

The Science of a Healthier Life®

LifeExtension.com

December 2023

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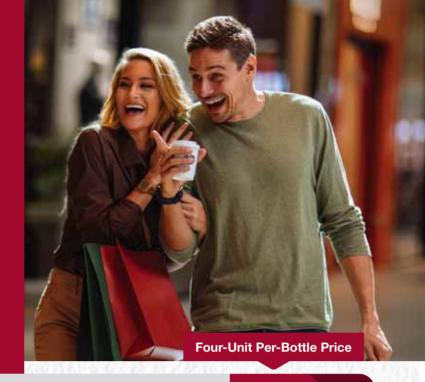
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Clinical studies show that two plant extracts promote restful sleep. One improved sleep efficiency by 74% while the other enhanced restorative sleep by 72%.

RFPORTS

22 PROTECT TELOMERES TO SLOW AGING

Shortened telomeres are associated with accelerated aging. Selenium + CoQ10 was clinically shown to reduce the shortening of telomeres in humans.



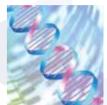
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Contributors

Michael Downey Mark Fields • John Johnson

Laurie Mathena • Brian McKnight • Patricia Weiser, PHARMD

Advertising

Chief Marketing Officer • Rey Searles • rsearles@lifeextension.com National Advertising Manager • JT Hroncich • 404-347-4170

Senior Director of Sales and Business Development

Carolyn Bouchard • cbouchard@lifeextension.com • 954-202-7685

Circulation & Distribution

Life Extension • 3600 West Commercial Blvd., Ft. Lauderdale, FL 33309

Editorial offices: 954-766-8433 • fax: 954-491-5306

Customer Service: 800-678-8989 • Email: customerservice@LifeExtension.com Wellness specialists: 800-226-2370 • Email: wellness@LifeExtension.com

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Gustavo Tovar Baez, MD, operates the Life Extension Clinic in Caracas, Venezuela. He is the first physician in Caracas to specialize in anti-aging medicine.

Ricardo Bernales, MD, is a board-certified pediatrician and general practitioner in Chicago, IL, focusing on allergies, bronchial asthma, and immunodeficiency.

Mark S. Bezzek, MD, FACP, FAARM, FAAEM, is board-certified in internal medicine, emergency medicine, and anti-aging/regenerative medicine. He is the director of Med-Link Consulting, which specializes in bioidentical hormone replacement therapy, natural alternatives, anti-aging, and degenerative diseases. He holds U.S. patents for a multivitamin/mineral supplement, an Alzheimer's/dementia compilation, and a diabetic regimen.

Thomas F. Crais, MD, FACS, a board-certified plastic surgeon, was medical director of the microsurgical research and training lab at Southern Baptist Hospital in New Orleans, LA, and currently practices in Sun Valley, ID.

William Davis, MD, is a preventive cardiologist and author of Wheat Belly: Lose the Wheat, Lose the Weight and Find Your Path Back to Health. He is also medical director of the online heart disease prevention and reversal program, Track Your Plaque (www.trackyourplaque.com).

Martin Dayton, MD, D0, practices at the Sunny Isles Medical Center in North Miami Beach, FL. His focus is on nutrition, aging, chelation therapy, holistic medicine, and oxidative medicine.

John DeLuca, MD, DC, is a 2005 graduate of St. George's University School of Medicine. He completed his internal medicine residency at Monmouth Medical Center in Long Branch, NJ, in 2008 and is board-certified by the American Board of Internal Medicine. Dr. DeLuca is a Diplomate of the American Academy of Anti-Aging Medicine and has obtained certifications in hyperbaric medicine, pain management, nutrition, strength and conditioning, and manipulation under anesthesia.

Sergey A. Dzugan, MD, PhD, was formerly chief of cardiovascular surgery at the Donetsk Regional Medical Center in Donetsk, Ukraine. Dr. Dzugan's current primary interests are antiaging and biological therapy for cancer, cholesterol, and hormonal disorders.

Patrick M. Fratellone, MD, RH, is the founder and executive medical director of Fratellone Associates. He completed his internal medicine and cardiology fellowship at Lenox Hill Hospital in 1994, before becoming the medical director for the Atkins Center for Complementary Medicine.

