

Annatto-E™ Synergy

Delta/gamma tocotrienols + black cumin seed oil



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Annatto-E™ Synergy is a unique tocopherols-free, tocotrienols-only product, containing 125 mg tocotrienols along with 1 g black cumin seed oil (*Nigella sativa*) per two softgel serving. Like tocopherols, tocotrienols (T3) have four isomers: alpha, beta, gamma and delta. Research indicates that the two most potent forms of tocotrienols are delta and gamma-T3. This product contains 90% delta and 10% gamma-T3, a makeup unique to annatto and not found in rice bran and palm oils (two of the other richest sources of tocotrienols). Combined tocotrienol and tocopherol concentrates from these oils, referred to as “tocotrienol-rich fractions,” usually contain 30-50% tocopherols; however, the most effective concentrates for reducing oxidative indicators and supporting cardiovascular health in human studies are those with low tocopherols and high tocotrienols. In fact, tocopherols may actively interfere with the beneficial cardiovascular and anti-proliferative properties of tocotrienols.¹⁻⁵

Annatto tocotrienols are tocopherol-free because they are extracted from food grade annatto. Annatto is the most commonly used carotenoid in foods, added to provide a naturally derived orange-yellow color.

Cardiovascular Health⁸⁻¹¹

Cardiovascular health is an area where tocotrienol-rich preparations have been shown to be more effective than tocopherols. Tocotrienols are potent lipophilic antioxidants and have demonstrated hypocholesterolemic effects, believed to result from reduced oxidation of unsaturated lipids in cell membranes and lipoprotein particles. Tocotrienols may reduce foam cell formation by reducing oxidation of LDL particles and reducing the surface expression of cellular adhesion molecules. Tocotrienols may also have a favorable influence on blood lipids by reducing the translation of HMG-CoA reductase mRNA as well as increasing the degradation of the enzyme post-transcriptionally (this enzyme is the rate-limiting step in the cholesterol synthesis pathway).⁶ Delta-T3 has been shown to be the most effective tocotrienol fraction in regard to reducing the expression of adhesion molecules involved in atherogenesis in the endothelium.⁶ Tocotrienols may also aid in the management of hypertension. Animal models have demonstrated improved endothelial nitric oxide synthase (eNOS) activity and reduced systolic blood pressure upon supplementation with gamma-T3.⁷

Neuroprotective Benefits¹²⁻¹⁶

Tocotrienols have been shown to protect neurons through mechanisms involving not only their antioxidant properties, but also through activation of protective signaling molecules. Animal studies demonstrate that tocotrienols are more effective than tocopherols at protecting neurons from glutamate-induced cell death.¹⁵ With mitochondrial dysfunction and oxidative damage increasingly believed to be involved in the pathogenesis of Alzheimer's disease and other forms of neurodegeneration, antioxidant tocotrienols may be beneficial additions to existing therapies. In fact, patients with Alzheimer's disease and mild cognitive impairment typically have significantly lower plasma levels of tocotrienols and tocopherols.¹²⁻¹⁶

Antiproliferative Factors¹⁷⁻²⁴

Tocotrienols, specifically the gamma and delta isomers, have exhibited significant anti-cancer activities demonstrated through multiple mechanisms: enhanced apoptosis, cell cycle arrest, reduced angiogenesis and inhibition of proliferation (both due to reduction in vascular endothelial growth factor and reduced blood supply), enhanced immune function (increased expression of interferon-gamma, IgA and IgG), reduced risk of initial cancer occurrence (possibly resulting from the antioxidant protection of DNA), and reduced inflammation (decrease in NF-κB, IL-1, IL-6, TNF-α, COX-2, 12-LOX), as well as protection of normal tissues from radiation injury by altering endothelial cell function.¹⁷⁻¹⁹ The potential effects of tocotrienols with cancer have been demonstrated in models of breast, prostate, colon, liver, pancreatic, lung, skin and stomach cancer, suggesting they target activity not limited to specific types of tissue.¹⁷⁻²⁴

Supplement Facts

Serving Size 2 softgels

Servings Per Container 30

Amount Per Serving	% Daily Value
Black Cumin Seed Oil (<i>Nigella sativa</i>)(seed)	1 g *
Vitamin E Isomers (as delta and gamma tocotrienols)	125 mg *

*Daily Value not established.

Other Ingredients: Medium chain triglycerides; bovine gelatin, water, glycerine, annatto (natural color) (softgel ingredients).



