LIFE EXTENSION®
The Science of a Healthier Life®
January/February 2023

FEATURE ARTICLES

Deliver *More* RESVERATROL *into* Your Body

PLUS: Page 34

How Fish Oil Protects the Heart

Increase AMPK to Better Manage Body Weight

Most people today consume excess calories.

This results in **mTOR** constantly running at high gear, which is a factor in unwanted **fat storage**.

Studies show that increasing **AMPK** activity turns down excess **mTOR**.[1]

Reduce Cell Fat Storage

Scientific studies show that increasing **AMPK** activity can encourage cells to store less fat and burn it as energy.[2,3]

AMPK Metabolic Activator was formulated based on data showing reduced **belly fat** in response to just one of its ingredients (*Gynostemma pentaphyllum*).[3]

This ***Gynostemma pentaphyllum + hesperidin*** formula is designed to support healthy **AMPK** cellular activation.

Item #02207

30 vegetarian tablets

GLUTEN FREE · 1 DAILY · NON GMO LE CERTIFIED

This supplement should be taken in conjunction with a healthy diet and regular exercise program. Individual results are not guaranteed, and results may vary.

References

1. *Anticancer Agents Med Chem*. 2013 Sep;13(7):967-70.
2. *Nutr J*. 2016;15:6.
3. *Obesity (Silver Spring)*. 2014;22(1):63-71.

This product is available at fine health food stores everywhere.

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Quercetin has demonstrated significant health benefits, but ***higher*** doses are often required to achieve optimal results.

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* Supplier Internal Study. Data on File. 2017

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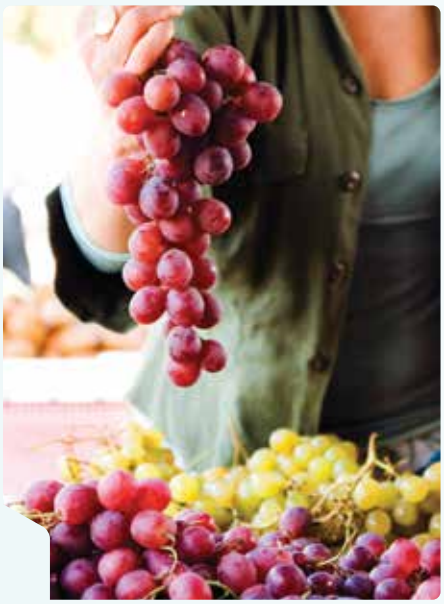

ON THE COVER: PAGE 18

DELIVER MORE RESVERATROL

Obtaining **resveratrol's** full benefits has been challenging.

Combining **resveratrol** with galactomannan *increases* **bioavailability** up to **10 times**.

DEPARTMENTS

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MEDICAL ADVISORY BOARD

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Richard Black, DO, is a dedicated nuclear medicine physician practicing as an independent contractor out of Cleveland, Ohio. Dr. Black is board-certified in internal medicine and nuclear medicine, and is licensed to practice medicine in multiple states throughout the United States.

John Boik, PhD, is the author of two books on cancer therapy, *Cancer and Natural Medicine* (1996) and *Natural Compounds in Cancer Therapy* (2001). He earned his doctorate at the University of Texas Graduate School of Biomedical Sciences with research at the MD Anderson Cancer Center, focusing on screening models to identify promising new anti-cancer drugs. He conducted his postdoctoral training at Stanford University's Department of Statistics.

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Deborah F. Harding, MD, is founder of the Harding Anti-Aging Center. She is double board-certified in internal medicine and sleep disorder medicine. She also earned the Cenegenics certification in age management medicine. She is a faculty member of the University of Central Florida Medical School.

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Peter H. Langsjoen, MD, FACC, is a cardiologist specializing in congestive heart failure, primary and statin-induced diastolic dysfunction, and other heart diseases. A leading authority on coenzyme Q10, Dr. Langsjoen has been involved with its clinical application since 1983. He is a founding member of the executive committee of the International Coenzyme Q10 Association, a fellow of the American College of Cardiology, and a member of numerous other medical associations.

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L. Ray Matthews, MD, FACS, is a professor of surgery and director of Surgical Critical Care at Morehouse School of Medicine in Atlanta, GA, and a trauma and critical care surgeon at Grady Memorial Hospital. He has published widely and is known as one of the top vitamin D experts. Dr. Matthews has spoken before the U.S. Food and Drug Administration several times, presenting a recent update about clinical research on vitamin D.

Ralph W. Moss, PhD, is the author of books such as *Antioxidants Against Cancer*, *Cancer Therapy*, *Questioning Chemotherapy*, and *The Cancer Industry*, as well as the award-winning PBS documentary *The Cancer War*. Dr. Moss has independently evaluated the claims of various cancer treatments and currently directs The Moss Reports, an updated library of detailed reports on more than 200 varieties of cancer diagnoses.

Michael D. Ozner, MD, FACC, FAHA, is a board-certified cardiologist who specializes in cardiovascular disease prevention. He serves as medical director for the Cardiovascular Prevention Institute of South Florida and is a noted national speaker on heart disease prevention. Dr. Ozner is also author of *The Great American Heart Hoax*,*The Complete Mediterranean Diet* and *Heart Attack Proof*. For more information visit www.drozner.com.

Jonathan V. Wright, MD, is medical director of the Tahoma Clinic in Tukwila, WA. He received his MD from the University of Michigan and has taught natural biochemical medical treatments since 1983. Dr. Wright pioneered the use of bioidentical estrogens and DHEA in daily medical practice. He has authored or co-authored 14 books, selling more than 1.5 million copies.

Xiaoxi Wei, PhD, is a chemist, expert in supramolecular assembly and development of synthetic transmembrane nanopores with distinguished selectivity via biomimetic nanoscience. She has expertise in ion channel function and characterization. She founded X-Therma Inc., a company developing a radical new highway towards non-toxic, hyper-effective antifreeze agents to fight unwanted ice formation in regenerative medicine and reduce mechanical icing.

In the News

Grape Powder Could Extend Lifespan by 4-5 Years

In a study the authors called "remarkable," researchers found that giving grape powder to mice reduced the risk of non-alcoholic fatty liver disease and **extended lifespan**.

To see if grape powder could modulate the harmful effects of a high-fat diet, researchers fed mice a typical Western (high-fat) diet. Half then received **5% standardized grape powder** while the other half didn't.

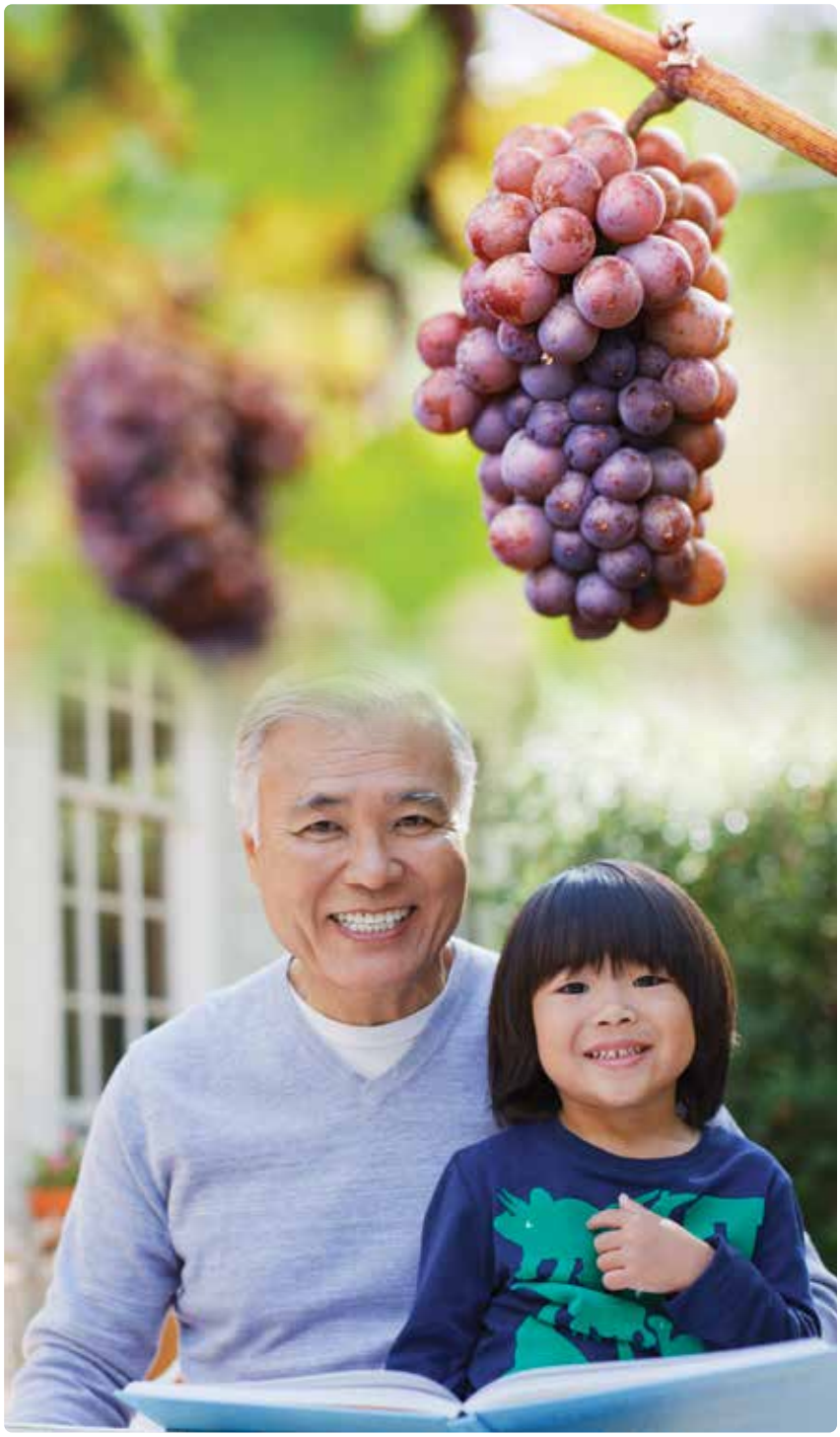
Compared to mice not fed the grape powder, the mice given grape powder saw beneficial increases in antioxidant genes, reductions in fatty liver, and extended lifespans.

The lead author estimated that when translated to humans, the extended lifespan would correspond to an additional **4-5 years** in the life of a human.

The grape powder used in this study was composed of fresh red, green and black grapes that were freeze-dried to retain their **bioactive** compounds.

Editor's Note: The researchers concluded: "These results suggest the potential of dietary grapes to modulate hepatic gene expression, prevent oxidative damage, induce fatty acid metabolism, ameliorate NAFLD (non-alcoholic fatty liver disease), and increase longevity when co-administered with a high-fat diet."

Foods 2022, 11(13), 1984.



Greater Potassium Intake May Lower Blood Pressure in Women with High-Sodium Diets

A study published in the *European Heart Journal* found a link between consuming a greater amount of potassium and lower blood pressure among women with a high intake of sodium.*

The participants were 11,267 men and 13,696 women enrolled in England's EPIC-Norfolk study. Sodium and potassium intake were estimated from urinary levels of these minerals.

Increased potassium intake was associated with declining blood pressure among women with high sodium intake. Each **1 gram** increase in potassium consumption was associated with a **2.4 mmHg** decrease in systolic blood pressure.

Editor's Note: "…in view of various studies showing that women are more sodium-sensitive—i.e., having a larger change in blood pressure in response to changes in sodium consumption—women with high sodium intake might specifically benefit more from an increase in potassium intake," the authors stated.

* *Eur Heart J.* 2022 Aug 7;43(30):2867-2875.

Taurine Supplementation Benefits Diabetes Patients

People with diabetes who received taurine supplements experienced improvements in glucose and other factors, according to the results of a review and meta-analysis of clinical trials, published in *Food Chemistry: Molecular Sciences*.*

Researchers analyzed five controlled trials including 209 participants, that evaluated the effects of taurine on individuals with type I or type II diabetes. Taurine doses ranged from **500 mg** daily to **1,000 mg** three times per day.

Participants who received taurine had lower fasting blood glucose, hemoglobin A1c (HbA1c, a marker of long-term glucose control), and insulin resistance, compared to those given a placebo.

Editor's Note: "Taurine emerges as a new option for the management of patients with diabetes," the scientists asserted.

* *Food Chem (Oxf).* 2022 Jul 30;4:100106.

Vitamin D Deficiency Linked to Breast Cancer

Most women with **breast cancer** were found to be deficient in **vitamin D**, according to the results of a study published in the journal *Progress in Nutrition*.*

Researchers analyzed the vitamin D status of 561 women, average age 55, with non-metastatic breast cancer.

In this group, **81%** of the women were *deficient* in vitamin D, and **11%** had *insufficient* levels of the vitamin.

Median *25-hydroxyvitamin D* blood levels were only **13.91 ng/mL** in this group of Turkish women.

Optimal ranges by U.S. standards are **30-80 ng/mL**. **Life Extension's** minimal target for *25-hydroxyvitamin D* is around **50 ng/mL**.

A significant portion of the world's population where supplementation is uncommon and sun exposure limited have very low blood levels of vitamin D.

Editor's Note: The researchers concluded that vitamin D levels should be measured in breast cancer patients and low levels should be corrected whenever diagnosed.

* Available at: https://www.mattioli1885journals.com/index.php/progressinnutrition/article/view/10428.

Clinical Trial Will Evaluate Form of Vitamin B1 in Alzheimer's Treatment

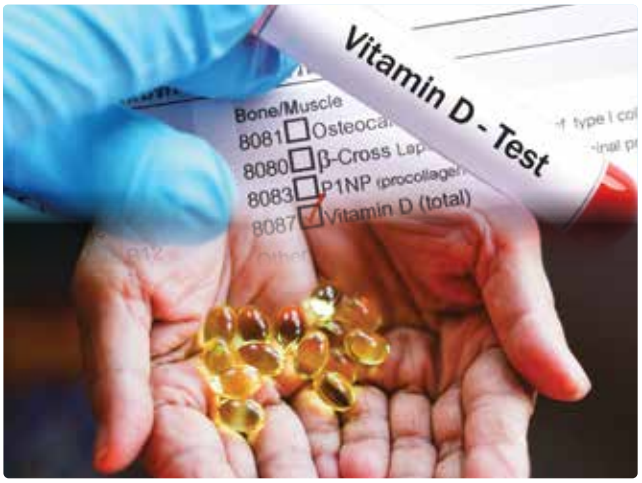
The Alzheimer's Disease Cooperative Study at the University of California San Diego (ADCS), in collaboration with Burke Neurological Institute, and Columbia University Irving Medical Center, plans to evaluate the effect of a high-dose form of thiamin (vitamin B1) known as **benfotiamine** in individuals with Alzheimer's disease, the ADCS announced.*

"The trial addresses tissue deficiency of thiamine-regulated metabolic pathways linked to Alzheimer's," the announcement stated.

Approximately 400 participants with mild Alzheimer's disease or mild cognitive impairment due to the disease will be enrolled at up to 50 U.S. clinical trial sites and will be evaluated during an 18-month period.

Editor's Note: A $45 million grant from the National Institutes of Health and National Institute on Aging is supporting this clinical trial, which is slated to begin in early 2023.

* Available at: https://ucsdnews.ucsd.edu/pressrelease/novel-treatment-approach-to-alzheimers-disease-uses-vitamin-b1-derivative Accessed September 21, 2022.



Vitamin D Supplementation May Help Critically Ill Patients

Findings from a meta-analysis review in *Critical Care* suggest that providing critically ill patients with **vitamin D** supplements may improve some outcomes, including **survival**.*

Researchers identified 16 trials that evaluated the association between vitamin D supplementation and mortality among critically ill individuals. Twelve studies reported intensive care unit (ICU) length of stay, nine reported 28-day mortality, and nine reported length of mechanical ventilation.

Study participants received vitamin D either by mouth, feeding tube, intramuscular injection or intravenously.

Vitamin D supplementation was associated with a **22%** lower risk of overall mortality compared to a placebo or standard care.

Among studies that reported 28-day mortality, vitamin D supplementation was associated with a trend toward a lower risk.

Patients who received vitamin D spent an average of 3.13 days less in the ICU and five fewer days on a ventilator than those who received a placebo.

Editor's Note: In patients admitted to the ICU, significantly reduced serum vitamin D levels "…are frequent and independently associated with higher incidence and severity of sepsis," the authors stated.

* *Crit Care.* 2022 Sep 6;26(1):268.

Less Fatigue with CoQ10

The results of a meta-analysis of clinical trials published in *Frontiers in Pharmacology* confirm an **anti-fatigue** effect in individuals who supplemented with **coenzyme Q10** (CoQ10).*

Researchers identified 13 randomized, controlled trials that compared fatigue scores among a total of 1,126 participants who received CoQ10 or a placebo.

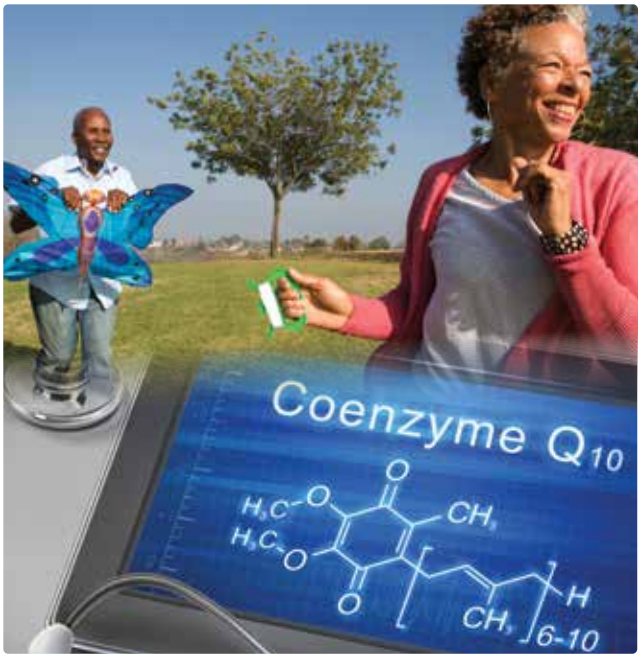
Analysis of the 13 trials showed a consistent, significant effect of CoQ10 in reducing fatigue.

When trials that included healthy participants were analyzed separately from trials that included patients with fatigue-associated diseases, both supplemented populations showed decreases in **fatigue**, however the effects were more significant among the unhealthy participants, who had more severe CoQ10 depletion.

Higher CoQ10 doses and longer duration of supplementation were correlated with greater reduction in **fatigue**.

Editor's Note: While the body makes some CoQ10, the authors remarked that studies have provided evidence that supplementing with CoQ10 does not affect the body's synthesis of the coenzyme.

* *Front Pharmacol.* 2022 Aug 24;13:883251.



Adequate Nutrient Intake Can Help You Live Longer

A study that utilized data from the National Health and Nutrition Education Survey (NHANES) 1999-2010, found an association between adequate intake of specific nutrients and a lower risk of dying during a median follow-up of 9.3 years, the *Journal of Nutrition* reported.*

Nutrient adequacy was calculated as the percentage of the RDA met by the participants according to age and gender.

Compared to participants whose **magnesium** intake was among the lowest one-third, those whose intake was among the top third had a **22%** lower adjusted risk of all-cause mortality, a **35%** lower risk of dying from cardiovascular disease and a **29%** lower risk of cancer death during follow-up.

Top consumers of **vitamin E**, **potassium**, and **fiber** had a **19%**, **18%** and **16%**, respectively, lower risk of premature **mortality**.

Editor's Note: "Americans are underconsuming essential nutrients while overconsuming several nutrients, including sodium, saturated fat, and added sugars," the authors asserted.

* *J Nutr.* 2021 Oct 1;151(10):3214-3222.

Protein Supplementation Benefits Lean Body Mass

A "systematic review of systematic reviews" published in *Sports Medicine* showed that the addition of protein supplementation to resistance training is associated with a greater increase in lean body mass (body mass minus fat mass) in comparison with resistance training alone.*

Researchers selected five systematic reviews with meta-analyses of randomized trials that compared the effects of resistance training alone to resistance training combined with protein and/or amino acid supplementation. The 46 studies included in the meta-analyses involved a total of 2,925 men and women over 50 years of age.

Supplemented groups received **12-40 grams** of protein or **3-10 grams** of amino acids while the control groups received a placebo or no supplementation.

Among the four meta-analyses that evaluated lean body mass, three found a significant increase in association with resistance training plus protein supplementation compared to resistance training without supplementation.

Editor's Note: There was also a significant benefit for protein supplementation combined with training on muscle mass alone.

* *Sports Med*. 2022 Oct;52(10):2511-2522.

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NT2 Collagen™ standardized cartilage Total Collagen	**40 mg** **10 mg**
Boron (calcium fructoborate as patented FruiteX-B® OsteoBoron®)	**1.5 mg**

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$^{\Delta}$ 3-O-acetyl-11-ketoB-boswellic acid.

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Resveratrol in the Prevention of Aging

WILLIAM FALOON

In **2003**, a plant compound called **resveratrol** emerged as the hottest topic in anti-aging medicine.

The sizzling enthusiasm came from a **Harvard** study showing an astounding **70%** increase in the **lifespans** of yeast given **resveratrol**.[1]

Several follow-up studies supported **lifespan** benefits in **resveratrol**-supplemented model organisms.[2]

What got scientists fired up are **mechanisms** behind resveratrol's **age-delaying** effects.

It turned out that **resveratrol** induced some of the favorable **gene expression** changes seen with **calorie restriction**.[1]

This has led to **resveratrol** appearing in thousands of published papers about the multiple disorders that it might protect against.

