens and in the macula lutea region of the retina. Lutein and zeaxanthin absorb blue light that enters the eye that can lead to light-associated damage of the lens and retina.<sup>17</sup>  
<sup>18</sup> Lutein also scavenges photo-induced reactive oxygen species.<sup>19</sup> Oxidative damage to lens proteins is considered one potential mechanism for cataract development, as lens proteins aggregate when subjected to oxidation.

Dietary sources of lutein and zeaxanthin include, in descending order of content, kale, spinach, romaine lettuce, broccoli, summer squash, Brussels sprouts, peas, and corn.<sup>20</sup> While the overall content in eggs is low, the yolk yields a highly bioavailable source. In supplement form, purified crystalline lutein falls in the “generally recognized as safe” or GRAS category, attesting to its quality and safety.<sup>21</sup>

The carotenoid lycopene may likewise protect against cataract development.<sup>22</sup> Lycopene is responsible for the red color in various fruits and vegetables.

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<sup>11</sup> Jacques PF, Taylor A, Moeller S, Hankinson SE, Rogers G, Rung W, Ludovico J, Willett WC, and Chylack LT. Long-term nutrient intake and 5-year change in nuclear lens opacities. *Arch Ophthalmol.* 2005;123:517-526.

<sup>12</sup> Ayala MN and Soderberg PG. Vitamin E can protect against ultraviolet radiation-induced cataract in albino rats. *Ophthalmic Res.* 2004;36:264-269.

<sup>13</sup> Ferrigno L, Aldigeri R, Rosmini F, Sperduto RD, and Maraini G. Associations between plasma levels of vitamins and cataract in the Italian-American Clinical Trial of Nutritional Supplements and Age-Related Cataract (CTNS): CTNS Report #2. *Ophthalmic Epidemiology.* 2005;12:71-80.

<sup>14</sup> Dorey CK, Granata L, Nichols CR, Cheng KM, and Craft NE. Dietary modulation of lens zeaxanthin in quail. *Experimental Eye Research.* 2005;81:464-477.

<sup>15</sup> Peponis V, Papathanasiou M, Kapranou A, Magkou C, Tyligada A, Melidonis A, Drosos T, and Sitaras NM. Protective role of oral antioxidant supplementation in ocular surface of diabetic patients. *Br J Ophthalmol.* 2002;86:1369-1373.

<sup>16</sup> Blades KJ, Patel S, and Aido KE. Oral antioxidant therapy for marginal dry eye. *European Journal of Clinical Nutrition.* 2001;55:589-597.

<sup>17</sup> Dorey CK, Granata L, Nichols CR, Cheng KM, and Craft NE. Dietary modulation of lens zeaxanthin in quail. *Experimental Eye Research.* 2005;81:464-477.

<sup>18</sup> Krinsky NI and Johnson EJ. Carotenoid actions and their relation to health and disease. *Molecular Aspects of Medicine.* 2005;26:459-516.

<sup>19</sup> Alves-Rodrigues A and Shao A. The science behind lutein. *Toxicology Letters.* 2004;150:57-83.

<sup>20</sup> Alves-Rodrigues A and Shao A. The science behind lutein. *Toxicology Letters.* 2004;150:57-83.

<sup>21</sup> Alves-Rodrigues A and Shao A. The science behind lutein. *Toxicology Letters.* 2004;150:57-83.

<sup>22</sup> Gale CR, Hall NF, Phillips DI, and Martyn CN. Plasma antioxidants vitamins and carotenoids and age-related cataract. *Ophthalmology.* 2001;108:1992-1998. Cited in Ferrigno L, Aldigeri R, Rosmini F, Sperduto RD, and Maraini G. Associations between plasma levels of vitamins and

Primary food sources include tomatoes and tomato products, but watermelon, papaya, pink grapefruit, and guava contain some lycopene. Lycopene is available in supplement form.

The antioxidant vitamins C and E offer additional protection against ultraviolet radiation-induced cataracts. Vitamin E appears to work by increasing glutathione (GSH) levels. GSH plays a major role in lens antioxidation, and research has demonstrated that lenticular levels of GSH rise in rats supplemented with alpha-tocopherol.<sup>23</sup> Treated animals suffered less lens opacification as a consequence to ultraviolet B exposure, compared to untreated animals. Some have postulated that topical (i.e., ophthalmic) administration of alpha-tocopherol may lead to higher lenticular uptake, though this remains to be proven.

As shown above, while certain vitamins and minerals may benefit human patients with age-related macular degeneration, a 2006 review published in the *American Journal of Ophthalmology* found little other convincing evidence in support of herbal or nutritional approaches for eye conditions.<sup>24</sup> Separating the hype from what's helpful can be hard, especially when no compendia exist that specifically document ocular benefits and side effects from herbs and supplements.<sup>25</sup> Bilberry, for example, is commonly thought to improve night vision, but a systematic review of placebo-controlled trials noted a complete absence of rigorous research on patients suffering from impaired night vision due to eye pathology.<sup>26</sup> While bilberry appears to be non-toxic in humans, its safety profile in animals is unknown.

