

**The CRF would like to thank Dr. Katie Bales for her time and work to create this valuable information for our members and those with CHM.*

Supplements

Note: Patients should consult with physician before taking.
Know the Science behind how medications and supplements can interact: <https://www.nccih.nih.gov/health/know-science/how-medications-supplements-interact>

1. Lutein:

What is it/ where is it found? Lutein is a yellow xanthophyll carotenoid found in egg yolks and many colorful fruits and vegetables. It can also be taken in an oral pill form.

Reported risks: None

Side effects: Oral pill is associated with upset stomach, headache, and unusual or unpleasant taste in your mouth.

Scientific studies:

1. Vision-related studies using Lutein in patients have shown benefit in Age-related macular degeneration (AMD) and Choroideremia. In one study, patients with AMD that added more Lutein rich foods to their diet displayed slower progression of the disease:
<https://econtent.hogrefe.com/doi/abs/10.1024/0300-9831/a000525>
2. In a study focused on the effects of Lutein on patients with Choroideremia, taking an oral pill (20mg) at dinner in a six-month study caused augmentation of macular pigment density.
https://ac.els-cdn.com/S0014483501911261/1-s2.0-S0014483501911261-main.pdf?_tid=d8143bb9-1fa1-4f83-bcb2-7d73b06478d1&acdnat=1546538708_b634165dec804d2378d7167e4d600159



2. Zeaxanthin:

What is it/ where is it found? Zeaxanthin is one of the most common carotenoid alcohols found in nature. Synthesized in plants and some microorganisms, it is the pigment that gives [paprika](#) (made from bell peppers), [corn](#), [saffron](#), [wolfberries](#), and many other plants and microbes their characteristic color. The name (pronounced *zee-uh-zan'-thin*) is derived from [Zea mays](#) (common yellow maize corn, in which zeaxanthin provides the primary yellow pigment), plus *xanthos*, the Greek word for "yellow" (see [xanthophyll](#)). Xanthophylls such as zeaxanthin are found in highest quantity in the [leaves](#) of most green [plants](#). Patients can add these zeaxanthin foods to their diet or take a supplement in an oral pill form, averaging 0.25mg per tablet.

Reported risks: None

Side effects: No known side effects.

Scientific studies:

1. <https://www.aoa.org/patients-and-public/caring-for-your-vision/diet-and-nutrition/lutein>,
<https://www.allaboutvision.com/nutrition/lutein.htm>
2. Vision-related studies have been conducted that monitor the effects of using zeaxanthin to treat AMD patients and to determine the effects in a photooxidation animal model of AMD. Additionally, clinical trials have been done in patients with AMD in the AREDS2 study, combining zeaxanthin with lutein omeg-3 fatty acid supplements.
<https://www.ncbi.nlm.nih.gov/pubmed/30506012>
3. Collectively the data from these studies support the use of zeaxanthin to decrease the progression of AMD and support retinal health:
 - a. Photooxidation study:
<https://www.tandfonline.com/doi/abs/10.1080/15569527.2018.1554667?journalCode=icot20>
 - b. Light-induced retinopathy study:

<https://www.ncbi.nlm.nih.gov/pubmed/29958415>

c. AREDS2 study:

<https://www.ncbi.nlm.nih.gov/pubmed/30506012>).

3. Formulation of high-dose antioxidants and zinc supplements: Age Related Eye Disease Study (AREDS):

What is it/ where is it found? Supplemental high-dose antioxidants and zinc supplements taken together daily: vitamin C (500 mg), vitamin E (400 IU), beta-carotene (15 mg), zinc oxide (80 mg), cupric oxide (2 mg) taken to prevent copper deficiency caused by zinc.

Reported risks: ***Increased risk for lung cancer in persons whom currently or previously smoked.