For example, a PubMed® search for "**resveratrol**" yields **16,000** citations over the past four decades, including 260 **clinical trials** since year 2002.

A review article published in **2021** concluded:

"Resveratrol could be an effective and safe compound for the prevention and treatment of aging and age-related diseases." [3]

We at **Life Extension** funded costly laboratory studies aimed at identifying what dose of **resveratrol** might enable **humans** to live *longer* and healthier lives.

The challenge, however, was finding a way to make resveratrol **bioavailable** to the **human** body.

Resveratrol is rapidly metabolized in the liver, kidneys, and other tissues despite relatively good intestinal absorption.[4,5]

This helps explain the **longevity-enhancing** effects of **resveratrol** found in flies, fish, worms, and yeast, but inconsistent benefits when tested in mammals.[2]

Intensive research has uncovered a way to protect **resveratrol** from rapid metabolic degradation.

It is now possible to better explore the potential of **resveratrol** to combat degenerative disorders and assist in the ***prevention*** *and* ***treatment of aging.***

In **1997**, a paper was published describing the biological effects of **resveratrol** as it relates to the prevention of **cancer** and other illnesses.[6]

This led to intensive investigations, thousands of published papers, resveratrol-focused conferences, and patents on resveratrol analogs.

The public reacted to the media blitz by ingesting **resveratrol** supplements and increasing their consumption of **red wine,** despite there being little resveratrol in red wine (and other foods).

Longevity Impact of Resveratrol

Published studies document the ability of **resveratrol** to **extend lifespans** in laboratory models.

A meta-analysis of 19 published papers indicated that resveratrol acts as a **life-extending** agent.[7] The species studied were yeast, roundworms, mice, fruit flies, and turquoise killifish.

Resveratrol has been shown to induce **autophagy** in **human** cells in test tubes (*in vitro*) and in the bodies of roundworms (*in vivo*).[3]

Autophagy is a cleansing process that promotes the clearance of internal cellular debris.

The induction of **autophagy** by **resveratrol** is thought to be a longevity-enhancing mechanism.

Bees fed with **resveratrol syrup** live longer than controls. [8] Depending on **resveratrol concentration**, mean and maximum lifespan of these bees increased by **33%** to **38%** respectively.

Short-lived **flies** fed with different resveratrol concentrations had mean lifespan extension of **10%** to **29%**, while other models found **resveratrol** also conveyed **neuroprotective** benefits. [2,9,10]

Resveratrol-fed **fish** lived ***longer*** and demonstrated better cognitive ability and locomotor function than the control fish group.[11] The fish fed **resveratrol** showed reduced markers of **senescent cells** and less buildup of a wear-and-tear residue called **lipofuscin**.

In a genetically altered strain of **mice** predisposed to neurodegenerative disease and accelerated aging, oral administration of **resveratrol** increased the median survival of these mice from 32 days to 42 days.[12] Resveratrol additionally helped preserve motor function and protect against degenerative changes in the brain.

Not all studies demonstrate these kinds of elongated lifespans. One study found that **resveratrol** delayed **vascular aging** in **rats** but had no effect on overall survival.[13]

Another study found that in **mice** fed a standard diet, resveratrol did not enhance lifespan.[14] In mice eating a **high-calorie** diet, however, resveratrol reduced the **risk of death** by **31%** and improved **insulin sensitivity**, suggesting it helps protect against diet-related metabolic diseases.[15]

Effect on Neurodegenerative Disorders

The aging brain is afflicted with neuroinflammation, autophagy defects, mitochondrial dysfunction, cell loss, and elevated oxidative status. This all contributes to memory loss and motor impairments.[16,17]

A large body of data shows how **resveratrol** protects against **neurodegenerative** disorders in rodents.[3]

Resveratrol-supplemented animals demonstrate improved **memory** performance, enhanced secretion of **neurotransmitters**, and increased production of new brain cells with beneficial decreases in **inflammation** and **oxidative stress**.[18-21]

A **human** trial using **200 mg** a day of **resveratrol** showed enhanced **memory performance** accompanied with improved glucose metabolism and hippocampal functional connectivity.[22]

Effect on Cardiovascular Disorders

Aging is associated with **endothelial dysfunction** that leads to arterial blockages and increased risks of cardiovascular diseases. [23]

In animal models, resveratrol was shown to exert a cardioprotective effect mainly through enhancing the production of endothelial **nitric oxide**, improving blood vessel **dilation**, reducing **blood pressure**, and ameliorating **oxidative stress**.[24-26]

Effect on other Disorders

Research findings show how resveratrol may help protect against **cancer, osteoporosis**, **sarcopenia** and possibly even **infertility**.[27-30]

What impresses scientists are the many **pathological** mechanisms of **aging** that resveratrol has been shown to thwart.

The challenge up to now has been how to deliver enough **bioavailable resveratrol** to the bloodstream to induce systemic (whole-body) effects.

Up to 10 Times Greater Bioavailability

Orally ingested resveratrol is rapidly metabolized and transformed primarily in the digestive tract and the liver.[4,5] This leaves very little *free* resveratrol in circulation.

Scientists found a solution to this by combining **resveratrol** with **galactomannan** fibers from **fenugreek seed.** This creates a **hydrogel** coating that allows greater resveratrol bioavailability.

Compared to unformulated resveratrol, this **resveratrol-galactomannan** hydrogel showed **up to 10 times** *greater* **bioavailability**.[31]

The graph on this page shows the magnitude of **resveratrol** increase and the longer period this proprietary **hydrogel** formulation of **resveratrol** remained in the blood compared to unformulated resveratrol.

It's Time for More Clinical Research!

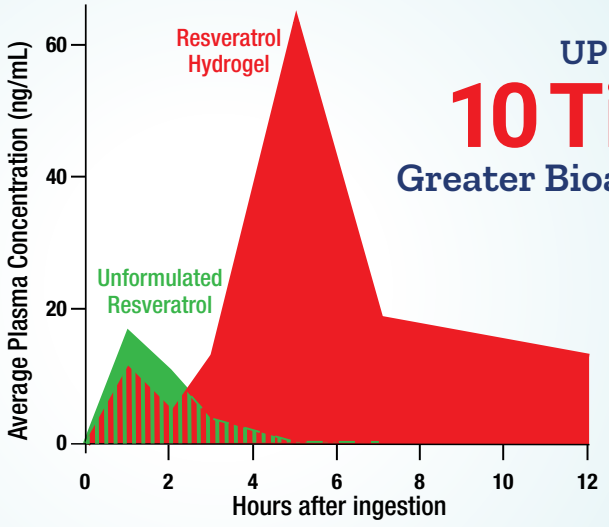
Resveratrol is a widely studied **plant extract** in the health and longevity fields.

Physician-scientists have been frustrated with **resveratrol research** because most of what is **orally** ingested is quickly degraded in the **human** body.

After oral administration in humans, a **resveratrol hydrogel** formula boosted plasma concentration (ng/mL) about **10-fold higher** than unformulated resveratrol.

530 mg of **Resveratrol Hydrogel** providing 80 mg of *trans*-resveratrol (red)

380 mg of unformulated resveratrol providing 80 mg of *trans*-resveratrol (green)



UP TO
10 Times
Greater Bioavailability[31]

Resveratrol Hydrogel

Unformulated Resveratrol

Adapted from: Joseph A, Balakrishnan A, Shanmughan P, et al. Micelle/Hydrogel Composite as a "Natural Self-Emulsifying Reversible Hybrid Hydrogel (N'SERH)" Enhances the Oral Bioavailability of Free (Unconjugated) Resveratrol. *ACS Omega.* 2022 Apr 19;7(15):12835-45.

With the advent of a new **bioavailable resveratrol**, far better dosing schedules can be tested, and consistently ***higher*** blood levels achieved.

The good news for consumers is lower cost, as fewer milligrams of resveratrol need to be ingested to achieve *higher* circulatory levels.

I look forward to this new **bioavailable resveratrol** being used in upcoming clinical trials that seek to extend healthy human longevity.

Your ongoing support enables us to fund many of these **human** studies.

For longer life,

William Faloon,
Co-Founder, Life Extension®

References

1. Howitz KT, Bitterman KJ, Cohen HY, et al. Small molecule activators of sirtuins extend Saccharomyces cerevisiae lifespan. *Nature.* 2003 Sep 11;425(6954):191-6.
2. Bhullar KS, Hubbard BP. Lifespan and healthspan extension by resveratrol. *Biochim Biophys Acta.* 2015 Jun;1852(6):1209-18.
3. Zhou DD, Luo M, Huang SY, et al. Effects and Mechanisms of Resveratrol on Aging and Age-Related Diseases. *Oxid Med Cell Longev.* 2021;2021:9932218.
4. Springer M, Moco S. Resveratrol and Its Human Metabolites-Effects on Metabolic Health and Obesity. *Nutrients.* 2019 Jan 11;11(1).
5. Walle T, Hsieh F, DeLegge MH, et al. High absorption but very low bioavailability of oral resveratrol in humans. *Drug Metab Dispos.* 2004 Dec;32(12):1377-82.
6. Jang M, Cai L, Udeani GO, et al. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. *Science.* 1997 Jan 10;275(5297):218-20.
7. Hector KL, Lagisz M, Nakagawa S. The effect of resveratrol on longevity across species: a meta-analysis. *Biol Lett.* 2012 Oct 23;8(5):790-3.
8. Rascon B, Hubbard BP, Sinclair DA, et al. The lifespan extension effects of resveratrol are conserved in the honey bee and may be driven by a mechanism related to caloric restriction. *Aging (Albany NY).* 2012 Jul;4(7):499-508.
9. Khan M, Park S, Kim HJ, et al. The Resveratrol Rice DJ526 Callus Significantly Increases the Lifespan of Drosophila (Resveratrol Rice DJ526 Callus for Longevity). *Nutrients.* 2019 Apr 29;11(5).
10. Islam MS, Jin YY, Chung HJ, et al. Effect of the Resveratrol Rice DJ526 on Longevity. *Nutrients.* 2019 Aug 5;11(8).
11. Yu X, Li G. Effects of resveratrol on longevity, cognitive ability and aging-related histological markers in the annual fish Nothobranchius guentheri. *Exp Gerontol.* 2012 Dec;47(12):940-9.
12. Gerhardt E, Graber S, Szego EM, et al. Idebenone and resveratrol extend lifespan and improve motor function of HtrA2 knockout mice. *PLoS One.* 2011;6(12):e28855.
13. da Luz PL, Tanaka L, Brum PC, et al. Red wine and equivalent oral pharmacological doses of resveratrol delay vascular aging but do not extend life span in rats. *Atherosclerosis.* 2012 Sep;224(1):136-42.
14. Pearson KJ, Baur JA, Lewis KN, et al. Resveratrol delays age-related deterioration and mimics transcriptional aspects of dietary restriction without extending life span. *Cell Metab.* 2008 Aug;8(2):157-68.
15. Baur JA, Pearson KJ, Price NL, et al. Resveratrol improves health and survival of mice on a high-calorie diet. *Nature.* 2006 Nov 16;444(7117):337-42.
16. Azam S, Haque ME, Balakrishnan R, et al. The Ageing Brain: Molecular and Cellular Basis of Neurodegeneration. *Front Cell Dev Biol.* 2021;9:683459.
17. Hou Y, Dan X, Babbar M, et al. Ageing as a risk factor for neurodegenerative disease. *Nat Rev Neurol.* 2019 Oct;15(10):565-81.
18. Torres-Perez M, Tellez-Ballesteros RI, Ortiz-Lopez L, et al. Resveratrol Enhances Neuroplastic Changes, Including Hippocampal Neurogenesis, and Memory in Balb/C Mice at Six Months of Age. *PLoS One.* 2015;10(12):e0145687.
19. Kodali M, Parihar VK, Hattiangady B, et al. Resveratrol prevents age-related memory and mood dysfunction with increased hippocampal neurogenesis and microvasculature, and reduced glial activation. *Sci Rep.* 2015 Jan 28;5:8075.
20. Sarubbo F, Ramis MR, Aparicio S, et al. Improving effect of chronic resveratrol treatment on central monoamine synthesis and cognition in aged rats. *Age (Dordr).* 2015 Jun;37(3):9777.
21. Gocmez SS, Gacar N, Utkan T, et al. Protective effects of resveratrol on aging-induced cognitive impairment in rats. *Neurobiol Learn Mem.* 2016 May;131:131-6.
22. Witte AV, Kerti L, Margulies DS, et al. Effects of resveratrol on memory performance, hippocampal functional connectivity, and glucose metabolism in healthy older adults. *J Neurosci.* 2014 Jun 4;34(23):7862-70.
23. Fajemiroye JO, da Cunha LC, Saavedra-Rodriguez R, et al. Aging-Induced Biological Changes and Cardiovascular Diseases. *Biomed Res Int.* 2018;2018:7156435.
24. Rajapakse AG, Yepuri G, Carvas JM, et al. Hyperactive S6K1 mediates oxidative stress and endothelial dysfunction in aging: inhibition by resveratrol. *PLoS One.* 2011 Apr 22;6(4):e19237.
25. Tasatargil A, Tanriover G, Barutcigil A, et al. Protective effect of resveratrol on methylglyoxal-induced endothelial dysfunction in aged rats. *Aging Clin Exp Res.* 2019 Mar;31(3):331-8.
26. Restini CBA, Garcia AFE, Natalin HM, et al. Resveratrol Supplants Captopril's Protective Effect on Cardiac Remodeling in a Hypertension Model Elicited by Renal Artery Stenosis. *Yale J Biol Med.* 2022 Mar;95(1):57-69.
27. Rauf A, Imran M, Butt MS, et al. Resveratrol as an anti-cancer agent: A review. *Crit Rev Food Sci Nutr.* 2018 Jun 13;58(9):1428-47.
28. Tou JC. Resveratrol supplementation affects bone acquisition and osteoporosis: Pre-clinical evidence toward translational diet therapy. *Biochim Biophys Acta.* 2015 Jun;1852(6):1186-94.
29. Kan NW, Ho CS, Chiu YS, et al. Effects of Resveratrol Supplementation and Exercise Training on Exercise Performance in Middle-Aged Mice. *Molecules.* 2016 May 18;21(5).
30. Pasquariello R, Verdile N, Brevini TAL, et al. The Role of Resveratrol in Mammalian Reproduction. *Molecules.* 2020 Oct 5;25(19).
31. Joseph A, Balakrishnan A, Shanmughan P, et al. Micelle/Hydrogel Composite as a "Natural Self-Emulsifying Reversible Hybrid Hydrogel (N'SERH)" Enhances the Oral Bioavailability of Free (Unconjugated) Resveratrol. *ACS Omega*. 2022 Apr 19;7(15):12835-45.

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Restore Youthful TESTOSTERONE LEVELS

BY MICHAEL DOWNEY

Men worry that low **testosterone** will decrease **muscle growth** and **libido**.

This is just the tip of iceberg.

Research indicates that low testosterone may affect mood and cause depression.[1]

It is *also* linked to an increased risk for **heart disease** and greater risk of ***death from any cause***.[2-7]

Serum testosterone declines over time. Beginning as early as **age 30**, testosterone levels start falling about **1% per year**.[8,9]

Scientists have identified **plant-derived nutrients** that help safely boost production of this hormone.

In one clinical study, a blend of **pomegranate** and **cacao** extracts was shown to increase **free testosterone** as much as **48%** in aging men.[10]

In preclinical studies, the flavonoid **luteolin** was shown to support testosterone production and reduce its conversion into estrogen.[11-14]

Declining Free Testosterone

The hormone **testosterone** is primarily produced in the **testicles** in men.[15,16] It is crucial for normal development of the male **reproductive system** and impacts the healthy function of organs and tissues ***throughout the body***.

To perform its vital roles, **testosterone** must be in a "**free**" or **biologically active** form to attach to testosterone receptors on various body cells.

However, only about **2%** of all circulating testosterone is in this **free***, unbound* form.[17] The rest circulates in the blood already *bound* to proteins.[15,18]

And, **free testosterone** declines with age.

Overweight men have a *higher* risk for low testosterone. That's because being overweight or obese is associated with increased levels of the enzyme **aromatase**, which converts testosterone into **estrogen**.[9,19]

Dangers of Low Testosterone

As testosterone levels decline with age, men experience well-known *low* **testosterone symptoms**. These include diminished sexual desire, erectile dysfunction, fatigue, reduced muscle mass and strength, and loss of youthful well-being.

But the effects go beyond these. **Testosterone deficiency** in men correlates with a greater risk of:[6,7,18,20-24]

- Cardiovascular disease,
- Osteoporosis,
- Chronic inflammation,
- Neurodegeneration, including cognitive decline and Alzheimer's disease,
- Metabolic syndrome and type II diabetes,
- Depression, and
- All-cause mortality.

A misguided fear that testosterone may cause **prostate cancer** hampered clinical progress for decades. In reality, low testosterone is associated with increased prostate cancer incidence in most studies.[25,26]

Clearly, there is a critical need to boost **free testosterone** levels in most aging men.

Promising Plant Extracts

Seeking a safe and **drug-free** way to elevate testosterone, scientists took note of a study presented at an endocrinology conference a decade ago.

In that study, healthy men and women who took **pomegranate juice** for just ***two weeks*** increased salivary **testosterone** levels by **23%-27%**. Mood and well-being measures also improved.[27]

After screening hundreds of plant extracts, scientists believed that both **pomegranate** and **cacao seed** extract, from the beans used to make cocoa and chocolate, might promote *higher* testosterone levels.

A study using testes cells from mice confirmed that both extracts could significantly raise **testosterone production**.[28]

In a rodent model, investigators found that a **pomegranate-cacao seed combination** boosted testosterone production by over **72%** in just six weeks.[29]

Boosting Testosterone in Men

To evaluate **pomegranate** and **cacao** extracts in humans, scientists gave men ranging from **36** to **55 years old** either a combination of these extracts or a placebo.[10]

After eight weeks, **free testosterone** levels in men receiving **400 mg** of the **pomegranate-cacao** blend were elevated by over **48%** compared to baseline.[10]

In addition, in men taking the pomegranate-cacao blend:[10]

- Overall **well-being** improved,
- Measures of **stress** dropped by **26%**, and
- Hand grip **strength** increased by almost **25%** compared to baseline.

The **pomegranate-cacao** group also reduced their symptoms on the **Aging Males' Symptoms scale** by **19%**.[10] These symptoms include:[30]

- Joint pain and muscle aches,
- Excessive sweating,
- Sleep problems and exhaustion,
- Anxiety and irritability,
- Depression and feeling burned out, and
- Decrease in libido and other sexual problems.

A similar study was done on ***younger*** men, aged **21 to 35**.[10]

Even in these younger men, a blend of pomegranate and cacao extracts increased **free testosterone** by **25%**. Hand grip strength and the circumference of the upper arm increased as well.[10]

How Luteolin Helps

Luteolin is a flavonoid found in certain fruits, herbs, and vegetables, including celery, broccoli, parsley, and thyme.

This compound may support higher **testosterone** production and levels in **two** ways. Cell and animal studies demonstrate that luteolin:

- **Increases** an enzyme called **StAR** (steroid-ogenic acute regulatory protein), which is *required* for testosterone production to occur,[31] and
- **Inhibits** the enzyme **aromatase**, which converts testosterone into estrogen.[11,12]

A combination of **luteolin** and **pomegranate-cacao** extracts may support the production and maintenance of healthy **free testosterone** levels in men as they age.

WHAT YOU NEED TO KNOW

Boost Testosterone for Better Health

- **Testosterone** is crucial to healthy aging in men, but levels of this hormone begin to drop around age **30**.
- **Low testosterone** causes symptoms like fatigue, low libido, and reduced strength. It also *increases* the risk of cardiovascular disease and other disorders, and raises the risk of death from any cause.
- In clinical studies, a blend of **pomegranate** and **cacao seed extracts** increased bioactive **free testosterone** in men by as much as **48%** and improved measures of stress, hand grip strength, and more.
- Preclinical studies show that the flavonoid **luteolin** may support optimal testosterone levels and maintain healthy testosterone and estrogen balance.

Summary

Beginning around age **30**, levels of the hormone **testosterone** in men begin to *decline*.

Low testosterone can result in symptoms like erectile dysfunction, fatigue, and reduced muscle mass, and poses a serious risk to overall health.

Pomegranate and **cacao seed** extracts *boost* testosterone production. In a clinical study, this combination increased **free testosterone** by **48%** and improved measures of stress-resilience and strength.[10]

Preclinical data found that the flavonoid **luteolin** also supports higher testosterone levels.

Together, these nutrients may help aging men support *higher* testosterone levels and quality of life.

HOW TO CHECK YOUR TESTOSTERONE LEVEL

The best way to check your testosterone status is through simple **blood tests**.

