

Senolytic Synergy™

Cellular Senescence Support*



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Senolytic Synergy™ is uniquely formulated to enhance overall cellular health and to support healthy aging.* This formula contains a synergistic blend of well-researched ingredients that help attenuate cellular aging by selectively supporting the clearance of senescent cells and promoting a healthy inflammatory response.* Each 2-capsule serving provides 200 mg of curcuminoid powder (as Curcumin C3 Complex®), 200 mg of quercetin, and 200 mg of red grape powder (as Vinia®), along with 100 mg of fisetin and 100 mg of Senactiv® — agents with senolytic properties.* Senolytic Synergy™ is designed to help optimize cellular longevity for adults 35 years and older or those who show signs of early aging (progeroid populations) and for those individuals with inflammatory conditions and oxidative damage due to an accumulation of senescent cells.*

Ingredient Highlights

- Senactiv®, a proprietary blend of standardized extracts from the *Panax notoginseng* root and *Rosa canina* L. fruit that promote senescent cell clearance*
- Fisetin, a unique flavonoid that supports senescent cell apoptosis*
- Quercetin is included to support redox balance and healthy aging*
- Curcumin C3 Complex® featuring three highly bioactive forms of curcumin standardized to contain 95% curcuminoids
- Vinia®, a patented red grape powder containing the whole matrix of red grape micronutrients and polyphenols, including resveratrol
- Gluten-free and soy-free
- Non-GMO

Aging and Cellular Senescence

Aging is associated with an increased risk of developing chronic disorders, impaired physical resilience, and mortality. Cellular senescence is an irreversible growth arrest of normal cells with a resistance to apoptosis, and it is one of the hallmarks of aging that is associated with age-related diseases (ARDs).¹ The accumulation of senescent cells (SCs) is induced by a variety of intracellular and extracellular stressors, such as oxidative stress, inflammatory cytokines, bioactive lipids, abnormal cell growth, DNA damage, decreased autophagy, mechanical stress, presence of advanced glycation end products, and limited telomere replication capacity, creating a favorable environment for the onset of an ARD with disease progression.^{2,3} These inducers activate senescence-promoting transcription factor cascades that alter gene expression and epigenetic changes to DNA, and they upregulate tumor suppressor pathways and enforce replicative cell arrest.^{2,4} SCs have various phenotypes, including senescence-associated beta-galactosidase (SA-β-Gal) activity, senescence-associated secretory phenotype, apoptotic cell death resistance, cellular flattening and hypertrophy, nuclear structure alterations, mitochondrial expansion, and the upregulation of cell cycle inhibitors and pro-survival effectors.¹

Senolytic Agents

Senolytics are small molecules that target and selectively induce apoptosis or autophagy of SCs.⁵ Phytocompounds that have been shown to have senolytic and anti-inflammatory properties include quercetin, fisetin, ginsenoside Rg1, resveratrol, and curcumin.^{3,6} Research has demonstrated that SC clearance by these plant compounds may delay ARD and extend health span.³

Benefits*

- Enhances overall cellular health
- Promotes healthy cellular aging
- Supports tissue regeneration
- Helps mitigate age-related decline in cellular division
- Supports apoptosis and autophagy of senescent cells

Supplement Facts

Serving Size 2 capsules
Servings Per Container 30

Amount Per Serving	% Daily Value
Curcuminoid Powder (as Curcumin C3 Complex®) (Curcuma longa)(rhizomes) (containing three curcuminoids: Curcumin, bisdemethoxycurcumin, demethoxycurcumin) [standardized to contain 95% curcuminoids]	200 mg *
Quercetin	200 mg *
Red Grape Powder (Vinia®)(Vitis vinifera)(cells)	200 mg *
Fisetin (Cotinus coggryia)(branch)	100 mg *
Senactiv® Proprietary Blend [standardized extract from Ginseng (Panax notoginseng)(root) and Dog Rose (Rosa canina L.)(fresh fruit)]	100 mg *

*Daily Value not established.

Other Ingredients: Partially hydrolyzed guar gum, ascorbyl palmitate, Quillaja extract, silicon dioxide, vegetable stearate.