Norman R. Gay, MD, is proprietor of the Bahamas Anti-Aging Medical Institute in Nassau, Bahamas. A former member of the Bahamian Parliament, he served as Minister of Health and Minister of Youth and Sports.

Mitchell J. Ghen, DO, PhD, holds a doctorate in holistic health and anti-aging and serves on the faculty of medicine at the Benemerita Universidad Autonoma De Puebla, Mexico, as a professor of cellular hematopoietic studies.

Gary Goldfaden, MD, is a clinical dermatologist and a lifetime member of the American Academy of Dermatology. He is the founder of Academy Dermatology of Hollywood, FL, and COSMESIS Skin Care.

Miguelangelo Gonzalez, MD, is a certified plastic and reconstructive surgeon at the Miguelangelo Plastic Surgery Clinic, Cabo San Lucas.

Richard Heifetz, MD, is a board-certified anesthesiologist in Santa Rosa, CA, specializing in the delivery of anesthesia for office-based, plastic/cosmetic surgery, chelation therapy, and pain management.

Roberto Marasi, MD, is a psychiatrist in Brescia and in Piacenza, Italy. He is involved in anti-aging strategies and weight management.

Maurice D. Marholin, DC, DO, is a licensed chiropractic physician and board-certified osteopathic family physician. While training at the University of Alabama, he completed fellowships in Clinical Nutrition and Behavioral Medicine. He is currently in private practice in Clermont. FL.

Professor Francesco Marotta, MD, PhD, of Montenapoleone Medical Center, Milan, Italy, is a gastroenterologist and nutrigenomics expert with extensive international university experience. He is also a consulting professor at the WHO-affiliated Center for Biotech & Traditional Medicine, University of Milano, Italy and honorary resident professor, Nutrition, Texas Women's University. He is the author of more than 130 papers and 400 lectures.

Philip Lee Miller, MD, is founder and medical director of the Los Gatos Longevity Institute in Los Gatos. CA

Michele G. Morrow, D0, FAAFP, is a board-certified family physician who merges mainstream and alternative medicine using functional medicine concepts, nutrition, and natural approaches.

Filippo Ongaro, MD, is board-certified in antiaging medicine and has worked for many years as flight surgeon at the European Space Agency. He is a pioneer in functional and antiaging medicine in Italy where he also works as a journalist and a writer.

Lambert Titus K. Parker, MD, an internist and a board- certified anti-aging physician, practices integrative medicine from a human ecology perspective with emphasis on personalized brain health, biomarkers, genomics and total health optimization. He serves as the Medical Director of Integrative Longevity Institute of Virginia, a 501(c)3 Non-Profit Medical Research Institute. He also collaborates on education and research for Hampton Roads Hyperbaric Therapy.

Ross Pelton, RPh, PhD, CCN, is scientific director for Essential Formulas. Inc.

Patrick Quillin, PhD, RD, CNS, is a clinical nutritionist in Carlsbad, CA, and formerly served as vice president of nutrition for Cancer Treatment Centers of America, where he was a consultant to the National Institutes of Health.

Allan Rashford, MD, graduated from the University of Iowa Medical School. Upon completing medical training, he became chief of medicine at St. Francis Hospital in South Carolina, and he was later named president of the Charleston Medical Society.

Marc R. Rose, MD, practices ophthalmology in Los Angeles, CA, and is president of the Rose Eye Medical Group. He is on the staff of Pacific Alliance Medical Center, Los Angeles, and other area hospitals.

Michael R. Rose, MD, a board-certified ophthalmologist with the Rose Eye Medical Group in Los Angeles, CA, is on the staff of the University of Southern California and UCLA.

Ron Rothenberg, MD, is a full clinical professor at the University of California San Diego School of Medicine and founder of California HealthSpan Institute in San Diego.

Roman Rozencwaig, MD, is a pioneer in research on melatonin and aging. He practices in Montreal, Canada, as research associate at Montreal General Hospital, Department of Medicine, McGill University.

Michael D. Seidman, MD, FACS, is the director of skull base surgery and wellness for the Adventist Health System in Celebration, FL.

Ronald L. Shuler, BS, DDS, CCN, LN, is involved in immunoncology for the prevention and treatment of cancer, human growth hormone secretagogues, and osteoporosis. He is board-certified in anti-aging medicine.