In men, the optimal ranges for **free** and **total** testosterone in the blood are:

- Free testosterone: **15-25 pg/mL**
- Total testosterone: **600-900 ng/dL**

References

1. Nead KT. Androgens and depression: a review and update. *Curr Opin Endocrinol Diabetes Obes.* 2019 Jun;26(3):175-9.
2. Bassil N, Morley JE. Late-life onset hypogonadism: a review. *Clin Geriatr Med.* 2010 May;26(2):197-222.
3. Marin P, Arver S. Androgens and abdominal obesity. *Baillieres Clin Endocrinol Metab.* 1998 Oct;12(3):441-51.
4. Seidell JC, Bjorntorp P, Sjostrom L, et al. Visceral fat accumulation in men is positively associated with insulin, glucose, and C-peptide levels, but negatively with testosterone levels. *Metabolism.* 1990 Sep;39(9):897-901.
5. Travison TG, Morley JE, Araujo AB, et al. The relationship between libido and testosterone levels in aging men. *J Clin Endocrinol Metab.* 2006 Jul;91(7):2509-13.
6. Araujo AB, Dixon JM, Suarez EA, et al. Clinical review: Endogenous testosterone and mortality in men: a systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2011 Oct;96(10):3007-19.
7. Michaud JE, Billups KL, Partin AW. Testosterone and prostate cancer: an evidence-based review of pathogenesis and oncologic risk. *Ther Adv Urol.* 2015 Dec;7(6):378-87.
8. Brawer MK. Testosterone replacement in men with andropause: an overview. *Rev Urol.* 2004;6 Suppl 6(Suppl 6):S9-S15.
9. Kazi M, Geraci SA, Koch CA. Considerations for the diagnosis and treatment of testosterone deficiency in elderly men. *Am J Med.* 2007 Oct;120(10):835-40.
10. Nutraceutical L. Internal Study. A randomized, double blind, placebo controlled study to evaluate the efficacy and safety of a novel herbal composition improving aging males' symptoms. Data on file. 2018.
11. Li F, Wong TY, Lin SM, et al. Coadministrating luteolin minimizes the side effects of the aromatase inhibitor letrozole. *J Pharmacol Exp Ther.* 2014 Nov;351(2):270-7.
12. Lu DF, Yang LJ, Wang F, et al. Inhibitory effect of luteolin on estrogen biosynthesis in human ovarian granulosa cells by suppression of aromatase (CYP19). *J Agric Food Chem.* 2012 Aug 29;60(34):8411-8.
13. Cormier M, Ghouili F, Roumaud P, et al. Influences of flavones on cell viability and cAMP-dependent steroidogenic gene regulation in MA-10 Leydig cells. *Cell Biol Toxicol.* 2018 Feb;34(1):23-38.
14. Martin LJ, Touaibia M. Improvement of Testicular Steroidogenesis Using Flavonoids and Isoflavonoids for Prevention of Late-Onset Male Hypogonadism. *Antioxidants (Basel).* 2020 Mar 13;9(3).
15. Available at: https://www.ncbi.nlm.nih.gov/books/NBK526128/. Accessed October 13, 2022.
16. Kohn FM. Testosterone and body functions. *Aging Male.* 2006 Dec;9(4):183-8.
17. Hinson J, Raven P, Chew S. Hormonal Control of Reproduction Part I. In: Hinson J, Raven P, Chew S, editors. *The Endocrine System*: Churchill Livingstone; 2010:87-98.
18. Edwards RZ. Testosterone Deficiency. In: Rakel D, ed. *Integrative Medicine*: Elsevier; 2018:630-7.e1.
19. Kalyani RR, Dobs AS. Androgen deficiency, diabetes, and the metabolic syndrome in men. *Curr Opin Endocrinol Diabetes Obes.* 2007 Jun;14(3):226-34.
20. Zhang X, Zhao H, Horney J, et al. Testosterone Deficiency, Long-Term Testosterone Therapy, and Inflammation. *J Cardiovasc Pharmacol Ther.* 2021 Nov;26(6):638-47.
21. Li Y, Liu M, Cui Y, et al. Increased risk of testosterone deficiency is associated with the systemic immune-inflammation index: a population-based cohort study. *Front Endocrinol (Lausanne).* 2022 2022-August-16;13:974773.
22. Avsar O. Is testosterone perspective available for neurodegenerative diseases? *Neuropsychiatry.* 2018 01/01;08(05).
23. Muraleedharan V, Jones TH. Testosterone and the metabolic syndrome. *Ther Adv Endocrinol Metab.* 2010 Oct;1(5):207-23.
24. Kheirkhah F, Hosseini SR, Hosseini SF, et al. Relationship between testosterone levels and depressive symptoms in older men in Amirkola, Iran. *Caspian J Intern Med.* 2014 Spring;5(2):65-70.
25. Morgentaler A, Rhoden EL. Prevalence of prostate cancer among hypogonadal men with prostate-specific antigen levels of 4.0 ng/mL or less. *Urology.* 2006 Dec;68(6):1263-7.
26. Hoffman MA, DeWolf WC, Morgentaler A. Is low serum free testosterone a marker for high grade prostate cancer? *J Urol.* 2000 Mar;163(3):824-7.
27. Smail N, Al-Dujaili E. *Pomegranate juice intake enhances salivary testosterone levels and improves mood and well being in healthy men and women.* 2012.
28. Nutraceutical L. Laila Nutraceutical Internal Study. Evaluating testosterone production activating capacity of herbal extracts in MA-10 mouse leydig cells. Data on file. 2018.
29. Nutraceutical L. Laila Nutraceutical Internal Study. Tesnor raises testosterone levels in rats: in vivo study. Data on file. 2018.
30. Moore C, Huebler D, Zimmermann T, et al. The Aging Males' Symptoms scale (AMS) as outcome measure for treatment of androgen deficiency. *Eur Urol.* 2004 Jul;46(1):80-7.
31. Couture R, Mora N, Al Bittar S, et al. Luteolin modulates gene expression related to steroidogenesis, apoptosis, and stress response in rat LC540 tumor Leydig cells. *Cell Biol Toxicol.* 2020 Feb;36(1):31-49.

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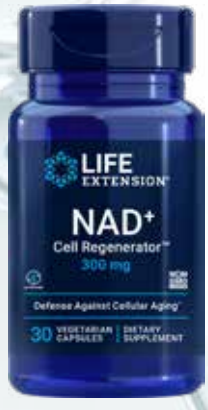

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References
1. *Rev Urol*. 2004;6 Suppl 6(Suppl 6):S9-S15.
2. *Am J Med*. 2007 Oct;120(10):835-40.
3. Laila Nutraceutical Internal Study. Data on file. 2019.
4. *Cell Biol Toxicol*. 2020 Feb;36(1):31-49.
5. *J Pharmacol Exp Ther*. 2014 Nov;351(2):270-7.
6. *J Agric Food Chem*. 2012 Aug 29;60(34):8411-8.

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FISH OIL AND HEART ATTACK RISK

BY STAN FREEDMAN

Ingestion of omega-3s is associated with lower rates of **heart attack** and **cardiac-related death**.[1]

An observational study found that those with the *highest* blood levels of **omega-3s** live almost ***five years longer*** than those with the lowest blood levels.[2]

The average dietary intake of **EPA** and **DHA** for typical Americans is too low.[3-5]

Eating cold-water fish and/or supplementing with **fish oil** is a smart, heart-healthy move.

How Fish Oil Prevents Heart Disease

Omega-3 fatty acids are healthy fats that serve multiple roles.

They are particularly concentrated in **brain** and **heart muscle**.[6,7]

Omega-3 fatty acids are essential for balancing **inflammatory** responses.[8]

Getting enough omega-3s helps counter several major contributors to heart and blood vessel disease, including:

1. **Elevated triglycerides**. High levels of these fats in the blood correlate with an *increased* risk of heart disease. Taking omega-3s *reduces* triglyceride levels.[9-11] The **American Heart Association** has issued a science advisory that **EPA** and **DHA** doses of **2,000–4,000 mg** per day are recommended for lowering triglycerides.[12]

2. **High blood pressure**. Increasing intake of omega-3 fatty acids can modestly reduce blood pressure, a major risk factor for heart disease.[13,14]

3. **Insulin resistance**. When cells do not respond to the hormone insulin appropriately, the body cannot optimally manage blood sugar. Fish oil intake is associated with *improved* insulin sensitivity in people with some existing degree of metabolic disease.[11,15]

4. **Blood clotting**. Heart attacks and strokes are frequently caused by abnormal clotting (thrombosis) within blood vessels.[16] Higher intake of omega-3s can *reduce* the formation of blood clots.[17-19]

5. **Chronic inflammation**. Persistent inflammation is a major driver of **atherosclerosis**, the buildup of plaque in arteries. Omega-3s reduce the production of pro-inflammatory compounds and serve as precursors to *anti*-inflammatory compounds.[6-8,20,21]

The above actions may help slow or *halt* the development and progression of **cardiovascular disease**.

Observational Studies

The **omega-3 index** is a blood test that measures the percentage of omega-3s in the blood. The *higher* the number, the *more* **omega-3s** in the body.

An index of **8%** or higher is considered ideal.[22]

In an observational study that evaluated close to ***30,000 individuals***, having an **omega-3 index** of **8%** or greater predicted about a **30%** lower ***risk of death*** due to **coronary artery disease** than an omega-3 index below **4%**.[22]

The **Framingham Heart Study** is one of the largest and longest-running observational studies in existence.[2,23] It has consistently found that a *higher* omega-3 index is associated with significantly *lower* risk of **total mortality** and cardiovascular-related events such as **stroke** and **heart attack**.

The Framingham study even found that the **omega-3 index** is as good at predicting risk of death as factors like smoking, high blood pressure, diabetes, and age.[2] Those with a *higher* index live almost **five years longer** on average than those with a low index.

In one of the papers from the Framingham study, people with the highest omega-3 index levels compared to those with the lowest, had a **34%** lower risk of all cause mortality and their risk of developing cardiovascular diseases was **39%** lower.[23]

WHAT YOU NEED TO KNOW

Omega-3s Promote Heart Health

- Low intake of **omega-3 fatty acids** is associated with increased risk for cardiovascular disease and death.
- Daily intake of fish oil is associated with reduced rates of heart disease, and cardiovascular disease outcomes like heart attack and stroke.
- **Life Extension** suggests daily supplementation with about **2,000 mg** of EPA + DHA from highly purified fish oil.

Results from Clinical Studies

Data from many **clinical trials** show that increased intake of fish oil correlates with reduced risk for **heart disease** and cardiac-related **mortality**.[1]

The Food and Drug Administration (FDA) published a **Qualified Health Claim** stating that increased consumption of EPA and DHA may reduce risk for high blood pressure and coronary heart disease.[24]

Oral intake of **omega-3** has been linked with:[25]

- *Prevention* of the development of heart disease, and
- Improved outcomes for those who *already* suffer from heart disease.

One recent, large meta-analysis[26] found that taking fish oil was associated with reduced development of **coronary heart disease** compared to those who did not receive fish oil.

Another meta-analysis found that **fish oil** is associated with a *reduced* risk of developing **coronary heart disease** and all **cardiovascular disease**, and **cardiovascular mortality**.[1]

These newer studies add to decades of evidence showing that fish oil helps protect the **heart**.

Boosting the Benefits of Fish Oil

Olive extract and **sesame lignans** add to the health benefits of fish oil.

OLIVE EXTRACT

Research shows that people who consume the most **olive oil** have a lower risk of dying from *cardiovascular* events.[27-29]

Olive oil contains unique ***polyphenols*** including *oleuropein, tyrosol,* and *hydroxytyrosol*.[30-32] High-phenolic **extra virgin olive oil** is the best food source of these compounds.

In a study in people over age 65, those who ingested the *highest* amount of **hydroxytyrosol** from virgin olive oil and wine lived **9.2 years** *longer* on average.[33]

Extracts of the **olive leaf**, concentrated and standardized to provide maximum polyphenol content, have been shown to protect cultured heart-muscle cells from destruction caused by **oxidative damage**.[34]

SESAME SEEDS

Sesame seeds contain high concentrations of polyphenols called **lignans**. They have demonstrated activity related to lowering blood lipid levels, fighting inflammation and cancer, neutralizing free radicals, and enhancing **vitamin E** bioavailability.[35,36]

Metabolism of **sesame lignans** by intestinal microflora creates the compounds *enterolactone* and *enterodiol*, both of which may have protective effects against **hormone-related diseases** such as breast cancer.[37,38]

Sesame lignans may help enhance the effects of **omega-3s** in the body.

Summary

Modern Western diets are usually lacking in **omega-3 fatty acids** like **DHA** and **EPA**.

Lower blood levels of omega-3s have been correlated with increased risk for coronary artery occlusion and cardiovascular events like **stroke** and **heart attacks**.

Life Extension suggests most readers supplement with about **2,000 mg** of EPA + DHA each day from highly purified fish oil. •

References

1. Hu Y, Hu FB, Manson JE. Marine Omega-3 Supplementation and Cardiovascular Disease: An Updated Meta-Analysis of 13 Randomized Controlled Trials Involving 127 477 Participants. J *Am Heart Assoc.* 2019 Oct;8(19):e013543.
2. McBurney MI, Tintle NL, Vasan RS, et al. Using an erythrocyte fatty acid fingerprint to predict risk of all-cause mortality: the Framingham Offspring Cohort. *Am J Clin Nutr.* 2021 Oct 4;114(4):1447-54.
3. Serhiyenko V. Omega-3 Polyunsaturated Fatty Acids, Metabolic Syndrome and Diabetes Mellitus. *Current Research in Diabetes & Obesity Journal.* 2018 02/06;5(4).
4. Srigley CT, Rader JI. Content and composition of fatty acids in marine oil omega-3 supplements. *J Agric Food Chem*. 2014 Jul 23;62(29):7268-78.
5. Papanikolaou Y, Brooks J, Reider C, et al. U.S. adults are not meeting recommended levels for fish and omega-3 fatty acid intake: results of an analysis using observational data from NHANES 2003-2008. *Nutr J.* 2014 Apr 2;13:31.
6. Surette ME. The science behind dietary omega-3 fatty acids. *CMAJ.* 2008 Jan 15;178(2):177-80.
7. Calder PC. Docosahexaenoic Acid. *Ann Nutr Metab*. 2016;69 Suppl 1:7-21.
8. Gutierrez S, Svahn SL, Johansson ME. Effects of Omega-3 Fatty Acids on Immune Cells. *Int J Mol Sci*. 2019 Oct 11;20(20).
9. Abdelhamid AS, Brown TJ, Brainard JS, et al. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. *Cochrane Database Syst Rev.* 2020 Feb 29;3:CD003177.
10. Shearer GC, Savinova OV, Harris WS. Fish oil -- how does it reduce plasma triglycerides? *Biochim Biophys Acta.* 2012 May;1821(5):843-51.
11. Thota RN, Acharya SH, Garg ML. Curcumin and/or omega-3 polyunsaturated fatty acids supplementation reduces insulin resistance and blood lipids in individuals with high risk of type 2 diabetes: a randomised controlled trial. *Lipids Health Dis*. 2019 Jan 26;18(1):31.
12. Skulas-Ray AC, Wilson PWF, Harris WS, et al. Omega-3 Fatty Acids for the Management of Hypertriglyceridemia: A Science Advisory From the American Heart Association. *Circulation.* 2019 Sep 17;140(12):e673-e91.

13. Campbell F, Dickinson HO, Critchley JA, et al. A systematic review of fish-oil supplements for the prevention and treatment of hypertension. *Eur J Prev Cardiol*. 2013 Feb;20(1):107-20.
14. Miller PE, Van Elswyk M, Alexander DD. Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure: a meta-analysis of randomized controlled trials. *Am J Hypertens.* 2014 Jul;27(7):885-96.
15. Gao H, Geng T, Huang T, et al. Fish oil supplementation and insulin sensitivity: a systematic review and meta-analysis. *Lipids Health Dis.* 2017 Jul 3;16(1):131.
16. Alkarithi G, Duval C, Shi Y, et al. Thrombus Structural Composition in Cardiovascular Disease. *Arterioscler Thromb Vasc Biol.* 2021 Sep;41(9):2370-83.
17. Watson PD, Joy PS, Nkonde C, et al. Comparison of bleeding complications with omega-3 fatty acids + aspirin + clopidogrel--versus--aspirin + clopidogrel in patients with cardiovascular disease. *Am J Cardiol.* 2009 Oct 15;104(8):1052-4.
18. Pryce R, Bernaitis N, Davey AK, et al. The Use of Fish Oil with Warfarin Does Not Significantly Affect either the International Normalised Ratio or Incidence of Adverse Events in Patients with Atrial Fibrillation and Deep Vein Thrombosis: A Retrospective Study. *Nutrients.* 2016;8(9):578.
19. Tomic-Smiljanic M, Vasiljevic D, Lucic-Tomic A, et al. Influence of different supplementation on platelet aggregation in patients with rheumatoid arthritis. *Clin Rheumatol.* 2019 Sep;38(9):2443-50.
20. Laight D. Can fish oils help to prevent cardiovascular disease? *Prescriber*. 2021;32(7):21-5.
21. Hutchinson AN, Tingo L, Brummer RJ. The Potential Effects of Probiotics and omega-3 Fatty Acids on Chronic Low-Grade Inflammation. *Nutrients*. 2020 Aug 11;12(8).
22. Harris WS, Del Gobbo L, Tintle NL. The Omega-3 Index and relative risk for coronary heart disease mortality: Estimation from 10 cohort studies. *Atherosclerosis.* 2017 Jul;262:51-4.
23. Harris WS, Tintle NL, Etherton MR, et al. Erythrocyte long-chain omega-3 fatty acid levels are inversely associated with mortality and with incident cardiovascular disease: The Framingham Heart Study. *J Clin Lipidol*. 2018 May - Jun;12(3):718-27 e6.
24. Available at: https://www.fda.gov/food/cfsan-constituent-updates/fda-announces-new-qualified-health-claims-epa-and-dha-omega-3-consumption-and-risk-hypertension-and. Accessed September 18, 2022.
25. Zhang X, Ritonja JA, Zhou N, et al. Omega-3 Polyunsaturated Fatty Acids Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2022 Jun 7;11(11):e025071.
26. Wu G, Ji Q, Huang H, et al. The efficacy of fish oil in preventing coronary heart disease: A systematic review and meta-analysis. *Medicine (Baltimore).* 2021 Sep 17;100(37):e27253.
27. Katsiki N, Perez-Martinez P, Lopez-Miranda J. Olive Oil Intake and Cardiovascular Disease Prevention: "Seek and You Shall Find". *Curr Cardiol Rep.* 2021 May 7;23(6):64.
28. Torres-Collado L, Garcia-de la Hera M, Lopes C, et al. Olive oil consumption and all-cause, cardiovascular and cancer mortality in an adult mediterranean population in Spain. *Front Nutr.* 2022;9:997975.
29. Guasch-Ferre M, Hu FB, Martinez-Gonzalez MA, et al. Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study. *BMC Med.* 2014 May 13;12:78.
30. Tripoli E, Giammanco M, Tabacchi G, et al. The phenolic compounds of olive oil: structure, biological activity and beneficial effects on human health. Nutr Res Rev. 2005 Jun;18(1):98-112.
31. Tejada S, Pinya S, Del Mar Bibiloni M, et al. Cardioprotective Effects of the Polyphenol Hydroxytyrosol from Olive Oil. *Curr Drug Targets.* 2017 Oct 05;18(13):1477-86.
32. Virruso C, Accardi G, Colonna-Romano G, et al. Nutraceutical properties of extra-virgin olive oil: a natural remedy for age-related disease? *Rejuvenation Res.* 2014 Apr;17(2):217-20.
33. De la Torre R, Corella D, Castaner O, et al. Protective effect of homovanillyl alcohol on cardiovascular disease and total mortality: virgin olive oil, wine, and catechol-methylation. *Am J Clin Nutr.* 2017 Jun;105(6):1297-304.

34. Bali EB, Ergin V, Rackova L, et al. Olive leaf extracts protect cardiomyocytes against 4-hydroxynonenal-induced toxicity in vitro: comparison with oleuropein, hydroxytyrosol, and quercetin. *Planta Med.* 2014 Aug;80(12):984-92.
35. Wu MS, Aquino LBB, Barbaza MYU, et al. Anti-Inflammatory and Anticancer Properties of Bioactive Compounds from Sesamum indicum L.-A Review. *Molecules*. 2019 Dec 4;24(24):4426.
36. Majdalawieh AF, Dalibalta S, Yousef SM. Effects of sesamin on fatty acid and cholesterol metabolism, macrophage cholesterol homeostasis and serum lipid profile: A comprehensive review. *Eur J Pharmacol.* 2020 Oct 15;885:173417.
37. Coulman KD, Liu Z, Hum WQ, et al. Whole sesame seed is as rich a source of mammalian lignan precursors as whole flaxseed. *Nutr Cancer*. 2005;52(2):156-65.
38. Liu Z, Saarinen NM, Thompson LU. Sesamin is one of the major precursors of mammalian lignans in sesame seed (Sesamum indicum) as observed in vitro and in rats. *J Nutr.* 2006 Apr;136(4):906-12.