<https://www.nei.nih.gov/research/clinical-trials/age-related-eye-disease-studies-aredsareds2/aredsareds2-frequently-asked-questions>

Side Effects: ***See below

Scientific Studies:

1. Age-related macular degeneration neovascular (NV) AREDS study has been conducted for over a decade and recently had a 10 year follow up report in 2011. This study supports the use of high-dose antioxidants and zinc supplements to reduce the risk of progression to advanced AMD in participants.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3728272/pdf/nihms436398.pdf>

Side effects associated with each supplement:

-vitamin C (500 mg): diarrhea, nausea

-vitamin E (400 IU): headache, dizziness, unusual weakness or tired feeling, diarrhea, stomach cramps

-beta-carotene (15 mg): high doses could turn skin yellow or orange; special precautions: consult with physician before taking if pregnant or breast-feeding, smoking, history of asbestos exposure, angioplasty

[WebMd%3Bhttps://www.webmd.com/vitamins/ai/ingredientmono-999/beta-carotene](https://www.webmd.com/vitamins/ai/ingredientmono-999/beta-carotene)

-zinc oxide (80 mg): diarrhea, nausea, metallic taste, kidney and stomach damage; special precautions: Routine zinc supplementation is not recommended without the advice of a healthcare professional

[Webmed%3Bhttps://www.webmd.com/vitamins/ai/ingredientmono-982/zinc](https://www.webmd.com/vitamins/ai/ingredientmono-982/zinc)

-Copper; cupric oxide (2 mg): Copper is likely safe when taken by mouth in amounts no greater than 10 mg daily; special precautions: Possibly unsafe when taken by mouth in large amounts, adults should consume no more than 10 mg of copper per day. Kidney failure and death can occur with as little as 1 gram of copper sulfate. Symptoms of copper overdose include nausea, vomiting, bloody diarrhea, fever, stomach pain, low blood pressure, anemia and heart problems. Other precautions include pregnancy and breast-feeding, children, hemodialysis, certain hereditary conditions, including idiopathic copper toxicosis and childhood cirrhosis and Wilson's disease.

<https://www.webmd.com/vitamins/ai/ingredientmono-902/copper>

4. Formulation of high-dose antioxidants and zinc supplements: Age Related Eye Disease Study 2 (AREDS2):

What is it/ where is it found? The primary goal of the AREDS2 was to evaluate the efficacy and safety of lutein plus zeaxanthin and/or omega-3 long-chain polyunsaturated acid (LCPUFA) supplementation in reducing the risk of developing advanced AMD. The study also assessed the reduction in zinc and the omission of beta-carotene from original AREDS

formulation. Patients took lutein (10 mg), Zeaxanthin (2 mg), DHA (350 mg), EPA (650 mg) along with vitamin C (500 mg), vitamin E (400 IU), beta-carotene (15 mg/ 0mg), zinc oxide (80 mg/ 25 mg), cupric oxide (2 mg) taken to prevent copper deficiency caused by zinc, multi-vitamin-mineral supplement with recommended dietary allowance (RDA) doses (Centrum). The study found that while omega-3 fatty acids had no effect on the formulation, lutein and zeaxanthin together appeared to be a safe and effective alternative to beta-carotene.

Reported risks: None

Side effects associated with each supplement: ***See below

Scientific Studies:

1. Clinical study:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3485447>

2. NEI press release article:

<https://nei.nih.gov/news/pressreleases/050513>

Side effects associated with each supplement:

-vitamin C (500 mg): diarrhea, nausea.

-vitamin E (400 IU): headache, dizziness, unusual weakness or tired feeling, diarrhea, stomach cramps.

-cupric oxide (2 mg): Copper is likely safe when taken by mouth in amounts no greater than 10 mg daily; special precautions: Possibly unsafe when taken by mouth in large amounts, adults should consume no more than 10 mg of copper per day. Kidney failure and death can occur with as little as 1 gram of copper sulfate. Symptoms of copper overdose include nausea, vomiting, bloody diarrhea, fever, stomach pain, low blood pressure, anemia and heart problems. Other precautions include pregnancy and breast-feeding, children, hemodialysis, certain hereditary conditions, including idiopathic copper toxicosis and childhood cirrhosis and Wilson's disease.

