Lutein SAP

Science-based lutein/zeaxanthin combination for optimal eye support

Lutein and zeaxanthin are carotenoid pigments vital for human health.* Structurally, the critical difference between lutein and zeaxanthin is their ionone ring.* The hydroxy group of lutein and zeaxanthin, which are xanthophylls, enables them to cross blood-ocular and blood-brain barriers.* Both lutein and zeaxanthin are predominantly present in the lens and macular region of the eyes.* Lutein and zeaxanthin are potent antioxidants and help eye health, especially in conditions associated with sunlight damage, such as cataracts and age-related macular degeneration.* Lutein and zeaxanthin have been shown to help reduce the risk of developing cataracts and improve macular pigment optical density.*

NFH's **Lutein SAP** provides high-quality non-GMO lutein and zeaxanthin in a synergistic combination for optimal eye health support.*

SUPPLEMENT FACTS

Serving Size: 1 Softgel

	Amount Per Serving	% Daily Value
Vitamin E (as D-*alpha*-tocopherol, (from non-GMO sunflower)	1 mg AT	**
Lutein (from marigold [*Tagetes erecta*] flower)	25 mg	**
Zeaxanthin (from marigold [*Tagetes erecta*] flower)	5 mg	**

**Daily Value not established

Other ingredients: Sunflower oil, bovine gelatin, glycerin, purified water, beeswax, annatto extract, and rosemary extract.

This product is non-GMO.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

Lutein SAP contains 60 softgels per bottle.

DIRECTIONS FOR USE

Adults: Take 1 softgel daily with a meal containing oil/fat, or as directed by your healthcare practitioner.

INDICATIONS

Lutein SAP can help:

- Mitigate age-related macular degeneration and development of cataracts
- Protect eyes from sunlight damage
- Improve macular pigment optical density
- Support cognitive health and promote working memory
- Support cardiovascular health by maintaining healthy blood-pressure levels and enhancing antioxidant status
- Promote respiratory and skin health

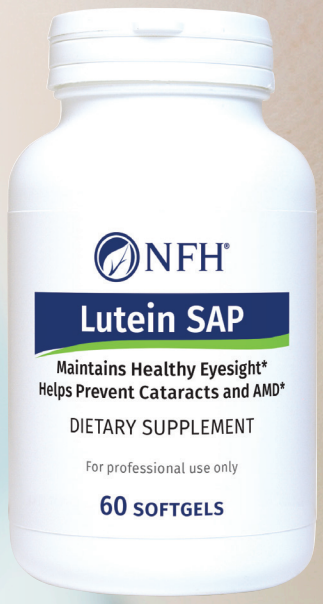
CAUTIONS, AND WARNINGS

Do not use if you are allergic to plants of the Asteraceae/Compositae (e.g., daisy) family.
Colour, size and smell may vary from one lot to another.
Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Lutein SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

*** 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.**



Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH

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INTRODUCTION

Lutein and zeaxanthin are carotenoid pigments vital for human health. Structurally, the critical difference between lutein and zeaxanthin is their ionone ring. While lutein has two types of ionone rings, a β-ionone, and an ε-ionone ring, zeaxanthin has two β-ionone rings.[1] The hydroxy group of lutein and zeaxanthin, which are xanthophylls, enables them to cross blood-ocular and blood-brain barriers.[2] Both lutein and zeaxanthin are predominantly present in the lens and macular region of the eyes.[3] The concentration of lutein and zeaxanthin is 1,000 times higher in the macula's centre than in other human tissues.[4] The concentration of total macular carotenoids is 1 mM, and it includes lutein, zeaxanthin, and *meso*-xanthin in a 1:1:1 ratio.[2] Absorption of lutein and zeaxanthin follows an identical biological process; they undergo passive diffusion and are absorbed in the mucosal layer of the small intestine, and then packaged into chylomicrons for transportation.[5, 6] The metabolic wastes are excreted in the feces, and some polar metabolites are excreted through urine.[7]

PHYSIOLOGICAL ROLES

Lutein and zeaxanthin are powerful antioxidant agents. They quench the singlet oxygen and other reactive oxygen species (ROS) that cause lipid-peroxidation damage.[8] Their antioxidant potential helps lower the risk of DNA damage resulting in malignancy.[9] These xanthophylls act as blue light protectors, thereby preventing retinal damage.[10] Their protective effect on the eyes is also connected to brain health. They can regulate the normal functioning of the brain regions that control visual perception, cognition, decision-making, and motor coordination.[11] Lutein and zeaxanthin also have a cardioprotective effect, as they prevent cholesterol oxidation in the heart's arteries.[12] The anti-inflammatory effect is another pivotal biological function of lutein and zeaxanthin, as they can reduce the expression of inflammatory modulators like C-reactive protein.[13] They also have an anticarcinogenic capacity; an increase in these carotenoid levels has been shown to potentially lower cancer risk.[14]