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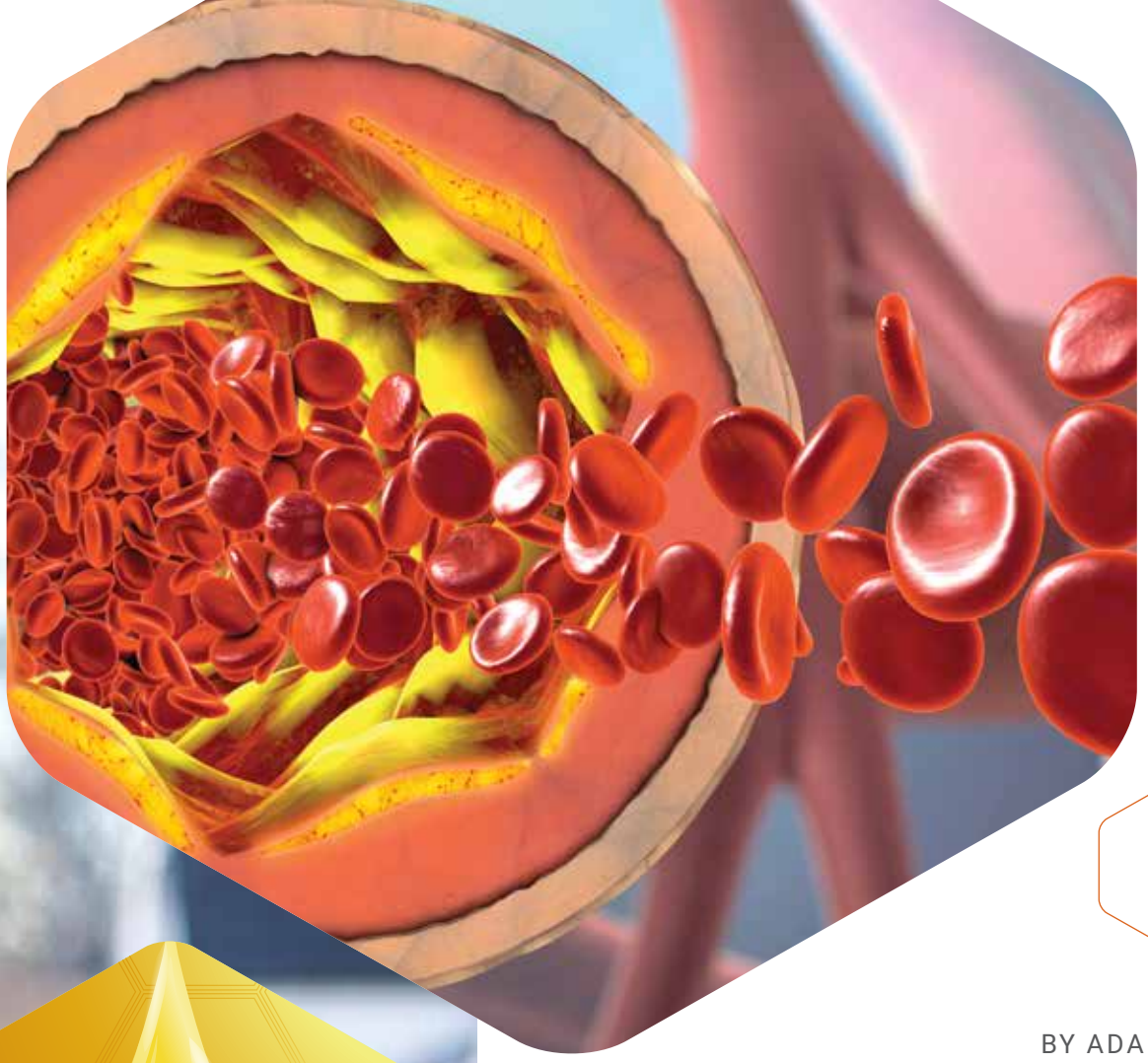
Role of CoQ10 in Aging



BY ADAM CRUZ

Coenzyme Q10 (CoQ10) is found in *every* **cell** in our body.

The *highest* amount is located in the **mitochondria**, the energy power houses of our cells.[1]

With age, **mitochondrial function** and **CoQ10** synthesis decline, contributing to a range of degenerative conditions.[2,3]

Research has shown that supplemental **CoQ10** improves **mitochondrial function** as well as organ performance.[1,4-8]

As a defense against the assaults of aging, **CoQ10** has been shown to suppress factors involved in nearly all chronic disorders.[1,6,7]

Heart Function

CoQ10 is no newcomer to **heart health**.[1,9,10]

It has been prescribed in **Japan** to treat heart failure for ***decades***. Research has shown it to be safe.[11]

One recent review paper presented preclinical and clinical evidence on the roles that CoQ10 plays in preventing and relieving heart disease, including:[1]

- Preventing the accumulation of oxidized LDL cholesterol in arteries,
- Decreasing stiffness of blood vessels, and
- Improving the function of the cells that line the inside of the blood vessels.

Clinical studies have shown that CoQ10 intake has clear benefits for the heart.

A clinical trial assessed the effects of CoQ10 supplementation against moderate-to-severe **heart failure**. Patients received either **CoQ10** or **placebo** over a two-year period.

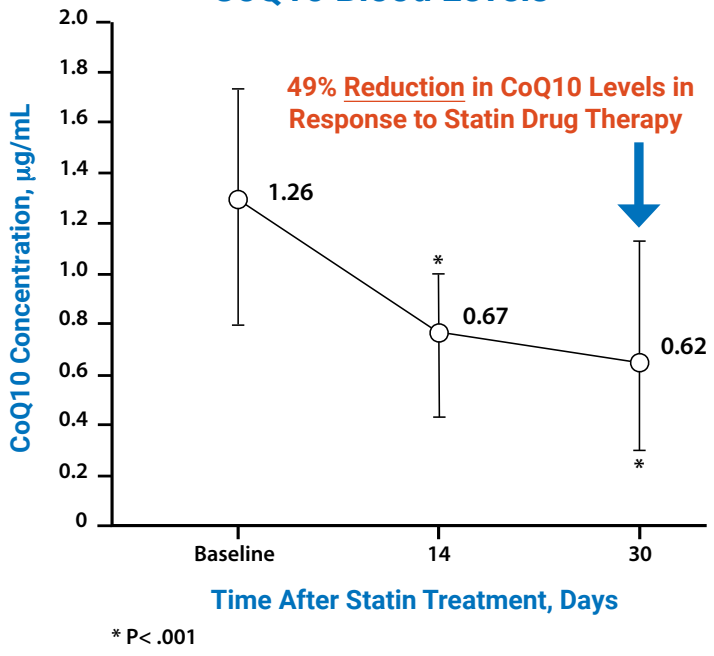
Those taking **100 mg** of **CoQ10** three times daily had a remarkable ***43% reduction*** in major cardiovascular events like heart attack, stroke, or death, compared to the **placebo** group.[10] Both groups were on standard drug therapy.

In another study, **heart attack** survivors were randomized to receive either **CoQ10** or a low-potency vitamin **placebo**.

The group receiving **120 mg** a day of **CoQ10** for one year had reduced rates of total cardiac events by **45%** and of nonfatal heart attacks by **46%** compared to the placebo group.[12]

Statin drugs prescribed to lower **LDL cholesterol** further reduce **coenzyme Q10 synthesis** in the body. Those using a statin are often advised to supplement with CoQ10.[13,14]

Statin Treatment Decreases CoQ10 Blood Levels



Source: *Arch Neurol.* 2004;61(6):889-892.

This study of people with an average age of 70 shows CoQ10 blood levels at baseline of only **1.26 mcg/mL**. Optimal levels should be between **2-3 mcg/mL**. Statin drug use causes these already low CoQ10 blood levels to drop to **0.62 mcg/mL**. According to cardiologist Peter Langsjoen, MD, heart failure patients should strive for CoQ10 blood levels of around **4 mcg/mL** and higher.[62]

WHAT YOU NEED TO KNOW

Brain Aging

Mitochondrial dysfunction is believed to play a role in the development of brain-aging diseases like Parkinson's and Alzheimer's.[15,16]

Studies show that **CoQ10** may help protect as follows:

- In patients with early **Parkinson's disease**, taking daily CoQ10 at a dosage of **1,200 mg/day** led to **44%** less **functional decline** than taking a placebo.[17]
- A study of patients with **Huntington's disease**, a progressive brain disorder, found that subjects given **300 mg** of CoQ10 twice daily for one year tended to have less **cognitive decline** than a placebo group.[18]
- In a mouse model of **Alzheimer's disease**, CoQ10 *decreased* the amount of beta-amyloid, a protein that accumulates in the brains of Alzheimer's patients, and *improved* the animals' cognitive and behavioral performance.[19]

Inflammation

Chronic inflammation is a driver of many different age-related chronic disorders.[20]

Meta-analyses of randomized controlled clinical trials have concluded that CoQ10 supplementation can significantly lower **inflammatory** markers.[21,22]

Another meta-analysis of randomized controlled trials reported CoQ10 supplementation significantly lowers markers of **inflammation** in individuals with metabolic syndrome. The authors described the ability of CoQ10 to inhibit oxidative stress, while also improving blood **sugar control** and **liver function**.[23]

CoQ10 Promotes Healthy Longevity

- **Coenzyme Q10 (CoQ10)** is essential for the production of energy by the mitochondria.
- CoQ10 deficiency has been found in many **age-related diseases** and processes, including brain aging and cardiovascular disease.
- One clinical trial showed that oral intake of CoQ10 *slowed* the age-related decline in **vitality**, **physical performance**, and health-related **quality of life**.
- CoQ10 intake can also help prevent **cardiovascular disease** by a variety of mechanisms.
- CoQ10 has been shown in one study to reduce the risk of major cardiovascular events including heart attack, stroke, and death in heart failure patients by **43%**.
- CoQ10 may help protect against neurodegenerative diseases like **Alzheimer's** and **Parkinson's diseases**.
- CoQ10 has many other benefits, such as reducing skin wrinkles, and improving lung function.

Systemic Indicators of Reduced Aging

CoQ10 has demonstrated other benefits that include:

- **Reducing wrinkles**. A clinical trial showed that daily intake of CoQ10 (**50** or **150 mg**) significantly reduced skin **wrinkles** and improved skin **smoothness** compared with a placebo.[4]
- **Enhancing physical performance**. Men were assigned to take either CoQ10 (**100 mg**) or a placebo daily, then underwent fitness tests. **Mean power** was *increased* in those taking CoQ10 compared to a placebo.[24]
- **Improving lung function**. Patients with **chronic obstructive pulmonary disease** (**COPD**), a lung disease, who took **90 mg** of CoQ10 daily for two months showed improvements in **heart rate** and a measure of how well oxygen moves from the lungs to the blood during exercise,[8] along with improvements in **hypoxemia** (low blood oxygen) at rest.
- In **asthma** patients, oral CoQ10 resulted in *improvement* in air flow.[25]

Cellular Energy

Preclinical evidence has shown that **CoQ10** is particularly promising for addressing a key aging factor: **mitochondrial dysfunction**.[1,3,5,26-28]

The mitochondria are responsible for **energy production** in our cells.[29] Damage to these structures is a contributor to **aging**, playing a role in various age-related disorders and a shorter lifespan.[3,5,27]

Some of this damage is caused by **oxidative stress**. CoQ10 *reduces* oxidative stress in cells.[1,26]

Deficiency of CoQ10 is linked to *increased* oxidative stress and mitochondrial dysfunction,[30] while **oral CoQ10** intake has shown evidence of protecting against the progression of aging and development of age-related diseases.[1,4,9,12,28]

CoQ10 slows common **symptoms of aging**, including decreased vitality, physical performance, and quality of life.

In a clinical trial, elderly participants received either a **placebo** or a combination of **CoQ10** and **selenium**. Participants took **200 mg** of CoQ10 and **200 mcg** of selenium each day. Over ***four years***, those taking the **CoQ10-selenium** showed improved health-related quality of life and more days out of the hospital.[9]

Summary

The nutrient **CoQ10** has shown promise in preventing and slowing degenerative disorders, including cardiovascular events and **brain aging**.

It functions via multiple mechanisms to enhance **mitochondria energy** output while combating **chronic inflammation** and **oxidative stress**.

Together, these effects may help slow certain aging processes and reduce symptoms of aging. •

References

1. Rabanal-Ruiz Y, Llanos-Gonzalez E, Alcain FJ. The Use of Coenzyme Q10 in Cardiovascular Diseases. *Antioxidants (Basel)*. 2021 May 10;10(5).
2. Barcelos IP, Haas RH. CoQ10 and Aging. *Biology (Basel)*. 2019 May 11;8(2).
3. Haas RH. Mitochondrial Dysfunction in Aging and Diseases of Aging. *Biology (Basel)*. 2019 Jun 17;8(2).
4. Zmitek K, Pogacnik T, Mervic L, et al. The effect of dietary intake of coenzyme Q10 on skin parameters and condition: Results of a randomised, placebo-controlled, double-blind study. *Biofactors*. 2017 Jan 2;43(1):132-40.
5. Bratic A, Larsson NG. The role of mitochondria in aging. *J Clin Invest.* 2013 Mar;123(3):951-7.
6. Dludla PV, Orlando P, Silvestri S, et al. Coenzyme Q10 Supplementation Improves Adipokine Levels and Alleviates Inflammation and Lipid Peroxidation in Conditions of Metabolic Syndrome: A Meta-Analysis of Randomized Controlled Trials. *Int J Mol Sci.* 2020 May 4;21(9).
7. Fan L, Feng Y, Chen G-C, et al. Effects of coenzyme Q10 supplementation on inflammatory markers: A systematic review and meta-analysis of randomized controlled trials. *Pharmacological Research.* 2017 2017/05/01/;119:128-36.
8. Fujimoto S, Kurihara N, Hirata K, et al. Effects of coenzyme Q10 administration on pulmonary function and exercise performance in patients with chronic lung diseases. *Clin Investig.* 1993;71(8 Suppl):S162-6.
9. Johansson P, Dahlstrom O, Dahlstrom U, et al. Improved Health-Related Quality of Life, and More Days out of Hospital with Supplementation with Selenium and Coenzyme Q10 Combined. Results from a Double Blind, Placebo-Controlled Prospective Study. *J Nutr Health Aging.* 2015 Nov;19(9):870-7.
10. Mortensen SA, Rosenfeldt F, Kumar A, et al. The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. *JACC Heart Fail*. 2014 Dec;2(6):641-9.
11. Hidaka T, Fujii K, Funahashi I, et al. Safety assessment of coenzyme Q10 (CoQ10). *Biofactors.* 2008;32(1-4):199-208.
12. Singh RB, Neki NS, Kartikey K, et al. Effect of coenzyme Q10 on risk of atherosclerosis in patients with recent myocardial infarction. *Mol Cell Biochem.* 2003 Apr;246(1-2):75-82.
13. Rundek T, Naini A, Sacco R, et al. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol.* 2004 Jun;61(6):889-92.
14. Deichmann R, Lavie C, Andrews S. Coenzyme q10 and statin-induced mitochondrial dysfunction. *Ochsner J*. 2010 Spring;10(1):16-21.
15. Spindler M, Beal MF, Henchcliffe C. Coenzyme Q10 effects in neurodegenerative disease. *Neuropsychiatr Dis Treat.* 2009;5:597-610.
16. Liu J, Wang LN, Zhan SY, et al. Coenzyme Q10 for Parkinson's disease. *Cochrane Database of Systematic Reviews.* 2012 (5).
17. Shults CW, Oakes D, Kieburtz K, et al. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. *Arch Neurol*. 2002 Oct;59(10):1541-50.
18. Group HS. A randomized, placebo-controlled trial of coenzyme Q10 and remacemide in Huntington's disease. *Neurology.* 2001 Aug 14;57(3):397-404.
19. Dumont M, Kipiani K, Yu F, et al. Coenzyme Q10 decreases amyloid pathology and improves behavior in a transgenic mouse model of Alzheimer's disease. *J Alzheimers Dis*. 2011;27(1):211-23.
20. Chung HY, Kim DH, Lee EK, et al. Redefining Chronic Inflammation in Aging and Age-Related Diseases: Proposal of the Senoinflammation Concept. *Aging Dis*. 2019 Apr;10(2):367-82.
21. Zhai J, Bo Y, Lu Y, et al. Effects of Coenzyme Q10 on Markers of Inflammation: A Systematic Review and Meta-Analysis. *PLoS One.* 2017;12(1):e0170172.
22. Mantle D, Heaton RA, Hargreaves IP. Coenzyme Q10 and Immune Function: An Overview. *Antioxidants (Basel)*. 2021 May 11;10(5).
23. Dludla PV, Orlando P, Silvestri S, et al. Coenzyme Q(10) Supplementation Improves Adipokine Levels and Alleviates Inflammation and Lipid Peroxidation in Conditions of Metabolic Syndrome: A Meta-Analysis of Randomized Controlled Trials. *Int J Mol Sci*. 2020 May 4;21(9).
24. Gokbel H, Gul I, Belviranl M, et al. The effects of coenzyme Q10 supplementation on performance during repeated bouts of supramaximal exercise in sedentary men. *J Strength Cond Res*. 2010 Jan;24(1):97-102.
25. Comhair SA, Grandon D, Khan A, et al. Coenzyme Q in asthma. *Am J Respir Crit Care Med*. 2015 Jun 1;191(11):1336-8.
26. Nakazawa H, Ikeda K, Shinozaki S, et al. Coenzyme Q10 protects against burn-induced mitochondrial dysfunction and impaired insulin signaling in mouse skeletal muscle. *FEBS Open Bio.* 2019 Feb;9(2):348-63.
27. Salvioli S, Bonafe M, Capri M, et al. Mitochondria, aging and longevity--a new perspective. *FEBS Lett.* 2001 Mar 9;492(1-2):9-13.
28. Tian G, Sawashita J, Kubo H, et al. Ubiquinol-10 supplementation activates mitochondria functions to decelerate senescence in senescence-accelerated mice. *Antioxid Redox Signal*. 2014 Jun 1;20(16):2606-20.
29. Available at: https://www.genome.gov/genetics-glossary/Mitochondria. Accessed October, 20, 2022.
30. Zhong X, Yi X, da Silveira ESRC, et al. CoQ10 Deficiency May Indicate Mitochondrial Dysfunction in Cr(VI) Toxicity. *Int J Mol Sci.* 2017 Apr 24;18(4).
31. Liguori I, Russo G, Curcio F, et al. Oxidative stress, aging, and diseases. *Clin Interv Aging*. 2018;13:757-72.

Fisetin

The Longevity Flavonoid

Fisetin, a flavonoid found in strawberries and apples, is currently being studied for its effectiveness as a **senolytic** in humans.[1]

In preclinical studies, fisetin:

- Mimics effects of **calorie reduction**[2]
- Targets longevity pathways[2-6]
- Extends lifespan of mice by about **10%**[7]
- Removes **senescent** cells through **senolytic** action[7]
- Inhibits excess **mTOR** activation[8]

Fisetin is poorly *absorbed* due to its breakdown in the small intestines.

Bio-Fisetin solves this problem by enclosing **fisetin** with a compound from the fenugreek herb.

A **human** trial showed **bioavailability** of this **fisetin** compound increased up to ***25 times*** compared to fisetin by itself.[9]

Just one capsule daily of **Bio-Fisetin** helps manage **senescent cells** and may support overall longevity.

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30 vegetarian capsules

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References

1. Available at: https://www.mayo.edu/research/clinical-trials/cls-20438802. Accessed June 22, 2020,
2. *Life Sci.* 2018 Jan 15;193:171-9.
3. *Mini Rev Med Chem.* 2018;18(13):1151-7.
4. *Nutr Res Pract.* 2017 Oct;11(5):430-4.
5. *Biochem Biophys Res Commun.* 2015 Nov 27;467(4):638-44.
6. *Int Immunopharmacol.* 2017 Apr;45:135-47.
7. *EBioMedicine.* 2018 Oct;36:18-28.
8. *J Nutr Biochem.* 2013 Aug;24(8):1547-54.
9. *Manufacturer's study (in press for future publication).* 2020.

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ASTAXANTHIN is a carotenoid that benefits the brain, heart, skin, and immune system. Research suggests that astaxanthin can play a role in promoting cardiovascular health.[1]

Found naturally in seafood and algae, as little as **50%** of **astaxanthin** is normally ***absorbed*** in the bloodstream.[2,3]

Life Extension® combines **4 mg** of **astaxanthin** with a blend of four different **phospholipids**, which has been shown to enhance carotenoid ***absorption*** by **several-fold**.[4]

References
1. *Nutrients*. 2020 Jun; 12(6): 1896.
2. *Mol Nutr Food Res*. 2012 Sep;56(9):1385-97.
3. *Eur J Pharm Sci*. 2003 Jul;19(4):299-304.
4. *Int J Pharm*. 2011 June 30; 412(1-2):99-105.