(<https://www.webmd.com/vitamins/ai/ingredientmono-902/copper>)

-Lutein (10mg): Lutein is a type of vitamin called a carotenoid. It is related to beta-carotene and vitamin A. Foods rich in lutein include egg yolks, broccoli, spinach, kale, corn, orange pepper,

kiwi fruit, grapes, orange juice, zucchini, and squash. Lutein is absorbed best when it is taken with a high-fat meal. Many people think of lutein as "the eye vitamin." It is commonly taken by mouth to prevent eye diseases such as an eye disease that leads to vision loss in older adults (age-related macular degeneration or AMD), and cataracts. There is no good scientific evidence to support the use of lutein for other conditions. Many multivitamins contain lutein. They usually provide a relatively small amount, such as 0.25 mg per tablet. (<https://www.webmd.com/vitamins/ai/ingredientmono-754/lutein>)

-Zeaxanthin (2mg): Zeaxanthin is one of the most common carotenoid alcohols found in nature. Synthesized in plants and some micro-organisms, it is the pigment that gives [paprika](#) (made from bell peppers), [corn](#), [saffron](#), [wolfberries](#), and many other plants and microbes their characteristic color. The name (pronounced *zee-uh-zan'-thin*) is derived from [Zea mays](#) (common yellow maize corn, in which zeaxanthin provides the primary yellow pigment), plus *xanthos*, the Greek word for "yellow" (see [xanthophyll](#)). Xanthophylls such as zeaxanthin are found in highest quantity in the [leaves](#) of most green [plants](#) (<https://lpi.oregonstate.edu/mic/dietary-factors/phytochemicals/carotenoids#sources>). Patients can add these zeaxanthin foods to their diet or take a supplement in an oral pill form, averaging 0.25mg per tablet.

(<https://www.aoa.org/patients-and-public/caring-for-your-vision/diet-and-nutrition/lutein>, <https://www.allaboutvision.com/nutrition/lutein.htm>).

-Zinc (80 mg): diarrhea, nausea, metallic taste, kidney and stomach damage; special precautions: Routine zinc supplementation is not recommended without the advice of a healthcare professional.

(Webmed;<https://www.webmd.com/vitamins/ai/ingredientmono-982/zinc>).

Additional resources for AREDS/AREDS2:

<https://www.nei.nih.gov/research/clinical-trials/age-related-eye-disease-studies-aredsareds2/aredsareds2-frequently-asked-questions>

5. Tauroursodeoxycholic Acid (TUDCA):

What is it/ where is it found? Taurine-conjugated derivative tauroursodeoxycholic acid (TUDCA) is a bile salt that is found naturally occurring in the body. When regular bile salts reach the intestines, they can be metabolized by bacteria into ursodeoxycholic acid and then later bound to a taurine molecule to become TUDCA. Clinical trial using the synthetic bile acid, TUDCA, as a treatment for liver cirrhosis used a daily dose of 750 mg in an oral pill form.

<https://link.springer.com/article/10.1007%2Fs11596-013-1095-x>

-Reported risks of TUDCA treatment: Treatment in patients with primary sclerosing cholangitis (PSC) suggests that high doses for long periods of time may be toxic.

<https://www.ncbi.nlm.nih.gov/pubmed/19585548>

Side effects: High doses of TUDCA can cause diarrhea and weight loss (no reference/link added).

Scientific studies: Multiple vision-related studies using TUDCA treatment have been done in animal models with one clinical trial recruiting patients with rhegmatogenous retinal detachment.

Animal studies:

-photoreceptor degeneration: collectively these studies have shown preserved retinal function and structure with TUDCA treatment.