KEY ROLE OF LUTEIN/ZEAXANTHIN IN EYE HEALTH

Many clinical studies have proved the efficiency of lutein and zeaxanthin in improving eye-related health issues such as age-related macular degeneration, macular pigment ocular density (MPOD), and cataracts.[15,16,17] A clinical trial on patients with early age-related macular degeneration (AMD) showed that supplementation of lutein and zeaxanthin could significantly increase the mean retinal sensitivity (MRS) which corresponds to an increase in retinal sensitivity.[18] Another trial showed that these carotenoids improved visual function by enhancing the macular pigment.[19] A proven increase in red-green (RG) colour discrimination sensitivity was noted after the supplementation of 10 mg of lutein for the first six months and a 10 mg increase in the dosage for the next six months; a similar dosage for zeaxanthin followed.[20] A substantial increase in contrast and glare sensitivity, especially in the mesopic condition, corresponded to the enhancement in the serum lutein levels after receiving 20 mg of lutein supplementation daily for a year.[21] Both carotenoids help reduce discomfort, disability, and temporary blindness due to photopigment bleaching by filtering the scattered light.[22] In patients affected by cataracts, a significant improvement in visual acuity was noticed after supplementation of 45 mg per week of lutein.[23] The Age-Related Eye Disease Study 2 (AREDS2), a clinical trial conducted in the US, showed that lutein and zeaxanthin could help reduce the risk of AMD. The results corroborated evidence that individuals with lower macular carotenoid levels were likely to develop macular disorders.[24]

LUTEIN/ZEAXANTHIN IN MENTAL HEALTH

The human brain is the second organ to accumulate lutein and zeaxanthin. The cognitive health of obese individuals is related to harming mental and cognitive health. The supplementation of these carotenoids can significantly increase cognitive flexibility.[25] A study revealed that individuals with lower MPOD showed poorer performance on the mini–mental-state examination. Also, they had inferior prospective memory. Solving a trail-making task was more challenging for these individuals, who also had slower and more variable reaction times on a choice reaction-time task, respectively.[26] Also, breast-milk lutein concentration helps enrich brain lutein in infants, which can improve recognition memory scores.[27] A systematic review with 1,371 participants revealed a direct correlation between cognitive functions, macular pigment, and the intake of lutein and zeaxanthin (10 mg to 22.33 mg of lutein and 2 mg to 4.7 mg of zeaxanthin per day).[28] Another randomized, double-masked, placebo-controlled study on healthy individuals showed that 10 mg of lutein and 2 mg of zeaxanthin daily could substantially enhance complex attention and reasoning ability.[29] Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) significantly improved in the carotenoid-supplemented individuals. Also, the errors in working-memory tasks were fewer when compared to the control group. This clinical study studied the efficiency of 20 mg of lutein and 4 mg of zeaxanthin per day. It also included 20 mg of *meso*-zeaxanthin, 2 g of fish oil, and 30 mg of vitamin E as the study supplement.[30]

POSITIVE EFFECTS OF LUTEIN/ZEAXANTHIN IN CARDIOVASCULAR HEALTH

Evidence shows that lutein is a potential factor in preventing cardiovascular complications like atherosclerosis. A preclinical study showed that the atherosclerotic lesion reduced size when the plasma lutein levels increased in the mouse model.[31] The presence of serum carotenoids is inversely proportional to early atherosclerosis, assessed by carotid intima-media thickness (IMT).[32] Coronary heart disease can significantly increase the risk of stroke; the effective antioxidants lutein and zeaxanthin can slow down the progressive shortening of telomere length and, thus, can reduce the risk of stroke.[33] A systematic review including 31 longitudinal, 33 cross-sectional, and 3 intervention studies showed a significant association between blood pressure and lutein levels. This study proposed that there can be an association between inflammatory markers and lutein.[34] A randomized, placebo-controlled study on 117 healthy nonsmokers revealed that increased plasma lutein levels could directly impact and reduce the expression of cardiovascular disease–related biomarkers and decrease lipid peroxidation.[35]