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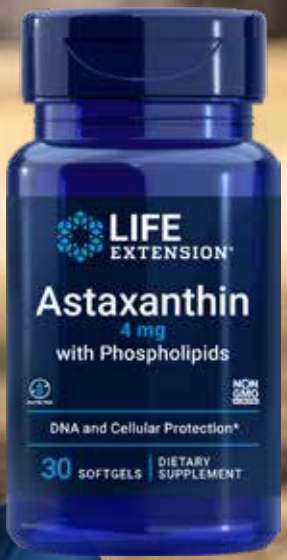

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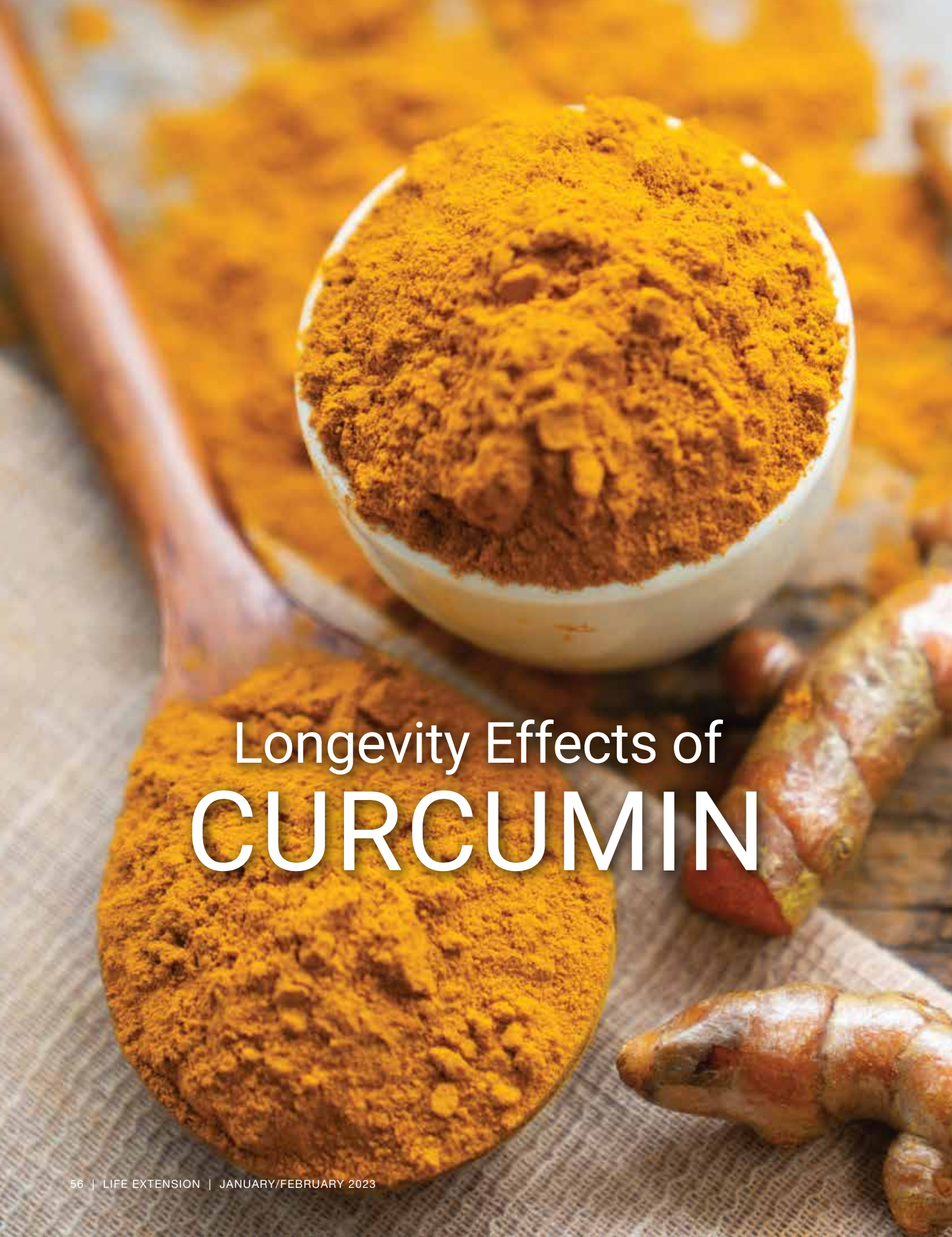
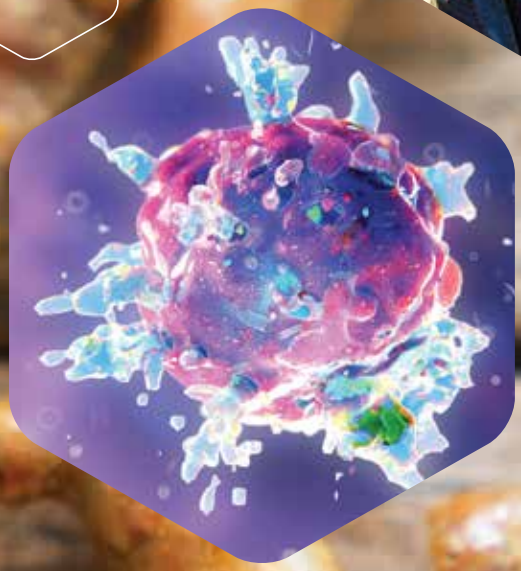


Longevity Effects of CURCUMIN

BY JIM RYDER



The spice **turmeric** has been used in Indian cooking and traditional medicine for ***thousands*** of years.[1]

There is some evidence from epidemiological studies that populations that regularly consume turmeric have *lower* rates of **Alzheimer's** as well as better-preserved cognition.[2]

A large body of scientific evidence reveals that turmeric's benefits are mainly attributable to the compound known as **curcumin**.

Research shows that **curcumin** helps *prevent* processes that drive **aging** and **chronic disorders**, including **cell senescence** and **chronic inflammation**.[3-5]

The overall effect may be to improve healthy **longevity**.

The Power of Curcumin

Curcumin is a yellowish pigment found in **turmeric**, a plant in the ginger family.

In studies, curcumin intake has been shown to **extend lifespan** of diverse species, from roundworms to mice.[6-11] In a study of fruit flies, for example, it increased the average lifespan by **26%**.[9]

In addition, research suggests it can help in the management of many conditions including metabolic syndrome, elevated lipids, arthritis, and more.[12]

A number of studies have found that curcumin supplementation led to improvements in **cognition** and **memory**.[13]

How does curcumin deliver its benefits? Science has identified several drivers of aging and chronic disease. **Curcumin** affects many of them[3-5] in ways that improve health.

Protecting Telomeres

Every strand of **DNA** in our body has protective end caps, called **telomeres**, that help maintain the stability and function of the genetic material.

As we age, these telomeres ***shorten***. When they are too short, the cell becomes dysfunctional or die. Shortened telomeres limit regeneration and stem cell function.

Telomerase is an enzyme that *builds up* the **length** of existing **telomeres**.

Curcumin has been shown in preclinical studies to give a boost to this anti-aging enzyme. It can enhance the expression and activity of **telomerase**, increasing the health and life of cells.[14,15]

Support Brain Function

Research has identified specific brain benefits for curcumin.

In animal studies, curcumin has been shown to:[16-18]

- Form new neurons in the hippocampus,
- Improve performance on memory tests,
- Reduce neuroinflammation, and
- Protect against memory loss.

But the benefits of curcumin go beyond just neuroprotection.

Fighting Glycation

Glycation occurs when sugars attach to proteins, fats, or nucleic acids, causing deleterious structural and functional changes. It is a major contributor to accelerated aging and many diseases of older age.[19,20]

This process even occurs in people with normal blood glucose. In diabetics and prediabetics, glycation is accelerated, leading to faster aging and higher risk for chronic disorders.

Preclinical studies have shown that curcumin protects cells and tissues from the damage caused by ***glycation***.[21-25]

One team of researchers has shown that, in cell culture models, curcumin can also block harmful effects when glycation has already occurred, preventing the inflammation and cellular dysfunction caused by **advanced glycation end products**.[25]

Reducing Senescent Cells

As cells age, some become **senescent**. These cells are dysfunctional and emit protein degrading enzymes but refuse to die off to make room for healthy cells. Senescent cells also secrete inflammatory compounds that damage surrounding tissues.[26]

Curcumin has demonstrated **senolytic** activity in preclinical studies,[27,28] which means it has the potential to *reduce* the number of senescent cells in tissues. In other similar models, it has also been shown to help favorably modulate the secretion of inflammatory compounds from these cells.[4]

Regulating Vital Proteins

Maladaptive activity of various essential structural and functional proteins in cells has been tied to accelerated aging, metabolic abnormalities, and chronic inflammation.[3-5]

Curcumin modulates their activity in ways that *reverse* age-related changes and protect cells against age-related damage. It can:[3-5]

- Inhibit **nuclear factor-kappa B (NF-kB)**, a protein complex associated with chronic inflammation,
- Reduce activity of **mTOR**, a protein linked to rapid aging and metabolic abnormalities that contribute to chronic disease,
- Boost activity of **AMPK**, an enzyme that supports healthy metabolism,
- Enhance function of **sirtuins**, proteins critical for maintaining health and longevity, and
- Support activity of **Nrf2**, a protein that regulates the body's defenses against oxidative stress.

Other Anti-Aging Mechanisms

There are many more anti-aging actions of curcumin. Among other benefits, curcumin:

- Acts as a potent **free-radical scavenger**, helping to prevent the oxidative stress that accompanies most age-related chronic disease,[29]
- Triggers production of the body's *own* antioxidant enzymes,[3-5]
- Reduces chronic inflammation,[3] another driver of aging and age-related disease,
- Supports healthy mitochondrial function,[30] and
- Activates **autophagy**, cellular "housekeeping," to rejuvenate cells and keep them functioning optimally.[31]

These and other actions can help reduce risk for disease and prevent accelerated aging.

WHAT YOU NEED TO KNOW

An Anti-Aging Nutrient

- Scientists have identified processes that drive **aging** and risk for disease, including oxidative stress, chronic inflammation, glycation, cellular senescence, telomere loss, and more.
- **Curcumin**, a polyphenol in turmeric, has been found to influence every one of these processes in ways that improve health and may slow aging.
- In animal studies, curcumin intake is associated with **longevity** and reduced risk for chronic age-related disease.
- Human studies show that curcumin use improves **cognition** and memory.

Summary

Curcumin is a potent anti-inflammatory compound.

Research over the last few decades reveals that curcumin favorably influences known contributors to **aging** and **chronic disease**.

In animal studies, curcumin extends **lifespan** while reducing risk for many age-related disorders. •

References

1. Available at: https://www.ncbi.nlm.nih.gov/books/NBK92752/. Accessed September 23, 2022.
2. Sikora E, Scapagnini G, Barbagallo M. Curcumin, inflammation, ageing and age-related diseases. *Immun Ageing*. 2010 Jan 17;7(1):1.
3. Bahrami A, Montecucco F, Carbone F, et al. Effects of Curcumin on Aging: Molecular Mechanisms and Experimental Evidence. *Biomed Res Int*. 2021;2021:8972074.
4. Benameur T, Soleti R, Panaro MA, et al. Curcumin as Prospective Anti-Aging Natural Compound: Focus on Brain. *Molecules.* 2021 Aug 7;26(16).
5. Zia A, Farkhondeh T, Pourbagher-Shahri AM, et al. The role of curcumin in aging and senescence: Molecular mechanisms. *Biomed Pharmacother.* 2021 Feb;134:111119.
6. Lee KS, Lee BS, Semnani S, et al. Curcumin extends life span, improves health span, and modulates the expression of age-associated aging genes in Drosophila melanogaster. *Rejuvenation Res.* 2010 Oct;13(5):561-70.
7. Liao VH, Yu CW, Chu YJ, et al. Curcumin-mediated lifespan extension in Caenorhabditis elegans. *Mech Ageing Dev.* 2011 Oct;132(10):480-7.
8. Shen LR, Parnell LD, Ordovas JM, et al. Curcumin and aging. *Biofactors*. 2013 Jan-Feb;39(1):133-40.
9. Shen LR, Xiao F, Yuan P, et al. Curcumin-supplemented diets increase superoxide dismutase activity and mean lifespan in Drosophila. *Age (Dordr)*. 2013 Aug;35(4):1133-42.
10. Soh JW, Marowsky N, Nichols TJ, et al. Curcumin is an early-acting stage-specific inducer of extended functional longevity in Drosophila. *Exp Gerontol.* 2013 Feb;48(2):229-39.
11. Stepien K, Wojdyla D, Nowak K, et al. Impact of curcumin on replicative and chronological aging in the Saccharomyces cerevisiae yeast. *Biogerontology.* 2020 Feb;21(1):109-23.
12. Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. *Foods.* 2017 Oct 22;6(10).
13. Seddon N, D'Cunha NM, Mellor DD, et al. Effects of Curcumin on Cognitive Function—A Systematic Review of Randomized Controlled Trials. *Exploratory Research and Hypothesis in Medicine.* 2019 03/19;4(1):1-11.
14. Taka T, Changtam C, Thaichana P, et al. Curcuminoid derivatives enhance telomerase activity in an in vitro TRAP assay. *Bioorg Med Chem Lett*. 2014 Nov 15;24(22):5242-6.
15. Xiao Z, Zhang A, Lin J, et al. Telomerase: a target for therapeutic effects of curcumin and a curcumin derivative in Abeta1-42 insult in vitro. *PLoS One.* 2014;9(7):e101251.
16. Yu Y, Shen Q, Lai Y, et al. Anti-inflammatory Effects of Curcumin in Microglial Cells. *Front Pharmacol*. 2018;9:386.
17. Sunny A, Ramalingam K, Das S, et al. Bioavailable curcumin alleviates lipopolysaccharide-induced neuroinflammation and improves cognition in experimental animals. *Pharmacognosy Magazine*. 2019 April 1, 2019;15(62):111-7.
18. Dong S, Zeng Q, Mitchell ES, et al. Curcumin enhances neurogenesis and cognition in aged rats: implications for transcriptional interactions related to growth and synaptic plasticity. *PLoS One.* 2012;7(2):e31211.
19. Kim CS, Park S, Kim J. The role of glycation in the pathogenesis of aging and its prevention through herbal products and physical exercise. *J Exerc Nutrition Biochem*. 2017 Sep 30;21(3):55-61.

Boosting Bioavailability

On its own, curcumin has *low* **bioavailability**. Much of the curcumin you consume is not absorbed into the bloodstream.

Scientists discovered that combining curcumin with galactomannans, from the spice fenugreek, **boosts bioavailability** by more than ***45 times*** compared to unformulated curcumin.[32]

Combining curcumin with other nutrients, including **turmerones** from turmeric and **gingerols** from ginger root, may further increase its bioavailability and health benefits.

20. Simm A. Protein glycation during aging and in cardiovascular disease. *J Proteomics.* 2013 Oct 30;92:248-59.
21. Hu TY, Liu CL, Chyau CC, et al. Trapping of methylglyoxal by curcumin in cell-free systems and in human umbilical vein endothelial cells. *J Agric Food Chem*. 2012 Aug 22;60(33):8190-6.
22. Liu JP, Feng L, Zhu MM, et al. The in vitro protective effects of curcumin and demethoxycurcumin in Curcuma longa extract on advanced glycation end products-induced mesangial cell apoptosis and oxidative stress. *Planta Med.* 2012 Nov;78(16):1757-60.
23. Sajithlal GB, Chithra P, Chandrakasan G. Effect of curcumin on the advanced glycation and cross-linking of collagen in diabetic rats. *Biochem Pharmacol.* 1998 Dec 15;56(12):1607-14.
24. Lima TFO, Costa MC, Figueiredo ID, et al. Curcumin, Alone or in Combination with Aminoguanidine, Increases Antioxidant Defenses and Glycation Product Detoxification in Streptozotocin-Diabetic Rats: A Therapeutic Strategy to Mitigate Glycoxidative Stress. *Oxid Med Cell Longev.* 2020;2020:1036360.
25. Tang Y, Chen A. Curcumin eliminates the effect of advanced glycation end-products (AGEs) on the divergent regulation of gene expression of receptors of AGEs by interrupting leptin signaling. *Lab Invest*. 2014 May;94(5):503-16.
26. Ohtani N. The roles and mechanisms of senescence-associated secretory phenotype (SASP): can it be controlled by senolysis? *Inflamm Regen.* 2022 Apr 2;42(1):11.
27. Cherif H, Bisson DG, Jarzem P, et al. Curcumin and o-Vanillin Exhibit Evidence of Senolytic Activity in Human IVD Cells In Vitro. *J Clin Med.* 2019 Mar 29;8(4).
28. Yousefzadeh MJ, Zhu Y, McGowan SJ, et al. Fisetin is a senotherapeutic that extends health and lifespan. *EBioMedicine.* 2018 Oct;36:18-28.
29. Jakubczyk K, Druzga A, Katarzyna J, et al. Antioxidant Potential of Curcumin-A Meta-Analysis of Randomized Clinical Trials. *Antioxidants (Basel).* 2020 Nov 6;9(11).
30. de Oliveira MR, Jardim FR, Setzer WN, et al. Curcumin, mitochondrial biogenesis, and mitophagy: Exploring recent data and indicating future needs. *Biotechnol Adv.* 2016 Sep-Oct;34(5):813-26.
31. Rainey NE, Moustapha A, Petit PX. Curcumin, a Multifaceted Hormetic Agent, Mediates an Intricate Crosstalk between Mitochondrial Turnover, Autophagy, and Apoptosis. *Oxid Med Cell Longev*. 2020;2020:3656419.
32. Kumar D, Jacob D, Subash PS, et al. Enhanced bioavailability and relative distribution of free (unconjugated) curcuminoids following the oral administration of a food-grade formulation with fenugreek dietary fibre: A randomised double-blind crossover study. *J Funct Foods.* 2016;22:578-87.

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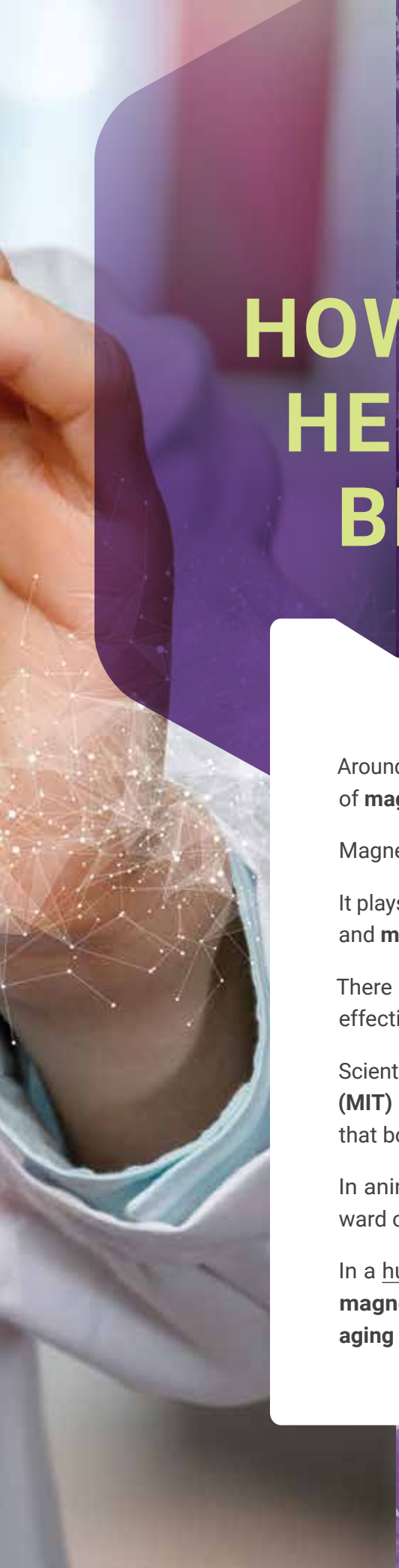
HOW MAGNESIUM HELPS *REVERSE* BRAIN AGING



BY DAVID CAMERON

Around **65%** of U.S. adults consume inadequate amounts of **magnesium** in their diet.[1,2]

Magnesium is especially important in the **brain**.

It plays key roles in cognitive function, including **learning** and **memory**.[3]

There are different forms of magnesium, but not all are effective at getting into the brain.

Scientists at the **Massachusetts Institute of Technology (MIT)** developed a form called **magnesium L-threonate** that boosts brain levels quickly and efficiently.[3-5]

In animal models, increasing brain magnesium helps ward off cognitive decline and dementia.[3-6]

In a human study of adults with cognitive impairment, **magnesium L-threonate** *reversed* measures of **brain aging** by an astonishing **nine years**.[7]

A Form for the Brain

Magnesium is essential for bone density, nerve function, and much more.[1,8-10]

Magnesium enables **brain cell** communication, particularly in areas critical for learning and formation of memories. Magnesium deficiency is associated with loss of **cognitive function**.[1,10-13]

MIT researchers developed **magnesium L-threonate** to more effectively elevate levels of magnesium in the brain.[3]

In a rodent study, **magnesium L-threonate** raised cerebral spinal fluid levels of **magnesium** by **54%**.[14]

How It Helps the Brain

Once in the brain, **magnesium** contributes to its healthy function in numerous ways.

For example, magnesium protects **synapses**, the **structural** communication connection points between brain cells.[11]

In animal studies, increasing brain levels of magnesium *increased* the total **number of synapses**, *improved* **synaptic plasticity** (the ability of synapses to adapt), and *stimulated* growth of new **brain cells**.[3-6,14,15]

This improved **cognitive function**, including **learning** and **memory**.