The evidence of harm from various supplements remains largely anecdotal, and the risk of side effects from drugs likely outweighs that of nutritional supplements.<sup>27</sup> Nevertheless, in order to help give clients a broader perspective concerning the potential dangers of opting for alternatives, Table 1 offers a summary of potential negative effects on the eye of various compounds, used either on the eye directly or ingested.

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cataract in the Italian-American Clinical Trial of Nutritional Supplements and Age-Related Cataract (CTNS): CTNS Report #2. *Ophthalmic Epidemiology*. 2005;12:71-80.

<sup>23</sup> Ayala MN and Soderberg PG. Vitamin E can protect against ultraviolet radiation-induced cataract in albino rats. *Ophthalmic Res*. 2004;36:264-269.

<sup>24</sup> West AL, Oren GA, and Moroi SE. Evidence for the use of nutritional supplements and herbal medicines in common eye diseases. *American Journal of Ophthalmology*. 2006;141(1):157-166.

<sup>25</sup> Fraunfelder FW. Ocular side effects from herbal medicines and nutritional supplements. *Am J Ophthalmol*. 2004;138:639-647.

<sup>26</sup> Canter PH and Ernst E. Anthocyanosides of *Vaccinium myrtillus* (Bilberry) for night vision – a systematic review of placebo-controlled trials. *Survey of Ophthalmology*. 2004;49(1):38-50.

<sup>27</sup> Bartlett H and Eperjesi F. Possible contraindications and adverse reactions associated with the use of ocular nutritional supplements. *Ophthal Physiol Opt*. 2005;25:179-194.

**Table 1, Herbs and supplements and their potentially adverse effects on the eye.**<sup>28 29</sup>

Herb or Nutrient	Usage (Ocular or Non-ocular)	Potential Negative Effects that Impact Eye Health
<b>Chamomile</b>	Ocular infection, irritation, epiphora, inflammation, hordeolum	<p>Self-limited IgE-mediated conjunctivitis, possibly including angioedema, can arise when applied topically as a tea.</p> <p>More likely to cause allergic reactions in atopic patients.</p> <p>May inhibit cytochrome enzymes, resulting in increased serum levels of co-administered drugs.</p>
<b>Echinacea</b>	Ocular infections	<p>Self-limited IgE-mediated conjunctivitis with lid edema can arise when applied topically.</p> <p>May cause eye irritation and conjunctivitis when ingested orally.</p> <p>Can inhibit cytochrome enzymes, resulting in increased serum levels of co-administered drugs.</p> <p>Immune stimulation caused by echinacea may counteract actions of corticosteroids or other immunosuppressive agents.</p> <p>Avoid in patients with autoimmune conditions.</p>
<b>Feverfew</b>	Inflammation	<p>May increase risk of bleeding; consider discontinuation prior to elective eye surgery.</p>
<b>Ginkgo</b>	May improve visual field defects in cases of low-tension glaucoma; promotes blood flow; may be neuroprotective	<p>Has been associated with causing retinal hemorrhage, retrobulbar hemorrhage, spontaneous hyphema, and orbital hemorrhage.</p>

<sup>28</sup> Schwartz SG and Chavis PS. Dietary supplements and the ophthalmologist. *Comp Ophthalmol Update*. 2005;6(3):153-159.

<sup>29</sup> Fraunfelder FW. Ocular side effects associated with dietary supplements and herbal medicines. *Drugs of Today*. 2005;41(8):537-545.

	and thereby benefit glaucoma patients. <sup>30</sup>	May increase risk of bleeding; consider discontinuation prior to elective eye surgery.  Effects can be additive with other agents that inhibit platelet function or clotting.
<b>Ginseng</b>	Immune hypofunction  Fatigue	May increase risk of bleeding; consider discontinuation prior to elective eye surgery.
<b>Goldenseal</b>	Ocular infections	Inhibits cytochrome P450 enzymes, resulting in increased effects of medications metabolized by this pathway.
<b>Licorice</b>	Promotes gastric and peptic ulcer healing.  Has been used to treat inflammation, including ocular inflammatory conditions.	Glucocorticoid and noradrenergic effects resulting in vasoconstriction may cause transient visual loss, central retinal vein occlusion or retinal vasospasm.  Usually requires large doses to produce ocular side effects.  May affect potassium levels and in some cases potentiate cardiac glycosides to the point of causing direct retinal toxicity.  Immune stimulation caused by licorice may counteract actions of corticosteroids or other immunosuppressive agents.
<b>Niacin</b>	Diabetes, osteoarthritis	May be associated with visual impairments, cystoid macular edema (from high doses of niacin), dry eye, eyelid edema, and superficial punctuate keratitis.
<b>St. John's Wort</b>	Depression, agitation	Induces cytochrome enzymes, decreasing effects of co-administered medications metabolized by the cytochrome P450 system.

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<sup>30</sup> Schwartz M and Yoles E. Neuroprotection: a new treatment modality for glaucoma? *Current Opinion in Ophthalmology*. 2000;11:107-111.