LUTEIN/ZEAXANTHIN IN OVERALL RESPIRATORY HEALTH

Oxidative stress is the leading cause of respiratory diseases like chronic obstructive pulmonary disease (COPD). The relationship between lutein and zeaxanthin levels with obstructive lung function was significant. However, the smoking status of the study population significantly affected the lutein and zeaxanthin concentrations.[36] A systematic review comprising 1 randomized, controlled study; 6 cross-sectional studies; 4 prospective studies; and 2 longitudinal studies emphasized that lutein and zeaxanthin supplementation significantly improved respiratory function and reduced mortality by alleviating the oxidative stress on the lungs. The incidence of bronchopulmonary dysplasia (BPD) is also reduced after supplementing these two carotenoids.[37]

LINK BETWEEN LUTEIN/ZEAXANTHIN AND SKIN HEALTH

The antioxidant potential of lutein and zeaxanthin helps in protecting the skin from damage that arises from UV exposure and free radicals. These carotenoids can absorb the blue wavelengths of visible light, thereby protecting the viable skin cells.[38] Preclinical studies on lutein and zeaxanthin showed that their supplementation could significantly diminish the adverse effects of ultraviolet B radiation by reducing increases in the percentage of proliferating cell-nuclear antigens.[39] A clinical intervention showed that daily supplementation of 10 mg of lutein and 2 mg of zeaxanthin promoted overall skin health, especially skin lightening, and firmness.[40]

SAFETY

Health Canada has established a maximum of 20 mg and 2.5 mg per day for lutein and zeaxanthin supplementation, respectively.[41]

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INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc) assessed and have been rated using a 5 star ★ rating classification.

Indication	Suggested Lutein SAP dosage	Supporting evidence and study outcome	Study design	Outcome measures	Safety	Evidence quality rating
Eye Health						
Macular health[1,2,3]	1 softgel/day	Significant improvement in contrast sensitivity (CS) in the supplemented group when compared to the placebo group. Similarly, a significant increase in macular pigment optical density and improvements in visual acuity (VA)	8 randomized, controlled studies (*n* = 1176; 6 to 36 months). 6 mg to 20 mg of lutein and 0.6 mg to 2 mg of zeaxanthin per day (some studies used antioxidant supplements).	Visual acuity (VA), contrast sensitivity (CS), glare recovery time (GRT), and subjective perception of visual quality.	No severe adverse effects were reported.	★★★★★
	1 softgel/day	Significant improvement in red-green (RG) colour discrimination sensitivity when macular pigment optical density (MPOD) levels are higher, and a substantial increase in macular pigment after receiving the supplements	Randomized, placebo-controlled study (*n* = 92; 12 months). 10 mg of lutein per day for the first 6 months and 20 mg of lutein per day for the next 6 months; similarly, 10 mg of zeaxanthin per day for the first 6 months and 20 mg of zeaxanthin per day for the next 6 months.	Chromatic detection thresholds using the Color Assessment and Diagnosis (CAD) test, spatial MPOD profiles, mean RG, and YB thresholds.	No severe adverse effects were reported.	★★★★
	1 softgel/day	Significant increase in plasma lutein and zeaxanthin levels in the supplemented group compared to the placebo group.	Randomized, double-blind, placebo-controlled study (*n* = 120; 6 months). 10 mg of lutein and 2 mg of zeaxanthin per day (+ vitamin C [180 mg], vitamin E [30 mg], zinc [15 mg], copper [< 1 mg], and resveratrol [1 mg], as well as 66 mg of fish oil that included 50% ω–3).	Macular Pigment Optical Density (MPOD) by the Modified Heidelberg Retina Angiograph.	No severe adverse effects were reported.	★★★
Age-related macular degeneration[4,5,6]	1 softgel/day	Significant improvements such as AMD progression prevention and deterioration of visual function were noticed after supplementing a combination of lutein and zeaxanthin with ω–3 LC-PUFA.	18 randomized, controlled studies (*n* = 630; 6 months to 6.3 years). 6 mg to 20 mg of lutein and 0.6 mg to 10 mg of zeaxanthin per day. Some studies additionally supplemented ω–3 long-chain polyunsaturated fatty acids (ω–3 LC-PUFA).	Best-corrected visual acuity (BCVA), MPOD, multifocal electroretinogram (mfERG), CS, and optical coherence tomography (OCT).	No severe adverse effects were reported.	★★★★★
	1 softgel/day	Significant increase in mean retinal sensitivity (MRS) and MPOD after receiving supplements, also N1P1 response densities showed substantial improvement.	Randomized, double-blind, placebo-controlled study (*n* = 112; 2 years). 10 mg or 20 mg of lutein or 10 mg of lutein and 10 mg of zeaxanthin per day.	Retinal sensitivities were measured by multifocal electroretinogram, visual threshold assessment, MRS, and mfERG responses.	No severe adverse effects were reported.	★★★
	1 softgel/day	Significant improvement in BCVA and MPOD, respectively, in the supplementation group that received 20 mg of lutein per day	Randomized, double-blind, placebo-controlled study (*n* = 108; 48 weeks). 10 mg or 20 mg of lutein or 10 mg of lutein and 10 mg of zeaxanthin per day.	MPOD, BCVA, CS, photo recovery time, and Amsler grid testing.	No severe adverse effects were reported.	★★★
MPOD[7,8,9,10,11,12]	1 softgel/day	Few studies observed significant MPOD improvement after 4 months of supplementation; the efficacy of doses lower than 5 mg of lutein was not observed.	34 randomized controlled studies, 6 non-RCTs and 6 single-arm studies (*n* = 3189; 5 weeks to 24 months). < 5 mg to ≥ 20 mg of lutein and 0.53 to 10.6 mg of zeaxanthin per day.	MPOD assessment.	No severe adverse effects were reported.	★★★★
	1 softgel/day	Significant MPOD improvement in all eccentricities, including chromatic contrast and recovery from photostress in the supplemented group compared to the placebo group	Randomized, double-blind, placebo-controlled study (*n* = 115; 1 year). 10 mg of lutein and 2 mg of zeaxanthin per day	MPOD assessment, photostress recovery, chromatic contrast, glare disability.	No severe adverse effects were reported.	★★★