Animal models of brain aging, dementia, Parkinson's disease, and brain injury *all* show that magnesium intake results in improvements in **cognition**.[3,4,6,14-18]

Magnesium L-threonate leads to *greater* improvements in memory, number of synapses, and other cognitive functions than other forms tested.[5,14]

Reversing Human Brain Aging

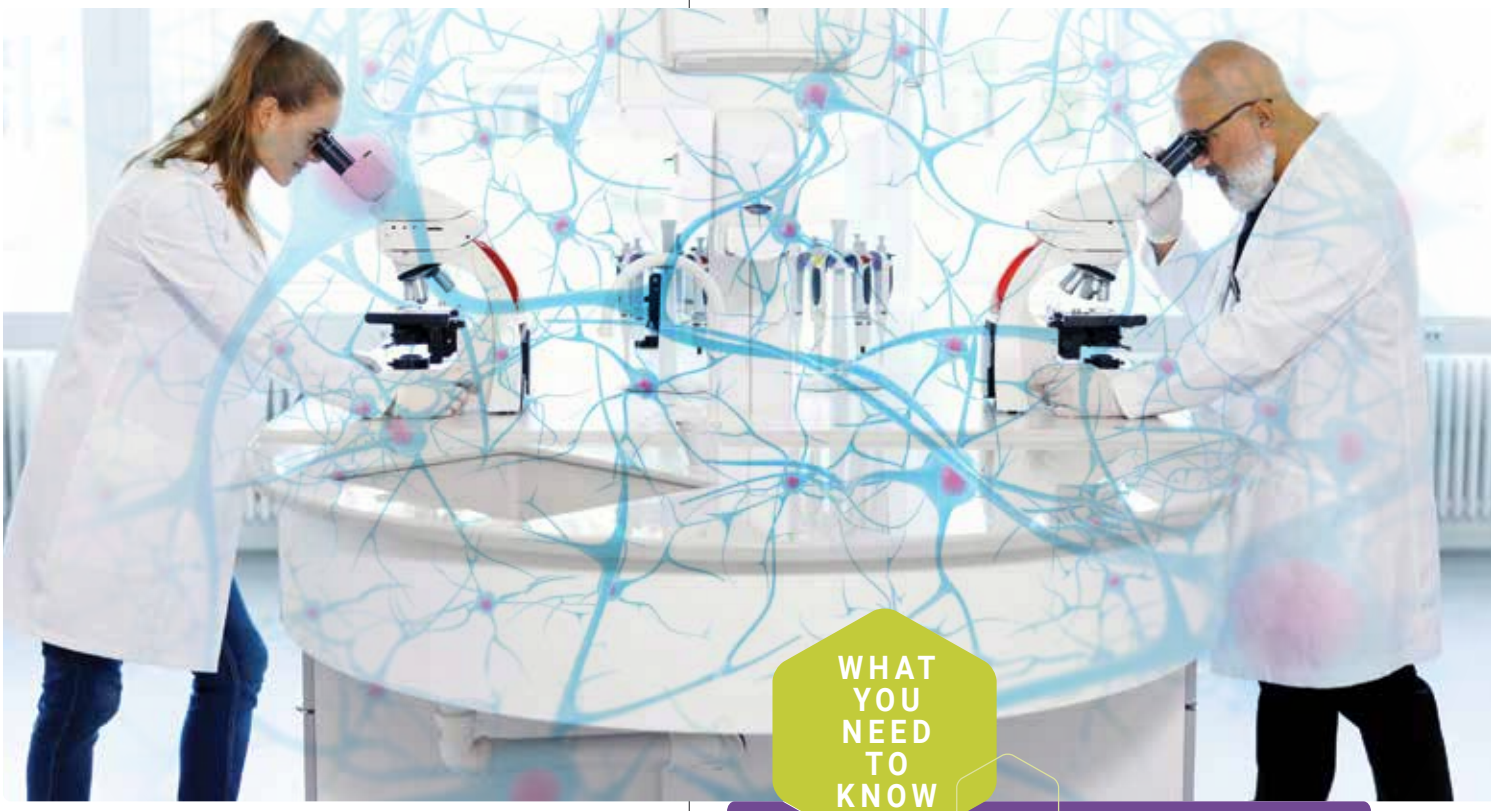
Scientists have long known that a **magnesium deficiency** can result in **cognitive** problems. Studies are now starting to demonstrate that *replenishing* magnesium can *improve* cognitive abilities.

In one clinical study, researchers gave older people with early cognitive impairment **1,500-2,000** mg (depending on body weight) of **magnesium L-threonate** or a **placebo** daily for 12 weeks.[7] Subjects began with some impairment in **executive functioning**, the ability to plan, adapt, focus, and make decisions.

At the beginning of the study, the participants averaged **57.8** years of age. However, their brain age based on cognitive functioning was **68.3** years old. By the end of the trial, those receiving magnesium L-threonate decreased their **brain age** a remarkable **nine years**.

Another human trial showed promising preliminary results in patients diagnosed with mild to moderate **dementia**. Even at this more advanced stage of cognitive decline, magnesium L-threonate led to improvements in **cognition** and **executive function**.[19]

Scientists have started to evaluate magnesium for neuropsychiatric conditions as well.



In a **2021** open-label, pilot study, 15 adults with moderate **ADHD** (attention deficit hyperactivity disorder) received **magnesium L-threonate** for up to 12 weeks.

Nearly half of the participants displayed clinical **improvements**. The authors concluded that supplementation was effective and well-tolerated.[20]

Summary

Magnesium deficiency is tied to health conditions including **cognitive decline**. Yet most adults do not get enough magnesium from their diets.

In the brain, magnesium is needed for the proper functioning of **synapses** involved in complex tasks such as learning and memory.

Magnesium L-threonate is easily absorbed and taken up into the brain, providing cognitive benefits as shown by animal and human studies. •

WHAT YOU NEED TO KNOW

Magnesium That Protects the Brain

- **Magnesium** is a mineral required for the function of hundreds of enzymes throughout the body.
- In the brain, it is needed for critical brain cell communication linked to cognitive functions like **learning** and **memory**.
- In animal models and human trials, magnesium L-threonate is tied to improvements in **cognitive function** and mental health.
- In one clinical study, magnesium L-threonate *reversed* measures of **brain aging** by **nine years**.

References

1. Kostov K, Halacheva L. Role of Magnesium Deficiency in Promoting Atherosclerosis, Endothelial Dysfunction, and Arterial Stiffening as Risk Factors for Hypertension. *Int J Mol Sci.* 2018 Jun 11;19(6).
2. Qu X, Jin F, Hao Y, et al. Magnesium and the risk of cardiovascular events: a meta-analysis of prospective cohort studies. *PLoS One.* 2013;8(3):e57720.
3. Slutsky I, Abumaria N, Wu LJ, et al. Enhancement of learning and memory by elevating brain magnesium. *Neuron.* 2010 Jan 28;65(2):165-77.
4. Huang Y, Huang X, Zhang L, et al. Magnesium boosts the memory restorative effect of environmental enrichment in Alzheimer's disease mice. *CNS Neurosci Ther.* 2018 Jan;24(1):70-9.
5. Sadir S, Tabassum S, Emad S, et al. Neurobehavioral and biochemical effects of magnesium chloride (MgCl2), magnesium sulphate (MgSO4) and magnesium-L-threonate (MgT) supplementation in rats: A dose dependent comparative study. *Pak J Pharm Sci.* 2019 Jan;32(1(Supplementary)):277-83.
6. Li W, Yu J, Liu Y, et al. Elevation of brain magnesium prevents synaptic loss and reverses cognitive deficits in Alzheimer's disease mouse model. *Mol Brain.* 2014 Sep 13;7:65.
7. Liu G, Weinger JG, Lu ZL, et al. Efficacy and Safety of MMFS-01, a Synapse Density Enhancer, for Treating Cognitive Impairment in Older Adults: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Alzheimers Dis.* 2016;49(4):971-90.
8. DiNicolantonio JJ, O'Keefe JH, Wilson W. Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. *Open Heart.* 2018;5(1):e000668.
9. Laires MJ, Monteiro CP, Bicho M. Role of cellular magnesium in health and human disease. *Front Biosci.* 2004 Jan 1;9:262-76.
10. Vink R. Magnesium in the CNS: recent advances and developments. *Magnes Res.* 2016 Mar 1;29(3):95-101.
11. Billard JM. Brain free magnesium homeostasis as a target for reducing cognitive aging. In: Vink R, Nechifor M, editors. *Magnesium in the Central Nervous System*. Adelaide (AU)2011.
12. Al-Ghazali K, Eltayeb S, Musleh A, et al. Serum Magnesium and Cognitive Function Among Qatari Adults. *Front Aging Neurosci.* 2020;12:101.
13. Chen C, Xun P, Unverzagt F, et al. Serum magnesium concentration and incident cognitive impairment: the reasons for geographic and racial differences in stroke study. *European journal of nutrition.* 2021 2021/04//;60(3):1511-20.
14. Sun Q, Weinger JG, Mao F, et al. Regulation of structural and functional synapse density by L-threonate through modulation of intraneuronal magnesium concentration. *Neuropharmacology.* 2016 Sep;108:426-39.
15. Jia S, Liu Y, Shi Y, et al. Elevation of Brain Magnesium Potentiates Neural Stem Cell Proliferation in the Hippocampus of Young and Aged Mice. *J Cell Physiol.* 2016 Sep;231(9):1903-12.
16. Shen Y, Dai L, Tian H, et al. Treatment Of Magnesium-L-Threonate Elevates The Magnesium Level In The Cerebrospinal Fluid And Attenuates Motor Deficits And Dopamine Neuron Loss In A Mouse Model Of Parkinson's disease. *Neuropsychiatr Dis Treat.* 2019;15:3143-53.
17. Liu C, Cheng Y, Guo Y, et al. Magnesium-L-threonate alleviate colonic inflammation and memory impairment in chronic-plus-binge alcohol feeding mice. *Brain Res Bull.* 2021 Sep;174:184-93.
18. Sen AP, Gulati A. Use of magnesium in traumatic brain injury. *Neurotherapeutics.* 2010 Jan;7(1):91-9.
19. Wroolie TE, Watson K, Chen K, et al. Open label trial of magnesium l-threonate in patients with dementia. Abstract from the 21st International Association of Gerontology and Geriatrics (IAGG) World Congress. *Innovation in Aging.* 2017;1(S1):170.
20. Surman C, Vaudreuil C, Boland H, et al. L-Threonic Acid Magnesium Salt Supplementation in ADHD: An Open-Label Pilot Study. *J Diet Suppl.* 2021;18(2):119-31.

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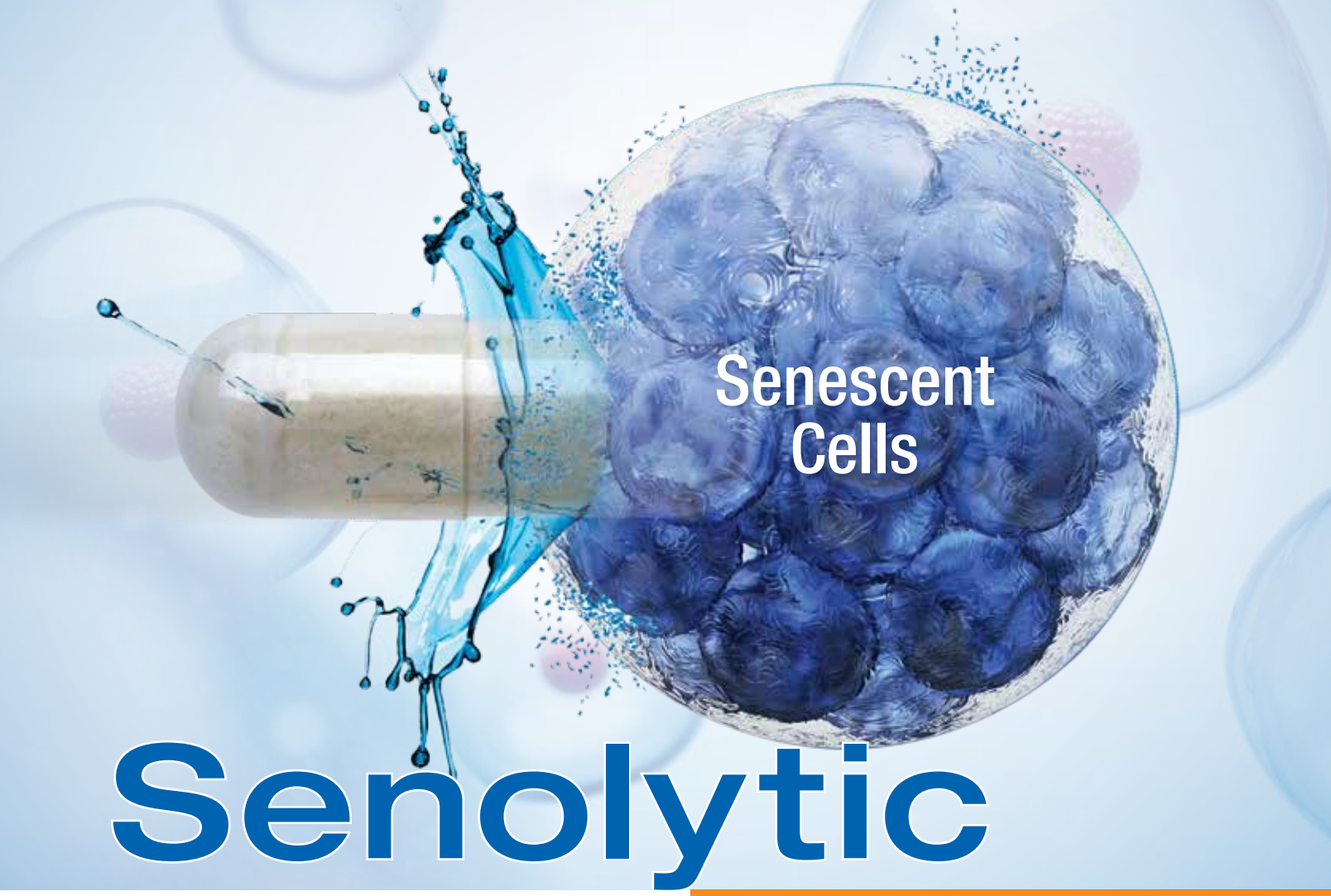

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Cataracts, Glaucoma, and Macular Degeneration

BY MARK STRATTON

As we age, conditions like **cataracts**, **glaucoma**, and **macular degeneration** threaten our vision.[1]

Scientists long ago discovered that **carotenoids** like **lutein** and **zeaxanthin** concentrate in the **macula** of the eye, where they help ***filter out*** damaging wavelengths of light.[2-4]

What few people know is these same **carotenoids** have *also* been shown to help protect the **eye lens** against **cataracts** and the **optic nerve** from **glaucoma** damage.[5-8]

Published studies continue to demonstrate whole-body benefits in those who ingest these plant-derived **carotenoids**.

CAROTENOIDS AND SYSTEMIC HEALTH

Carotenoids are a group of pigments found in many fruits and vegetables. They have demonstrated benefits in tissues throughout the body, including the **brain.**[7-9]

Taken up and concentrated in brain tissues, carotenoids have been found to be neuroprotective and supportive of cognitive function.[8]

Individuals with higher levels or higher intake of carotenoids have consistently been found to have better **cognitive** performance.[10-13]

A systematic review and meta-analysis found consistently lower blood levels of **lutein** and **zeaxanthin** in people diagnosed with **Alzheimer's** compared to healthy adults of the same age.[14]

Randomized clinical trials have also found significant improvements in cognitive functioning in those receiving a **carotenoid** supplement compared to those receiving a **placebo**.[15,16]

Those with *high* dietary intake of lutein and zeaxanthin have *lower* risk for **eye disease** and **vision loss**.

Modern Western diets rarely provide enough carotenoids.[17] Average lutein intake is low for adults.[18]

Oral intake of lutein-zeaxanthin supplements has been shown to boost the content of carotenoid pigments in the eyes and may improve whole-body health.[19,20]

Cataracts

Cataracts are a common degenerative disease that clouds the **lens** of the eye. The result is deteriorating vision and eventual blindness.

Cataracts are one of the most important leading causes of blindness in the world.[6] In modern societies, cataract surgery is rampant in people over age 65.

Studies show that people with the ***highest*** intake of lutein and zeaxanthin have the ***lowest*** rates of cataracts, age-related macular degeneration, and other age-related eye conditions.[5,21,22]

Glaucoma

In those with **glaucoma**, higher intake of **lutein** protects the photoreceptors and nerve cells of the retina against cell death. The result is less progression of visual loss and ***improved visual performance***.[22]

Studies have demonstrated that a larger dietary intake of carotenoids is associated with a lower risk of glaucoma.[22] In individuals already suffering from glaucoma, higher carotenoid levels in the retina consistently predict better visual performance.

Randomized controlled trials of carotenoid supplementation in patients with glaucoma demonstrate that they are effective at both boosting retinal levels of the nutrients and improving markers of visual function.[23,24]

Those with glaucoma should also follow conventional guidelines including taking steps to reduce intraocular pressure that slowly damages the optic nerve.

Macular Degeneration

When blue light and ultraviolet light hit the retina, they can damage **photoreceptors**, the cells that detect light.[2,25] Without photoreceptors, vision is not possible.[26]

Exposure to **blue light** is tied to an increased risk of age-related **macular degeneration,** the leading cause of severe vision loss and **blindness** in people over 60.[26]

Oxidative stress and inflammation further drive the progression of macular degeneration.[2]

Lutein and **zeaxanthin** in the retina defend against macular degeneration in multiple ways. They filter out harmful wavelengths of light *and* are potent **antioxidants** and **anti-inflammatories**.[2,4]

One study conducted over more than **20 years** found that people with the *highest* intake of lutein and zeaxanthin have a remarkable ***41% lower risk*** of advanced **macular degeneration**.[27]

Taking lutein and zeaxanthin doesn't just *prevent* macular degeneration. It may also ***reverse*** some visual loss that has occurred.[28]

Clinical studies show that oral intake of these carotenoids may slow the progression of macular degeneration in those who already have early signs of disease,[3,21,28-31] and may also support ***visual acuity*** (the ability to see sharply at a given distance).[28]

Other studies show that taking **lutein** and **zeaxanthin** improves eye health, enhances visual function, reduces nighttime glare, and improves visual contrast.[19,32-34]

In one recent trial, older adults who had difficulty with **night vision** took a placebo or a blend of **zeaxanthin** and **lutein** daily for six months.[35] Those taking the carotenoids had significant improvements in nighttime visual functions.

Digital Eye Strain

Threats to our eyes are all around us, from *ultraviolet rays* in sunlight to the blue light from our digital screens.

Gazing at smart phones, computers, tablets, LED televisions, and other digital screens increases exposure to **blue light**, which contributes to eye disease and vision loss.[25,26,36] The **LED lightbulbs** in most of our homes and workplaces also emit a high level of blue light.[36]

In addition to the long-term risk of **vision loss**, blue light is tied to **digital eye strain**, which causes symptoms like eye pain, dry eyes, headache, and blurred vision.[37]

The retina and macula are light-sensitive **eye tissues** that make vision possible. When the carotenoids lutein and zeaxanthin are orally ingested, they are taken up in these eye tissues where they help shield against harmful forms of light, including **ultraviolet** and **blue light.**[2,38,39]

The carotenoids **lutein** and **zeaxanthin** help shield the eyes from harmful blue light wavelengths, which can help protect against eye strain *and* vision loss.[28]

Retinopathy

Diabetic retinopathy is another cause of poor eyesight in older adults. Carotenoids protect against this condition as well.

In patients with **diabetic retinopathy**, body levels of **lutein** and **zeaxanthin** are typically *lower* than in normal subjects. Oral intake of these carotenoids has been shown to improve **visual clarity** and **contrast** in those displaying symptoms of diabetic eye disease.[40]

Ensuring adequate intake of lutein and zeaxanthin is vital for eye health at any age.[18]

Summary

In eye tissues, the carotenoids **lutein** and **zeaxanthin** help filter out harmful wavelengths of light that lead to vision loss.

These nutrients defend against most age-related **eye disorders** and the damage done by exposure to **blue light** from digital screens.

Studies long ago showed that *higher* intake of lutein and zeaxanthin boosts macular pigment density and *reduce* risk for **vision loss** from **macular degeneration**.

More recent data show these same carotenoids also help protect against **cataracts**, glaucoma-induced damage to the **optic nerve**, and **diabetic** eye disorders.

Evidence indicates that supplementing with carotenoids is supportive of optimal brain and cognitive function. •

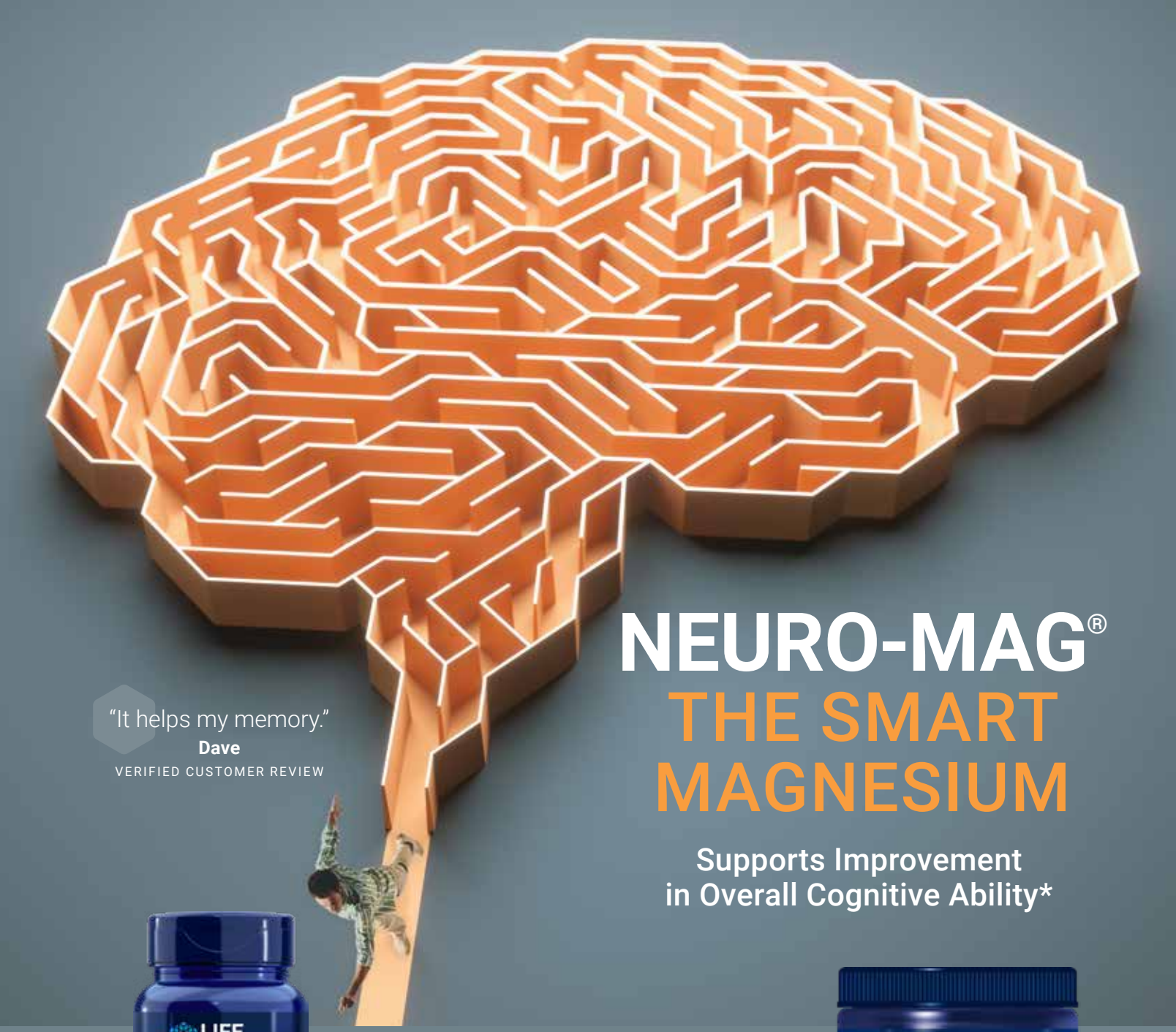
WHAT YOU NEED TO KNOW

Shield Your Eyes with Carotenoids

- Age-related **loss of vision** is commonly caused by cataracts, age-related macular degeneration, glaucoma, and diabetes.
- Exposure to **blue light** from digital screens and LED lights can accelerate loss of vision and cause eye strain.
- The eye is capable of concentrating carotenoids, particularly **lutein** and **zeaxanthin**, in the retina and macula—its light-sensitive tissues—to shield against dangerous ultraviolet and blue light.
- Studies show that oral intake of lutein and zeaxanthin can reduce the risk and slow the progression of *all* these age-related eye conditions. These nutrients have the potential to prevent degenerative vision loss, improve visual parameters in those with age-related degenerative eye conditions, and to delay progression of these conditions and the worsening of vision associated with them.