-Pde6brd1/rd1 (rd1)

https://link.springer.com/chapter/10.1007%2F978-3-319-17121-0_57

-Pde6brd10/rd10 (rd10):

<http://www.molvis.org/molvis/v12/a195/>

-Light induced retinal damage (LIRD):

<http://www.molvis.org/molvis/v12/a195/>

-P23H; dominant retinitis pigmentosa (RP):

<https://iovs.arvojournals.org/article.aspx?articleid=2187079>

<https://jneuroinflammation.biomedcentral.com/articles/10.1186/s12974-014-0186-3>

-Leber congenital amaurosis (LCA) model lecithin-retinol acyltransferase (LRAT):

<https://iovs.arvojournals.org/article.aspx?articleid=2127427>

-diabetic retinopathy: collectively these studies have shown decreased numbers of cell death and reduced endoplasmic reticulum stress.

-diabetic STZ rat model:

<https://www.sciencedirect.com/science/article/abs/pii/S0361923013001913>

-type 1 diabetes mouse model: [Fu et al., 2016](#)

J. Fu, M.H. Aung, M. Prunty, A. Hanif, J.H. Boatright, M.T. Pardue Tau ursodeoxycholic Acid Protects Visual Function in a Mouse Model of Type 1 Diabetes. ARVO E-abstracts 4781

- retinal cell culture:

<https://www.clinicalkey.com/-/content/playContent/1-s2.0-S0361923013001913?returnurl=https:%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0361923013001913%3Fshowall=true&referrer=https:%2F%2Fwww.ncbi.nlm.nih.gov%2F&scrollTo=%23hI0000236> and

<https://clinicaltrials.gov/ct2/show/NCT02841306?cond=rhegmatogenous+retinal+detachment&rank=2>

Clinical study

-rhegmatogenous retinal detachment: clinical trial currently recruiting patients; A single dose of ursodeoxycholic acid will be administered orally before surgery at different time-points in 16 subjects. Standard surgery will be performed and ocular samples will be collected during the procedure. Ursodeoxycholic acid treatment will be continued in treated patients during 3 months after surgery. The goal of the study is to see if TUDCA increases the survival of photoreceptor in the detached area and therefore improves patient outcomes.

<https://clinicaltrials.gov/ct2/show/NCT02841306?cond=rhegmatogenous+retinal+detachment&rank=2>

6. Bilberry Extract:

What is it/ where is it found? Bilberry extract has been used in a number of studies to investigate its role in slowing down retinal degeneration. Bilberry (*Vaccinium myrtillus* L.) contains high amounts of polyphenols (anthocyanins, resveratrol and proanthocyanidins) which could provide health benefits (Ogawa et al., 2014). Bilberry is a plant. The dried, ripe fruit and leaves are used to make medicine.

<https://www.webmd.com/vitamins/ai/ingredientmono-202/bilberry>

Reported risks: Bilberry fruit is considered safe when consumed in amounts typically found in foods, or as an extract for 6 months to a year. Bilberry leaves may be unsafe when taken orally (by mouth) in high doses or for long periods of time. Little is known about whether it is safe to use bilberry during pregnancy or while breastfeeding. Bilberry may interact with a cancer drug called erlotinib (Tarceval), anti-diabetes drugs, or medications that slow blood clotting.

<https://www.nccih.nih.gov/health/bilberry>

Side effects: When taken by mouth: The dried, ripe fruit of bilberry is likely safe for most people when eaten in typical food amounts. Bilberry fruit extracts are possibly safe when taken by mouth for medicinal uses for up to one year. Also, a specific combination product (Mirtogenol) containing bilberry and French maritime pine bark (Pycnogenol) has been used safely for up to 6 months. Bilberry leaf is possibly unsafe for most people when taken in high doses or for a long time. Bilberry might affect blood glucose levels. This could interfere with blood sugar control during and after surgery. Stop taking bilberry at least two weeks before a scheduled surgery.

<https://www.webmd.com/vitamins/ai/ingredientmono-202/bilberry>