Indication	Suggested Lutein SAP dosage	Supporting evidence	Study design	Outcome measures/ selection criteria for studies	Safety	Evidence quality rating
Eye Health (continued)						
MPOD (continued)	1 softgel/day	The study suggests that the supplement's efficacy was observed to be more significant in women compared to men.	Randomized, double-blind, placebo-controlled study (*n* = 115; 1 year). 10 mg of lutein and 2 mg of zeaxanthin per day. Additionally, 560 mg of docosahexaenoic acid (DHA), 420 mg of *gamma*-linolenic acid (GLA), 80 mg of vitamin C, 10 mg of vitamin E, 2 mg of vitamin B6, 200 µg of vitamin B_9, 1 µg of vitamin B_{12}, and 10 mg of zinc.	Complete ophthalmological exam including Amsler grid testing, BCVA, intra-ocular pressure (IOP) measurement, fundus exams, fundus photographs	No severe adverse effects were reported.	★★
	1 softgel/day	Significant improvement in central MPOD, a substantial increase in contrast and glare sensitivity, especially in the mesopic condition, and serum lutein levels, in the lutein-supplemented group.	Randomized, double-blind, placebo-controlled study (*n*= 120; 1 year). 20 mg of lutein per day.	MPOD, BCVA, contrast, and glare sensitivities; quality of life.	No severe adverse effects were reported.	★★★
	1 softgel/day	Significant improvement in MPOD with less than 28.25 mm of axial length at 6 months in the supplemented group.	Randomized, double-blind, placebo-controlled, single-center study (*n* = 44; 24 months). 20 mg of lutein per day.	MPOD, VA, change in CS, and change in electroretinogram (ERG) measurements.	No severe adverse effects were reported.	★★★
	1 softgel/day	Significant improvement in MPOD, similarly substantial improvement in PSR times and DG thresholds.	Randomized, double-blind, placebo-controlled study (*n* = 59; 12 months). 10 mg to 20 mg of lutein and 2 mg to 4 mg of zeaxanthin (1:1 ratio of zeaxanthin and *meso*-zeaxanthin).	Composite measure of visual performance in glare, MPOD, repeated-exposure photostress recovery (PSR) time, and DG threshold.	No severe adverse effects were reported.	★★★★
Cataract[13]	2 softgels/week	Significant improvement in visual acuity in the lutein-supplemented group; also a substantial improvement in glare sensitivity at low, medium, and high thresholds.	Randomized, double-blind, placebo-controlled study (*n* = 17; 2 years). 45 mg of lutein/week.	Visual acuity and glare sensitivity, biochemical and hematologic indexes.	No severe adverse effects were reported.	★★★
Mental Health						
Cognition[14,15]	1 softgel/day	Significant improvement in cognition and brain activity. Most of the included studies stated the direct correlation between cognitive functions, macular pigment, and the intake of lutein and zeaxanthin.	7 randomized, controlled studies, 11 observational studies (*n* = 1,371; 3 to 12 months). 10 mg to 22.33 mg of lutein and 2 mg to 4.7 mg of zeaxanthin per day.	MPOD, lutein, and zeaxanthin serum concentrations, cognitive function evaluation.	No severe adverse effects were reported.	★★★★★
	1 softgel/day	Significantly higher performance of visual memory tasks by the lutein-supplemented group. Improved MPOD helped in enhanced complex attention and reasoning ability.	Randomized, double-blind, placebo-controlled study (*n* = 51; 1 year). 10 mg of lutein and 2 mg of zeaxanthin per day.	Retinal and serum lutein and zeaxanthin levels, cognitive domain tests, Analysis of the Reliable Change Index.	No severe adverse effects were reported.	★★★
Working memory[16]	2 softgels/week	Significant improvement in Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) in the supplemented group. Errors in working-memory tasks of the supplemented group were significantly lesser than in the control group, and an enhancement was noticed in the cognitive load of the working-memory tasks.	Randomized, double-blind, placebo-controlled study (*n* = 60; 24 months). 20 mg of lutein and 4 mg of zeaxanthin per day (additionally, 20 mg of *meso*-zeaxanthin, 2 g of fish oil, and 30 mg of vitamin E).	Assessment of multiple cognitive domains, including visuospatial abilities, executive function, phonemic fluency, attention, immediate and delayed recall, language and orientation, skin carotenoid score, and tissue carotenoid concentrations.	No severe adverse effects were reported (one reported diarrhea, not related to supplement).	★★★