References

1. Pelletier AL, Rojas-Roldan L, Coffin J. Vision Loss in Older Adults. *Am Fam Physician.* 2016 Aug 1;94(3):219-26.
2. Bian Q, Gao S, Zhou J, et al. Lutein and zeaxanthin supplementation reduces photooxidative damage and modulates the expression of inflammation-related genes in retinal pigment epithelial cells. *Free Radic Biol Med.* 2012 Sep 15;53(6):1298-307.
3. Huang YM, Dou HL, Huang FF, et al. Effect of supplemental lutein and zeaxanthin on serum, macular pigmentation, and visual performance in patients with early age-related macular degeneration. *Biomed Res Int.* 2015;2015:564738.
4. Kijlstra A, Tian Y, Kelly ER, et al. Lutein: more than just a filter for blue light. *Prog Retin Eye Res.* 2012 Jul;31(4):303-15.
5. Ma L, Hao ZX, Liu RR, et al. A dose-response meta-analysis of dietary lutein and zeaxanthin intake in relation to risk of age-related cataract. *Graefes Arch Clin Exp Ophthalmol.* 2014 Jan;252(1):63-70.
6. Manayi A, Abdollahi M, Raman T, et al. Lutein and cataract: from bench to bedside. *Crit Rev Biotechnol.* 2016 Oct;36(5):829-39.
7. Ames BN. Prolonging healthy aging: Longevity vitamins and proteins. *Proc Natl Acad Sci U S A.* 2018 Oct 23;115(43):10836-44.
8. Tan BL, Norhaizan ME. Carotenoids: How Effective Are They to Prevent Age-Related Diseases? *Molecules.* 2019 May 9;24(9).
9. Eggersdorfer M, Wyss A. Carotenoids in human nutrition and health. *Arch Biochem Biophys.* 2018 Aug 15;652:18-26.
10. Christensen K, Gleason CE, Mares JA. Dietary carotenoids and cognitive function among US adults, NHANES 2011-2014. *Nutr Neurosci.* 2020 Jul;23(7):554-62.
11. Feeney J, Finucane C, Savva GM, et al. Low macular pigment optical density is associated with lower cognitive performance in a large, population-based sample of older adults. *Neurobiol Aging.* 2013 Nov;34(11):2449-56.
12. Renzi LM, Dengler MJ, Puente A, et al. Relationships between macular pigment optical density and cognitive function in unimpaired and mildly cognitively impaired older adults. *Neurobiol Aging.* 2014 Jul;35(7):1695-9.
13. Vishwanathan R, Iannaccone A, Scott TM, et al. Macular pigment optical density is related to cognitive function in older people. *Age Ageing.* 2014 Mar;43(2):271-5.
14. Qu M, Shi H, Wang K, et al. The Associations of Plasma/Serum Carotenoids with Alzheimer's Disease: A Systematic Review and Meta-Analysis. *J Alzheimers Dis.* 2021;82(3):1055-66.
15. Davinelli S, Ali S, Solfrizzi V, et al. Carotenoids and Cognitive Outcomes: A Meta-Analysis of Randomized Intervention Trials. *Antioxidants (Basel).* 2021 Feb 2;10(2).
16. Hammond BR, Jr., Miller LS, Bello MO, et al. Effects of Lutein/Zeaxanthin Supplementation on the Cognitive Function of Community Dwelling Older Adults: A Randomized, Double-Masked, Placebo-Controlled Trial. *Front Aging Neurosci.* 2017;9:254.
17. Hendrickson SJ, Willett WC, Rosner BA, et al. Food predictors of plasma carotenoids. *Nutrients.* 2013 Oct 11;5(10):4051-66.
18. Stringham JM, Johnson EJ, Hammond BR. Lutein across the Lifespan: From Childhood Cognitive Performance to the Aging Eye and Brain. *Curr Dev Nutr.* 2019 Jul;3(7):nzz066.
19. Stringham JM, Stringham NT. Serum and retinal responses to three different doses of macular carotenoids over 12 weeks of supplementation. *Exp Eye Res.* 2016 Oct;151:1-8.
20. Wilson LM, Tharmarajah S, Jia Y, et al. The Effect of Lutein/Zeaxanthin Intake on Human Macular Pigment Optical Density: A Systematic Review and Meta-Analysis. *Adv Nutr.* 2021 Dec 1;12(6):2244-54.
21. Lem DW, Davey PG, Gierhart DL, et al. A Systematic Review of Carotenoids in the Management of Age-Related Macular Degeneration. *Antioxidants (Basel).* 2021 Aug 5;10(8).
22. Lem DW, Gierhart DL, Davey PG. Carotenoids in the Management of Glaucoma: A Systematic Review of the Evidence. *Nutrients.* 2021 Jun 6;13(6).
23. Hunter AML, Loskutova E, Lingham G, et al. ARVO Annual Meeting Abstract. Higher macular pigment levels are associated with better contrast sensitivity and photostress recovery time in patients with open-angle glaucoma supplemented with carotenoids. *Invest Ophthalmol Vis Sci.* 2022;63(2699-A0063).
24. Loughman J, Loskutova E, Butler JS, et al. Macular Pigment Response to Lutein, Zeaxanthin, and Meso-zeaxanthin Supplementation in Open-Angle Glaucoma: A Randomized Controlled Trial. *Ophthalmol Sci.* 2021 Sep;1(3):100039.
25. Alaimo A, Linares GG, Bujjamer JM, et al. Toxicity of blue led light and A2E is associated to mitochondrial dynamics impairment in ARPE-19 cells: implications for age-related macular degeneration. *Arch Toxicol.* 2019 May;93(5):1401-15.
26. Algvere PV, Marshall J, Seregard S. Age-related maculopathy and the impact of blue light hazard. *Acta Ophthalmol Scand.* 2006 Feb;84(1):4-15.
27. Wu J, Cho E, Willett WC, et al. Intakes of Lutein, Zeaxanthin, and Other Carotenoids and Age-Related Macular Degeneration During 2 Decades of Prospective Follow-up. *JAMA Ophthalmol.* 2015 Dec;133(12):1415-24.
28. Liu R, Wang T, Zhang B, et al. Lutein and zeaxanthin supplementation and association with visual function in age-related macular degeneration. *Invest Ophthalmol Vis Sci.* 2014 Dec 16;56(1):252-8.
29. Berrow EJ, Bartlett HE, Eperjesi F. The effect of nutritional supplementation on the multifocal electroretinogram in healthy eyes. *Doc Ophthalmol.* 2016 Apr;132(2):123-35.
30. Huang YM, Dou HL, Huang FF, et al. Changes following supplementation with lutein and zeaxanthin in retinal function in eyes with early age-related macular degeneration: a randomised, double-blind, placebo-controlled trial. *Br J Ophthalmol.* 2015 Mar;99(3):371-5.
31. Ma L, Dou HL, Huang YM, et al. Improvement of retinal function in early age-related macular degeneration after lutein and zeaxanthin supplementation: a randomized, double-masked, placebo-controlled trial. *Am J Ophthalmol.* 2012 Oct;154(4):625-34 e1.
32. Nolan JM, Power R, Stringham J, et al. Enrichment of Macular Pigment Enhances Contrast Sensitivity in Subjects Free of Retinal Disease: Central Retinal Enrichment Supplementation Trials - Report 1. *Invest Ophthalmol Vis Sci.* 2016 Jun 1;57(7):3429-39.
33. Stringham JM, O'Brien KJ, Stringham NT. Macular carotenoid supplementation improves disability glare performance and dynamics of photostress recovery. *Eye Vis (Lond).* 2016;3:30.
34. Machida N, Kosehira M, Kitaichi N. Clinical Effects of Dietary Supplementation of Lutein with High Bio-Accessibility on Macular Pigment Optical Density and Contrast Sensitivity: A Randomized Double-Blind Placebo-Controlled Parallel-Group Comparison Trial. *Nutrients.* 2020 Sep 28;12(10).
35. Richer S, Novil S, Gullett T, et al. Night Vision and Carotenoids (NVC): A Randomized Placebo Controlled Clinical Trial on Effects of Carotenoid Supplementation on Night Vision in Older Adults. *Nutrients.* 2021 Sep 14;13(9).
36. Available at: https://www.reviewsce.com/ce/the-lowdown-on-blue-light-good-vs-bad-and-its-connection-to-amd-109744. Accessed October 13, 2022,
37. Available at: https://thevisioncouncil.org/blog/vision-council-shines-light-protecting-sight-and-health-multi-screen-era. Accessed October 13, 2022,
38. Xue C, Rosen R, Jordan A, et al. Management of Ocular Diseases Using Lutein and Zeaxanthin: What Have We Learned from Experimental Animal Studies? *J Ophthalmol.* 2015;2015:523027.
39. Loskutova E, Nolan J, Howard A, et al. Macular pigment and its contribution to vision. *Nutrients.* 2013 May 29;5(6):1962-9.
40. Hu BJ, Hu YN, Lin S, et al. Application of Lutein and Zeaxanthin in nonproliferative diabetic retinopathy. *Int J Ophthalmol.* 2011;4(3):303-6.
41. Cort A, Ozturk N, Akpinar D, et al. Suppressive effect of astaxanthin on retinal injury induced by elevated intraocular pressure. *Regul Toxicol Pharmacol.* 2010 Oct;58(1):121-30.
42. Kidd P. Astaxanthin, cell membrane nutrient with diverse clinical benefits and anti-aging potential. *Altern Med Rev.* 2011 Dec;16(4):355-64.
43. Fernandez-Albarral JA, de Hoz R, Ramirez AI, et al. Beneficial effects of saffron (Crocus sativus L.) in ocular pathologies, particularly neurodegenerative retinal diseases. *Neural Regen Res.* 2020 Aug;15(8):1408-16.
44. Heitmar R, Brown J, Kyrou I. Saffron (Crocus sativus L.) in Ocular Diseases: A Narrative Review of the Existing Evidence from Clinical Studies. *Nutrients.* 2019 Mar 18;11(3).
45. Li X, Sun M, Long Y. Cyanidin-3-O-Glucoside Attenuates Lipopolysaccharide-Induced Inflammation in Human Corneal Epithelial Cells by Inducing Let-7b-5p-Mediated HMGA2/PI3K/Akt Pathway. *Inflammation.* 2020 Jun;43(3):1088-96.
46. Nakaishi H, Matsumoto H, Tominaga S, et al. Effects of black currant anthocyanoside intake on dark adaptation and VDT work-induced transient refractive alteration in healthy humans. *Altern Med Rev.* 2000 Dec;5(6):553-62.
47. Pawlowska E, Szczepanska J, Koskela A, et al. Dietary Polyphenols in Age-Related Macular Degeneration: Protection against Oxidative Stress and Beyond. *Oxid Med Cell Longev.* 2019;2019:9682318.



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- **Saffron** has been shown to help support **vision** as demonstrated by doctors' eye exams.[1]
- **Alpha-carotene** further helps support **macular density**.[1]

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References
1. *JAMA Ophthalmol.* 2015;133(12):1415-24.
2. *Nutrients.* 2013 April;5(4):1169-85.
3. *Nutrition.* 2011 Sep;27(9):960-6.
4. *Free Radic Biol Med.* 2012;53(6):1298-307.
5. *J Ophthalmol.* 2015;2015:523027.
6. *Evid Based Complement Alternat Med.* 2012;2012:429124.
7. *Invest Ophthalmol Vis Sci.* 2010;51(12):6118-24.
8. *J Agric Food Chem.* 2003 Jun 4;51(12):3560-3.

ACHIEVING *SUSTAINED*

VITAMIN C BLOOD LEVELS

BY MICHAEL DOWNEY

Vitamin C supports the **immune system** and other aspects of health.

The human body cannot produce vitamin C.[1]

Daily intake is required to sustain vitamin C levels.

At doses above **200 mg**, however, **vitamin C** is only partially **absorbed** and rapidly meta-bolized by the body.[2]

By combining it with plant-based compounds, more **vitamin C** can be ***absorbed*** and ***maintained***.

Consumers can achieve nearly ***seven times*** greater vitamin C **bioavailability** compared to an equivalent dose of regular (unformulated) **vitamin C**.[3]

Absorbing More Vitamin C

Studies show that ***higher levels*** of vitamin C enhance immune function and may help reduce cardiovascular risks.[4,5]

At doses *over* **200 mg**, unformulated vitamin C is only *partially absorbed* and rapidly used by the body.

A new delivery system circumvents this problem. It elevates blood levels of vitamin C nearly **seven times** more than unformulated vitamin C—*and* it delivers higher levels ***over an extended period***.[3]

This improved delivery of vitamin C was achieved by combining two different **plant-based** formulation methods. Both have been used in the past to enhance **bioavailability** (absorbability) of other nutrients.

- The first method involves **liposomes**. These are small structures made of plant-derived **phospholipids**, the same types of compounds making up cell membranes of all living cells. Encapsulating vitamin C in liposomes improves its **absorption** into the bloodstream.

- But liposomes themselves can degrade. The second method uses a compound known as a **hydrogel** to *protect* the liposomes. A hydrogel is comprised of fiber called **galactomannans**, derived from fenugreek seeds. It surrounds and shields the liposomes, allowing for **sustained absorption** of the vitamin C released in the intestines.

Together, these techniques enable *more* **vitamin C** to be absorbed over a *longer* period of time.

Sustained Vitamin C Blood Levels

When regular, *unformulated* vitamin C is taken, blood levels peak about **one hour** after ingestion and then rapidly drop back to baseline.

When **liposomal hydrogel vitamin C** is taken, blood levels continue to rise up to ***four*** hours after ingestion *and* reach a ***much higher*** level. Taking this formulation just once a day leads to high around-the-clock vitamin C levels in the blood.

A recently **published** clinical study measured blood plasma levels of vitamin C and found: [3]

Taking **400 mg** of vitamin C in the **liposomal hydrogel** formula increased average *overall* body exposure to vitamin C over a 12-hour period by close to ***seven times*** compared to the same dose of unformulated vitamin C.

At **12 hours** after ingestion, this **liposomal hydrogel** formula maintained ***higher*** blood levels than the same dose of regular, unformulated vitamin C.

Defense Against Infections

Maintaining high levels of vitamin C can help it achieve its benefits, which include helping to improve **cardiovascular health**, initiate **tissue-healing** processes,[6,7] and reduce the risk, duration, and severity of the common cold.[8,9]

Vitamin C's most important function may be helping the **immune system** to defend against **viral** and other **infections**.[10]

Vitamin C fights infection by:

- Helping **neutrophils**, a first line of immune defense, reach an infection. In a study of participants with inadequate vitamin C status, daily vitamin C intake led to a **20% increase** in neutrophil migration.[11] In another study, vitamin C intake (with vitamin E) enhanced neutrophils' ability to kill infectious agents.[12]

- Promoting the growth, maturation, antibody production, and survival of **lymphocytes**.[13-16] Lymphocytes include B cells, T cells, and natural killer (NK) cells, all vital parts of the immune system's ability to recognize and attack foreign invaders.

- Providing **infection barrier support**. Vitamin C is required for the synthesis of **collagen**, a structural protein providing strength and durability to barrier tissues that prevent viruses, bacteria, and other infectious agents from entering the body in the first place.[17]

Liposomal hydrogel vitamin C makes it easier to achieve these and other health benefits.

Summary

Higher vitamin C levels can improve immune function and provide other benefits.

However, at doses greater than **200 mg**, unformulated vitamin C is partially absorbed and rapidly metabolized.

A **liposomal hydrogel** delivery system yields approximately **seven times** higher vitamin C plasma levels and maintains higher levels **all day long**. •

WHAT YOU NEED TO KNOW

More Efficient, Longer-Lasting Vitamin C

- **Vitamin C** is critical for immune function, protection against infection, cardiovascular health, and more. It is not made by the body and must be taken orally.
- Doses above **200 mg** of *unformulated* vitamin C are only partially absorbed and metabolize quickly.
- A new **liposomal hydrogel** formula protects the vitamin C, allowing *more* of it to be absorbed over a *longer* period of time. This results in significantly *higher* blood levels of vitamin C that persist for **24 hours**.

The Importance of High-Dose Vitamin C

- Maintaining optimal levels of **vitamin C** throughout the day delivers wide-ranging benefits, including:
- **Immune support.** Immune cells need vitamin C for activation and proper function, including fighting infections, reducing risk, duration, and severity of colds, and reducing breathing difficulties associated with airway irritation and asthma.[8,10-18]
- **Wound healing and tissue strengthening.** Vitamin C is required for the synthesis of **collagen**, which provides strength to connective tissues throughout the body (including skin, bones, and cartilage) and helps accelerate wound healing after injury.[19-21]
- **Cardiovascular protection.** Compared to those with the lowest levels, people with the *highest* blood levels of vitamin C may be ***less likely to die*** from all causes, cardiovascular disease and ischemic heart disease and have a ***42% lower risk of stroke.***[2,22-25]
- **Antioxidant activity.** Vitamin C can help prevent or reduce **oxidative damage**, a major contributor to aging and age-related disease.[26]

References

1. Available at: https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional. Accessed September 18, 2022.
2. Levine GN, Frei B, Koulouris SN, et al. Ascorbic acid reverses endothelial vasomotor dysfunction in patients with coronary artery disease. *Circulation.* 1996 Mar 15;93(6):1107-13.
3. Joseph A, Kumar D, Balakrishnan A, et al. Surface-engineered liposomal particles of calcium ascorbate with fenugreek galactomannan enhanced the oral bioavailability of ascorbic acid: a randomized, double-blinded, 3-sequence, crossover study. *RSC Adv.* 2021 Nov 23;11(60):38161-71.
4. Available at: https://lpi.oregonstate.edu/mic/vitamins/vitamin-C. Accessed September 18, 2022.
5. Schlueter AK, Johnston CS. Vitamin C: Overview and Update. *Journal of Evidence-Based Complementary & Alternative Medicine.* 2011;16(1):49-57.
6. Mohammed BM, Fisher BJ, Kraskauskas D, et al. Vitamin C promotes wound healing through novel pleiotropic mechanisms. *Int Wound J.* 2016 Aug;13(4):572-84.
7. Morelli MB, Gambardella J, Castellanos V, et al. Vitamin C and Cardiovascular Disease: An Update. *Antioxidants (Basel).* 2020 Dec 3;9(12).
8. Kim TK, Lim HR, Byun JS. Vitamin C supplementation reduces the odds of developing a common cold in Republic of Korea Army recruits: randomised controlled trial. *BMJ Mil Health.* 2022 Apr;168(2):117-23.
9. Bucher A, White N. Vitamin C in the Prevention and Treatment of the Common Cold. *Am J Lifestyle Med.* 2016 May-Jun;10(3):181-3.
10. Ang A, Pullar JM, Currie MJ, et al. Vitamin C and immune cell function in inflammation and cancer. *Biochem Soc Trans.* 2018 Oct 19;46(5):1147-59.
11. Bozonet SM, Carr AC, Pullar JM, et al. Enhanced human neutrophil vitamin C status, chemotaxis and oxidant generation following dietary supplementation with vitamin C-rich SunGold kiwifruit. *Nutrients.* 2015 Apr 9;7(4):2574-88.
12. de la Fuente M, Ferrandez MD, Burgos MS, et al. Immune function in aged women is improved by ingestion of vitamins C and E. *Can J Physiol Pharmacol.* 1998 Apr;76(4):373-80.
13. Huijskens MJ, Walczak M, Koller N, et al. Technical advance: ascorbic acid induces development of double-positive T cells from human hematopoietic stem cells in the absence of stromal cells. *J Leukoc Biol.* 2014 Dec;96(6):1165-75.
14. Huijskens MJ, Walczak M, Sarkar S, et al. Ascorbic acid promotes proliferation of natural killer cell populations in culture systems applicable for natural killer cell therapy. *Cytotherapy.* 2015 May;17(5):613-20.
15. Manning J, Mitchell B, Appadurai DA, et al. Vitamin C promotes maturation of T-cells. *Antioxid Redox Signal.* 2013 Dec 10;19(17):2054-67.
16. Tanaka M, Muto N, Gohda E, et al. Enhancement by ascorbic acid 2-glucoside or repeated additions of ascorbate of mitogen-induced IgM and IgG productions by human peripheral blood lymphocytes. *Jpn J Pharmacol.* 1994 Dec;66(4):451-6.
17. Carr AC, Maggini S. Vitamin C and Immune Function. *Nutrients.* 2017 Nov 3;9(11).
18. Hemila H. Vitamin C and common cold-induced asthma: a systematic review and statistical analysis. *Allergy Asthma Clin Immunol.* 2013 Nov 26;9(1):46.
19. Pinnell SR. Regulation of collagen biosynthesis by ascorbic acid: a review. *Yale J Biol Med.* 1985 Nov-Dec;58(6):553-9.
20. Bikker A, Wielders J, van Loo R, et al. Ascorbic acid deficiency impairs wound healing in surgical patients: Four case reports. *International Journal of Surgery Open.* 2016 03/01;2:15-8.
21. Ravetti S, Clemente C, Brignone S, et al. Ascorbic Acid in Skin Health. *Cosmetics.* 2019;6(4):58.
22. Khaw KT, Bingham S, Welch A, et al. Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. European Prospective Investigation into Cancer and Nutrition. *Lancet.* 2001 Mar 3;357(9257):657-63.
23. Myint PK, Luben RN, Welch AA, et al. Plasma vitamin C concentrations predict risk of incident stroke over 10 y in 20 649 participants of the European Prospective Investigation into Cancer Norfolk prospective population study. *Am J Clin Nutr.* 2008 Jan;87(1):64-9.
24. Gokce N, Keaney JF, Jr., Frei B, et al. Long-term ascorbic acid administration reverses endothelial vasomotor dysfunction in patients with coronary artery disease. *Circulation.* 1999 Jun 29;99(25):3234-40.
25. Hornig B, Arakawa N, Kohler C, et al. Vitamin C improves endothelial function of conduit arteries in patients with chronic heart failure. *Circulation.* 1998 Feb 3;97(4):363-8.
26. Monacelli F, Acquarone E, Giannotti C, et al. Vitamin C, Aging and Alzheimer's Disease. *Nutrients.* 2017 Jun 27;9(7).