Black Cumin Seed Oil – synergy with tocotrienols

The seeds of *Nigella sativa*, commonly known as black cumin, have been used in Western Asia for thousands of years as a spice, food preservative, and traditional remedy with efficacy across a wide range of health conditions, including hypertension, diabetes, digestive disorders, pain, diarrhea, and skin disorders.^{25, 26, 40} One of black cumin seed oil's primary active compounds—thymoquinone (TQ)—has shown antioxidant and anti-inflammatory properties, as well as anti-cancer and immuno-modulatory effects (via augmenting T-cell and natural killer cell activity), all of which may act synergistically with tocotrienols. This powerful compound is also a demonstrated hepato- and renal-protective agent.²⁷ In addition to TQ, black cumin seed oil contains carvacrol, a compound also found in oregano and thyme, which has anti-inflammatory, antioxidant, antitumor, immunomodulatory, and antimicrobial properties.²⁹⁻³¹

Animal models of chemically induced liver and kidney damage support the hepato- and nephro-protective effects of TQ. Furthermore, in animals experiencing ischemia/reperfusion, TQ normalizes levels of glutathione and lactate dehydrogenase.²⁷ Other studies support the role of TQ in enhancing the activity of related antioxidant enzymes, including catalase, glutathione peroxidase, glutathione S-transferase and superoxide dismutase.^{32,33}

TQ may also be a useful adjunct for autoimmune, allergic and inflammatory conditions.³² Compared to placebo, supplementation with black cumin seed oil resulted in significant improvement in disease activity in patients with rheumatoid arthritis. Animal models have also shown the anti-inflammatory and analgesic effects of TQ in rheumatoid arthritis by down-regulating pro-inflammatory cytokine expression.^{30,48,49} The combination of TQ's anti-inflammatory effects on mast cells with its role as an antihistamine offers a two-pronged mechanism to help alleviate symptoms of several respiratory disorders, including bronchial asthma and allergic rhinitis.^{34, 35} Isolated TQ and whole black cumin seed oil act as inhibitors of the inflammatory mediators, 5-LO, COX, PGD2, TNF-alpha, IL-1B, IL-6, NF-kB, eosinophils, and leukotrienes.^{34, 47} Animal models have shown the intact oil to have a greater effect on the reduction of inflammatory eicosanoids and reduced lipid peroxidation than TQ alone, suggesting a synergistic effect for compounds in the whole oil aside from isolated TQ.³⁴

Animal models of multiple sclerosis and ulcerative colitis point to TQ as a potential therapeutic aid, likely due to its modulation of T-cell activity, amelioration of oxidative stress and anti-inflammatory activity.^{41,46} The role of TQ in facilitating sufficient levels of antioxidant-replenishing enzymes may be why black cumin seed oil exhibits efficacy across such a wide range of health concerns.

TQ exhibits several functions that support its impressive potential as an anti-cancer agent, and these properties may be even more powerful when combined with tocotrienols, attacking carcinogenesis and proliferation on multiple fronts. Unlike many conventional chemotherapy drugs, TQ has been shown in animal models to be anti-proliferative against certain cancers (breast, lung, colorectal, pancreatic, prostate, and glioma/glioblastoma), while having only a limited influence on healthy cells.⁴³

TQ has shown anti-cancer properties via cell cycle arrest, reduced angiogenesis and metastasis, and activation of genes that regulate apoptosis.⁴⁰ Researchers believe black cumin seed oil's role in inhibiting 5-LOX may be partly responsible for the reduced proliferation and enhanced apoptosis demonstrated in several types of cancer.⁴³

Combining conventional chemotherapy drugs with TQ seems to enhance the efficacy of the conventional treatments, suggesting that black cumin seed oil may be a novel adjunct to more traditional cancer therapies. TQ has been shown to augment the cytotoxic effects of cisplatin, gemcitabine, paclitaxel, and doxorubicin.^{38,39}

In addition, animal models of post-menopausal and diabetes-induced osteoporosis suggest black cumin seed oil may also be beneficial for bone loss. Superoxide radicals play a role in osteoclast activity, so potent antioxidants may be helpful in supporting proper bone turnover.⁴⁴ Compared to controls, ovariectomized rats treated with black cumin seed oil before and after ovariectomy showed favorable changes in markers for bone turnover, including serum calcium levels and alkaline phosphatase, and the inflammatory markers TNF- α and IL-6.⁴⁵

Recommended Use :

- As a dietary supplement, take two softgels per day, or as directed by your health care practitioner.

For a list of references cited in this document, please visit:

http://catalog.designsforhealth.com/assets/itemresources/Annatto_E_Synergy_References.pdf

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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