Indication	Suggested Lutein SAP dosage	Supporting evidence	Study design	Outcome measures/ selection criteria for studies	Safety	Evidence quality rating
Cardiovascular and Metabolic Health						
Lipid peroxidation[17,18]	1 softgel/day	Significant association between blood pressure and lutein was reported in 6 studies, and LDL and lutein concentration are also associated. Cardiometabolic health can significantly improve with lutein consumption.	31 longitudinal, 33 cross-sectional, and 3 intervention studies (*n* = 387,569; 3 months to 15 years, including follow-up). 20 mg of lutein per day (few studies mentioned dietary lutein intake).	Systolic blood pressure, diastolic blood pressure, hypertension, non-fasting and fasting glucose, insulin, HOMA-IR, glycated hemoglobin, BMI, body fat percentage, and waist circumference.	No severe adverse effects were reported.	★★★★★
	1 softgel/day	Significant decline in malondialdehyde and C-reactive protein levels in the group supplemented with 20 mg of lutein. This study suggests a direct relationship between total antioxidant capacity and lutein supplementation.	Randomized, double-blind, placebo-controlled study (*n* = 117; 12 weeks). 10 mg or 20 mg of lutein per day.	Plasma carotenoid concentrations, plasma total antioxidant capacity (TAOC), plasma total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triacylglycerol concentrations; glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) activities; plasma malondialdehyde (MDA) level.	No severe adverse effects were reported.	★★★★
Respiratory Health						
Respiratory health[19]	1 softgel/day	Higher lutein/zeaxanthin intake showed significant improvement in respiratory function and thereby lower respiratory mortality, and it can also help in alleviating oxidative stress in patients affected by COPD.	1 randomized, controlled study; 6 cross-sectional studies; 4 prospective studies; and 2 longitudinal studies (*n* = 16,830; > weeks to 20 years, including follow-up). 140 µg to > 2 mg of lutein and 0.6 µg to 0.6 mg of zeaxanthin per day (microgram dosages were used for infant supplementation).	Bronchopulmonary dysplasia, asthma, respiratory function, chronic obstructive pulmonary disease (COPD), respiratory mortality.	No severe adverse effects were reported.	★★★★
Skin Health						
Skin tone[20]	1 softgel/day	Significant improvement in the overall skin tone was observed in the supplemented group. Similarly, skin lightening and improved skin conditions were also reported.	Randomized, double-blind, placebo-controlled study (*n* = 50; 12 weeks). 10 mg of lutein and 2 mg of zeaxanthin per day (or *meso*-zeaxanthin).	Overall skin tones—such as firmness, dryness, radiance, and texture—and the appearance of pores, facial discoloration, facial lines, and wrinkles.	No severe adverse effects were reported.	★★★

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