Senactiv® is a U.S. patented blend of two highly purified and fractionated extracts from *Panax notoginseng* and *Rosa canina* L. (dog rose fruit). It is the first senolytic compound shown to activate macrophage phagocytosis and clear SCs in exercised human skeletal muscle tissue.⁶ Compared to the placebo group, 5 mg of ginsenoside Rg1 (the *P. ginseng* bioactive in Senactiv®) facilitated SC clearance by decreasing SA-β-Gal (a biomarker of SC) by 63%, by reversing apoptosis, and by enhancing inducible nitric oxide synthase and interleukin-6 messenger RNA expression in human muscle tissue post-aerobic exercise. These findings suggest that Senactiv® may help clear damaged muscle tissue, reduce muscle soreness, and support regeneration of new muscle tissue.⁶ Additionally, in the same study, Rg1 supplementation resulted in marked increases in tumor suppressor p16^{INK4a} protein expression of endothelial progenitor cells in skeletal muscle post-exercise.⁷ P16^{INK4a} is a cellular senescence and oxidative stress-sensitive protein that is only detected in SCs. P16^{INK4a} induces macrophage phagocytosis to clear SCs in muscles and stimulates tissue repair during periods of inflammation.⁷

Fisetin (*Cotinus coggyria*) is a bioactive flavonol found in many fruits and vegetables that has shown anti-inflammatory and chemopreventive potential, and more recently, it has demonstrated senolytic activity, helping to overcome resistance of SCs to apoptosis.^{5,8} Fisetin-induced apoptosis in aged human umbilical vein endothelial cells.⁵ In premature aging mice, fisetin reduced inflammation, oxidative stress, and the proportion of SCs,⁵ whereas in the elderly mice, it was shown to reduce senescence markers in tissues and age-related pathologies and increase median and maximum lifespan.⁹ During anti-tumor treatment, fisetin was shown to inhibit the PI3K/AKT pathway (a pro-survival pathway in SCs) leading to SC death.⁵

Quercetin is a dietary flavonoid recently found to be a senolytic agent that may help promote healthy aging due to its antioxidative properties and its inhibitory effects on the anti-apoptotic PI3K pathway.^{3,5} Oxidative stress increases during the aging process, and SCs produce greater levels of inflammatory cytokines than normal cells. Quercetin was shown to effectively kill senescent human endothelial cells and mouse bone marrow-derived mesenchymal stem cells, likely due to its inhibitory effects on the anti-apoptotic PI3K pathway.³ In human mesenchymal stem cells, quercetin was used as a geroprotective agent against natural and accelerated aging.³

Curcumin (as Curcumin C3 Complex®) is a patented, unique composition of three bioactive, health-promoting curcuminoids: curcumin, bisdemethoxycurcumin, and dimethoxycurcumin. These are the strongest and best-researched constituents of the turmeric root. Curcumin exhibits healthy aging, and antioxidant and anti-inflammatory properties.* It has been reported to extend the lifespan of *C. elegans* and *Drosophila* due to its ability to regulate the expression of genes related to aging.³ The healthy aging mechanism of curcumin may be related to 5'-adenosine monophosphate-activated protein kinase, sirtuin, and PI3K/AKT, nuclear factor κB, and Nrf2 pathways.* Curcumin was shown to induce senescence in various cancer cell lines through its ability to inhibit telomerase activity, increase autophagic response, and induce the p53, p21, and p16 pathways.⁴

Red Grape Powder (as Vinia®) is a complex of red grape cells from the red grape skins, flesh, pulp, and seeds, providing the full spectrum of nutrients and polyphenols found in red grapes and wine, including resveratrol, tannins, quercetin, catechins, and anthocyanins. Polyphenols support the activation of the Nrf2 pathway to promote redox balance and a healthy inflammatory response.¹⁰ Oxidative stress and inflammation are major factors promoting cellular senescence.* Resveratrol has been shown to help prevent ARD in elderly populations and to extend the lifespans of model organisms.⁵ The antioxidant and healthy aging properties of resveratrol are related to its ability to increase sirtuin 1 (SIRT1) activity.⁵ SIRT1 levels are lower in response to oxidative stress from chronic inflammation and also during aging.⁵

Recommended Use: Take 2 capsules per day or as directed by your health-care practitioner.

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

<http://www.designsforhealth.com/techsheet-references/senolytic-synergy-references.pdf>



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