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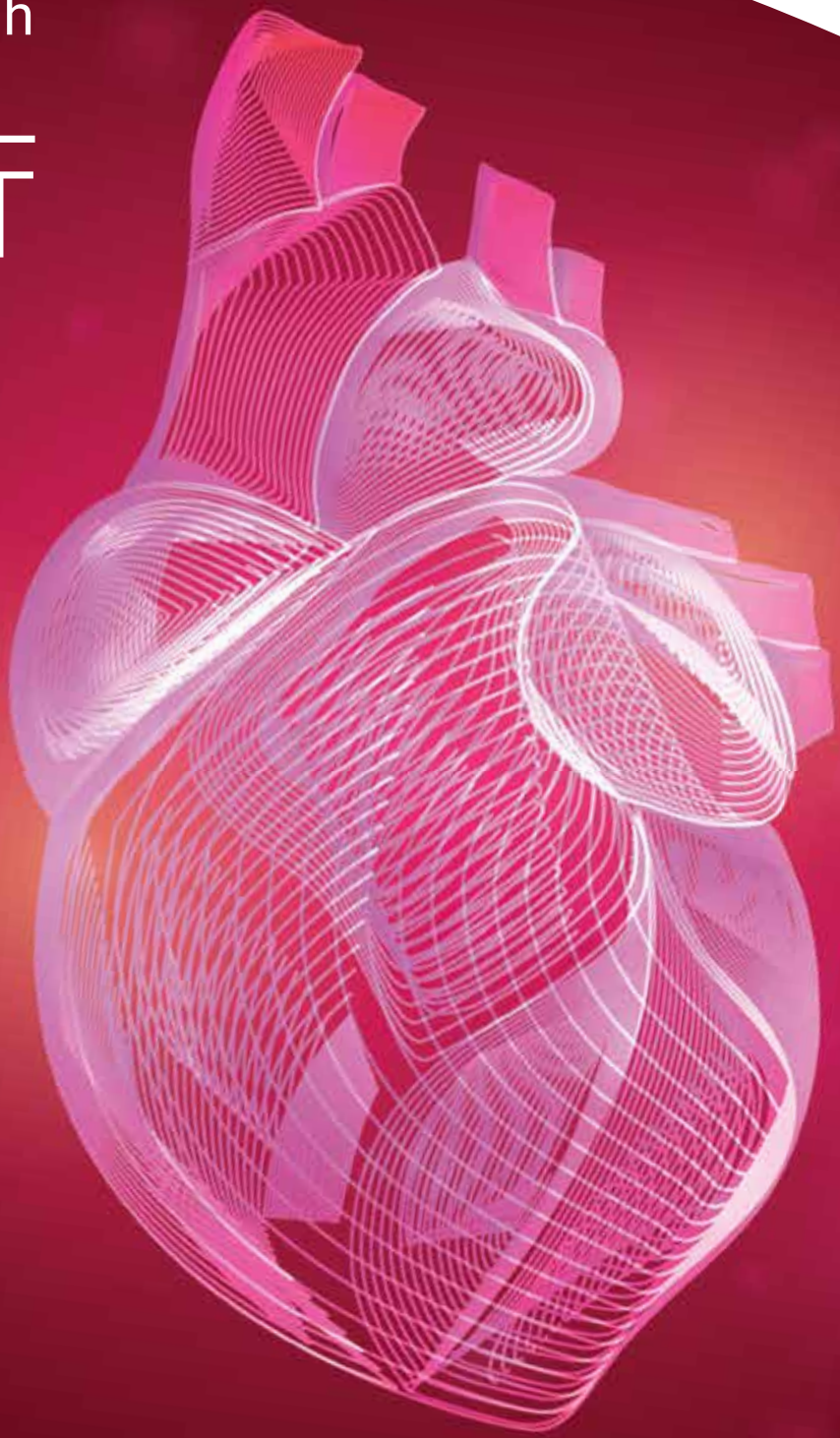

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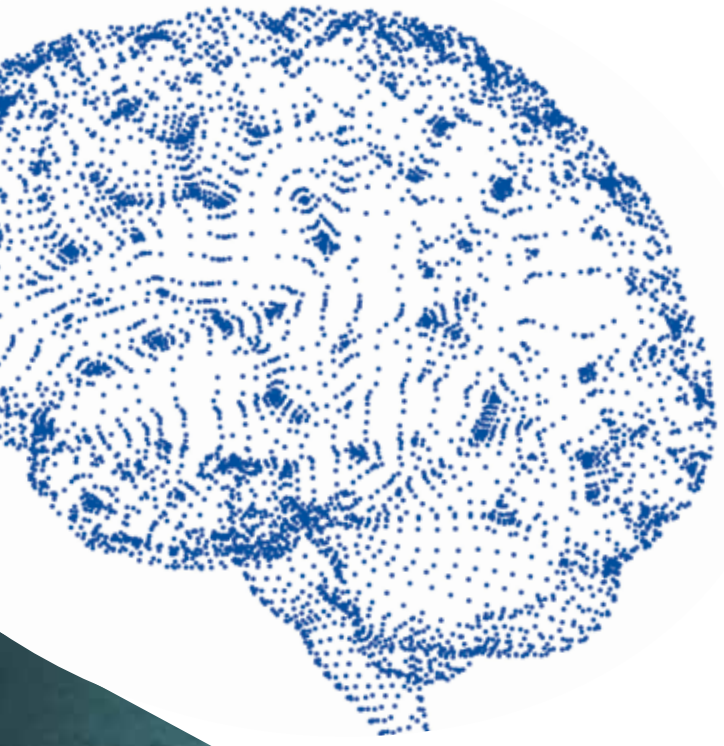
1. Akay Internal Study. Liposomal hydrogel vitamin C pharmacokinetics. Data on file. 2021.

How to Banish BRAIN FOG



BY MICHAEL DOWNEY

Losing your train of thought or finding it hard to pay attention is common as we get older.

If it starts to interfere with daily life, you may be experiencing what is known as **brain fog**.[1]

Brain fog refers to a general feeling of decreased **mental energy** and **focus**. It may be characterized by mental fatigue and clouding, forgetfulness, fuzzy thinking, confusion, and difficulty concentrating.

Scientists have identified two **plant-based** nutrients that can prevent or potentially reverse these alterations to bring back mental clarity, energy, and focus.

In clinical studies, **mango leaf extract**:[2,3]

- Improves reaction time,
- Reduces mental fatigue, and
- Boosts attention, performance accuracy, and working memory.

In other clinical studies, **peppermint oil** reduced the development of mental fatigue and improved aspects of memory and attention.[4]

Mango leaf extract and **peppermint oil** can provide a cognitive boost that may help replace ***fog with focus***.

What Causes Brain Fog?

The feeling of mental fatigue, foggy thinking, and difficulty concentrating is more than an annoyance. It can decrease **cognitive performance** and make it difficult to get work done.

In order to pinpoint underlying changes in the brain that may cause feelings of mental fogginess, scientists studied medical conditions that produce some of the same *mental symptoms*.

Their research showed that complaints consistent with **brain fog** have been reported by people with:[5-10]

- **Inflammatory disorders** of various types,
- **Allergies** (including seasonal allergies),
- **Immune disorders**, which increase inflammation, and
- **Dietary sensitivities**.

These observations led researchers to propose that brain fog may result from:[5-7]

- **Inflammation**,
- **Histamine** (the chemical that causes allergic symptoms),
- **Neurotransmitter imbalance**, and
- Impairments in **neuronal activity**.

Plant Extracts

Using this research, scientists identified **two** plant-derived nutrients that appear to have the potential to prevent or even *reverse* these underlying biological changes.

These two nutrients also had a track record of improving symptoms of brain fog:

- **Mango leaf extract** has been clinically shown to improve reaction time, reduce mental fatigue, and boost attention, performance accuracy, and working memory.[2,3]
- **Peppermint oi**l has been clinically shown to significantly reduce the development of mental fatigue and improve aspects of attention and memory.[4]

How Mango Leaf Protects the Brain

Long used in Asia and Africa to treat fatigue, **mango leaf** has more recently been shown to exert properties that are neuroprotective, anti-inflammatory, and anti-diabetic.[2]

These effects, which scientists suggested may help prevent brain fog, are believed to be largely attributable to the polyphenol compound **mangiferin**.

Mangiferin's capacity to **protect the brain** has been demonstrated in animal studies in which it:[2,11,12]

- Decreased neuroinflammation,
- Reduced oxidative stress, and
- Provided neurotransmitter support.

Other animal models found that **mangiferin** use prevented cognitive and memory impairment, key symptoms of **brain fog**.[13]

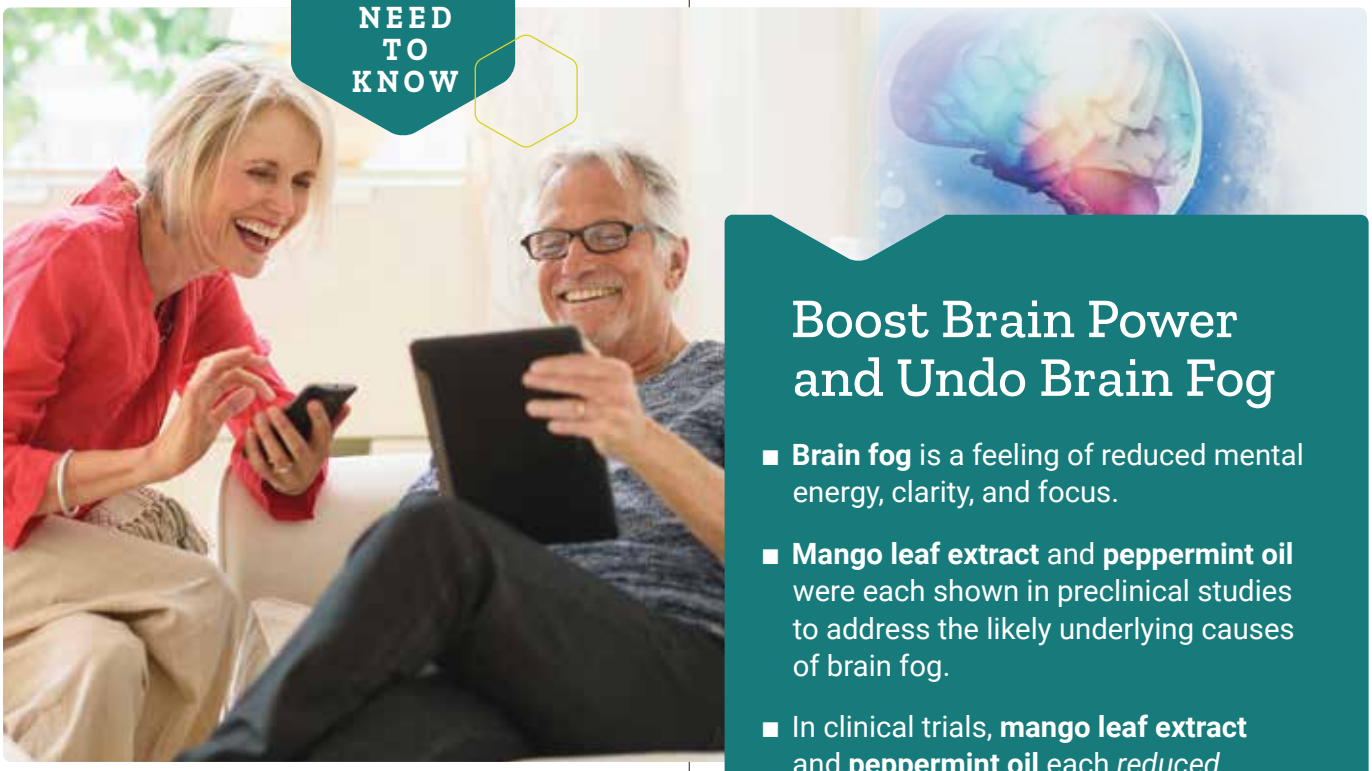
Mangiferin was also shown in rodent studies to exhibit **anti-allergic** properties,[14,15] suggesting potential benefits against brain fog associated with allergies.

Mango Leaf in Human Studies

Scientists conducted controlled **human** trials to evaluate whether **mango leaf extract** could treat symptoms consistent with **brain fog**.

They divided healthy adults into four groups. One group took a **mango leaf extract** containing **60% mangiferin**, the second group took **caffeine**, the third group took the extract *plus* caffeine, and the fourth took a **placebo**.

WHAT YOU NEED TO KNOW



Boost Brain Power and Undo Brain Fog

- **Brain fog** is a feeling of reduced mental energy, clarity, and focus.
- **Mango leaf extract** and **peppermint oil** were each shown in preclinical studies to address the likely underlying causes of brain fog.
- In clinical trials, **mango leaf extract** and **peppermint oil** each *reduced* mental fatigue while *improving* attention and working memory.
- Combined, these ingredients may maximize brain support and help erase symptoms of brain fog.

Compared to baseline, the **mango leaf** extract resulted in:[2]

- A remarkable **47%** *reduction* in **fatigue**, and
- An almost **5%** *improvement* in **reaction time**.

These improvements were significantly greater than those seen with caffeine alone *or* with a combination of caffeine and mango extract.

Tests of electrical activity in the brain showed that those taking **mango leaf extract** had increased activity in regions associated with complex cognitive processing, attention, and memory.[2]

In another clinical study, researchers gave healthy young adults either **300 mg** of the **mango leaf extract** or a placebo.

The extract *improved* areas of cognitive function, including aspects of:[3]

- **Attention**,
- **Performance accuracy**, and
- **Working memory**.

This evidence supports the use of **mango leaf extract** to enhance brain activity, reduce mental fatigue, and support mental focus and performance.

Peppermint's Brain Benefits

Peppermint is an herb traditionally used for medicinal properties, including aiding digestion and promoting calm.

Plants rich in **monoterpenes** have been shown in placebo-controlled studies to have **cognitive benefits**.[16,17] Peppermint oil contains many of these compounds, including menthol and menthone.[18]

Some human studies have shown that peppermint teas:[19]

- Improved **memory**, and
- Boosted **mental alertness**.

In addition, mint species have demonstrated the ability to modulate various **neurotransmitters** in the brain, such as **acetylcholine** and **GABA**. These neurotransmitters play pivotal roles in mental alertness, cognition, and mood.[4]

Clinical Trial of Peppermint Oil

In a controlled clinical trial, scientists gave healthy adults either **peppermint oil** containing **60% monoterpenes** or a placebo. Tests on aspects of memory, attention, and mood were administered.

The **peppermint oil** group significantly:[4]

- *Reduced* the development of **mental fatigue**,
- *Improved* aspects of **attention** and **working memory**.

The volunteers who received the **placebo** were severely fatigued within a few hours after the cognitive tests.[4]

Human studies overall demonstrate that **peppermint oil** and **mango leaf extract** can help restore mental clarity, focus, and energy.

A combination of these two ingredients may maximize their ability to clear away **brain fog**.

Summary

Scientists have identified two **plant-based** ingredients that can improve various aspects of **brain fog**.

Mango leaf extract and **peppermint oil** have each been shown to reduce mental fatigue, and improve attention, memory, and cognitive performance. •

References

1. Available at: https://health.clevelandclinic.org/brain-fog/. Accessed October 10, 2022.
2. Lopez-Rios L, Wiebe JC, Vega-Morales T, et al. Central nervous system activities of extract Mangifera indica L. *J Ethnopharmacol*. 2020 Oct 5;260:112996.
3. Wightman EL, Jackson PA, Forster J, et al. Acute Effects of a Polyphenol-Rich Leaf Extract of Mangifera indica L. (Zynamite) on Cognitive Function in Healthy Adults: A Double-Blind, Placebo-Controlled Crossover Study. *Nutrients*. 2020 Jul 23;12(8).
4. Kennedy D, Okello E, Chazot P, et al. Volatile Terpenes and Brain Function: Investigation of the Cognitive and Mood Effects of Mentha x Piperita L. Essential Oil with In Vitro Properties Relevant to Central Nervous System Function. *Nutrients*. 2018 Aug 7;10(8).
5. Hartgerink-Lutgens I, Vermeeren A, Vuurman E, et al. Disturbed cognitive functions after nasal provocation in patients with seasonal allergic rhinitis. *Clin Exp Allergy*. 2009 Apr;39(4):500-8.
6. Theoharides TC, Stewart JM, Hatziagelaki E, et al. Brain "fog," inflammation and obesity: key aspects of neuropsychiatric disorders improved by luteolin. *Front Neurosci*. 2015;9:225.
7. Balter LJ, Bosch JA, Aldred S, et al. Selective effects of acute low-grade inflammation on human visual attention. *Neuroimage*. 2019 Nov 15;202:116098.
8. Croall ID, Hoggard N, Aziz I, et al. Brain fog and non-coeliac gluten sensitivity: Proof of concept brain MRI pilot study. *PLoS One*. 2020;15(8):e0238283.
9. Makhlouf S, Messelmani M, Zaouali J, et al. Cognitive impairment in celiac disease and non-celiac gluten sensitivity: review of literature on the main cognitive impairments, the imaging and the effect of gluten free diet. *Acta Neurol Belg*. 2018 Mar;118(1):21-7.
10. Yelland GW. Gluten-induced cognitive impairment ("brain fog") in coeliac disease. *J Gastroenterol Hepatol.* 2017 Mar;32 Suppl 1:90-3.
11. Lei LY, Wang RC, Pan YL, et al. Mangiferin inhibited neuroinflammation through regulating microglial polarization and suppressing NF-kappaB, NLRP3 pathway. *Chin J Nat Med*. 2021 Feb;19(2):112-9.
12. Marquez L, Garcia-Bueno B, Madrigal JL, et al. Mangiferin decreases inflammation and oxidative damage in rat brain after stress. *Eur J Nutr.* 2012 Sep;51(6):729-39.
13. Lum PT, Sekar M, Gan SH, et al. Protective effect of mangiferin on memory impairment: A systematic review. *Saudi J Biol Sci*. 2021 Jan;28(1):917-27.
14. Sekar M. Molecules of Interest – Mangiferin – A Review. *Annual Research & Review in Biology*. 2015 01/10;5(4):307-20.
15. Garcia D, Escalante M, Delgado R, et al. Anthelminthic and antiallergic activities of Mangifera indica L. stem bark components Vimang and mangiferin. *Phytother Res.* 2003 Dec;17(10):1203-8.
16. Falcone PH, Nieman KM, Tribby AC, et al. The attention-enhancing effects of spearmint extract supplementation in healthy men and women: a randomized, double-blind, placebo-controlled, parallel trial. *Nutr Res.* 2019 Apr;64:24-38.
17. Falcone PH, Tribby AC, Vogel RM, et al. Efficacy of a nootropic spearmint extract on reactive agility: a randomized, double-blind, placebo-controlled, parallel trial. *J Int Soc Sports Nutr.* 2018 Dec 12;15(1):58.
18. Zhao H, Ren S, Yang H, et al. Peppermint essential oil: its phytochemistry, biological activity, pharmacological effect and application. *Biomed Pharmacother.* 2022 Oct;154:113559.
19. Moss M, Jones R, Moss L, et al. Acute consumption of Peppermint and Chamomile teas produce contrasting effects on cognition and mood in healthy young adults. *Plant Science today*. 2016;3:327-36.

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* *Br J Pharmacol.* 2004 Mar;141(5):825-30.

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References
1. *J Ethnopharmacol.* 2020 Oct 5;260:112996.
2. *Nutrients.* 2020 Jul 23;12(8).
3. *Nutrients*. 2018 Aug 7;10(8).

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