Sandra C. Kaufmann, MD, is a fellowship-trained and board-certified pediatric anesthesiologist as well as the Chief of Anesthesia at the Joe DiMaggio Children's Hospital in Hollywood, Florida. She is the founder of The Kaufmann Anti-Aging Institute and the author of the book The Kaufmann Protocol: Why we Age and How to Stop it (2018). Her expertise is in the practical application of anti-aging research.



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.



Aubrey de Grey, PhD, is a biomedical gerontologist and Editor-in-Chief of Rejuvenation Research, the world's highest-impact, peer-reviewed journal focused on intervention in aging. He received his BA and PhD from the University of Cambridge in 1985 and 2000 respectively. Dr. de Grey is a Fellow of both the Gerontological Society of America and the American Aging Association and sits on the editorial and scientific advisory boards of numerous journals and organizations.



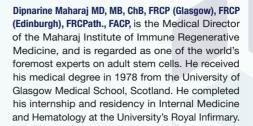
Deborah F. Harding, MD, is founder of the Harding Anti-Aging Center. She is double board-certified in internal medicine and sleep disorder medicine. She also earned the Cenegenics certification in age management medicine. She is a faculty member of the University of Central Florida Medical School.



Steven B. Harris, MD, has participated in groundbreaking hypothermia, cryothermia, and ischemia research. His research interests include antioxidant and dietary-restriction effects in animals and



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.





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 Heart Attacks Are Not Worth Dying For, The Great American Heart Hoax, and The Complete Mediterranean Diet. 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.





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Sleep, Obesity, and Dementia



WILLIAM FALOON

Those with **impaired sleep** suffer a tsunami of disorders, including higher dementia rates and unwanted weight gain.

In January 2022, I described data supporting a relationship between less-than-optimal sleep and obesity.1

Throughout 2022-2023, similar reports linking sleep disorders with excess body fat2-4 and cognitive deficits were published.5-8

Sleep deprivation harms overall health and increases all-cause mortality.9,10

Research published in 2023 reveals how lack of quality sleep can inflict structural brain damage. 11 The lead author of this study was quoted as saying that insufficient restorative sleep accelerated an indicator of brain aging by as much as 4.6 years!12

This **2023** study helps corroborate prior data linking decreased slow-wave sleep to cognitive decline and structural changes indicative of Alzheimer's 13-15

The challenge is what to do if you are unable to readily fall or stay asleep.

Encouraging news has emerged of non-drug approaches that have been shown to provide substantial help to sleep-challenged people in randomized controlled trials.

Widespread enhancements of restorative sleep would help reduce the epidemic burdens inflicted by aging. These include surplus body fat, neurodegeneration, and cardiovascular disorders.

SLOW-WAVE Sleep

Slow-wave sleep, also called deep sleep, is a stage of sleep that plays an influential role in growth and memory.49



The media relentlessly report on growing numbers of Americans not getting enough **sleep** hours.

One of every three American adults are sleep deprived.¹⁶

With aging, it's not just sleep **quantity**, but also sleep **quality** that matters.

Any intervention that improves **restorative sleep** can have major impacts on overall health and longevity.

Rising Prevalence of Sleep Disorders

Official statistics show that **50** to **70 million** Americans are afflicted with chronic or ongoing **sleep disorders**. ¹⁶ About **9%** to **15%** of the U.S. adult population suffer from insomnia. ¹⁷

In older adults, however, the number suffering from sleep disorders surges to between 40% and 70%.¹⁸

Inadequate sleep is not just about feeling miserable the next day. It significantly <u>increases</u> risks of lethal disorders.

Five-Fold Rise in Stroke Risk

Stroke continues to be a leading cause of long-term disability and death, striking 795,000 Americans each year.¹⁹

More than <u>half</u> of stroke survivors over age 64 suffer reduced mobility including **paralysis**.²⁰

A study published in April **2023** linked multiple sleep problems to a **five-fold** increase in the odds of



having a **stroke**.²¹ The nocturnal disorders included short, fragmented sleep, insufficient restful hours, and sleep apnea that impair the body's ability to regulate metabolism, inflammation, and blood pressure.

These findings are consistent with prior research linking unhealthy sleep to chronic conditions leading to blood vessel impairment associated with **stroke**.²²

Increased Heart Disease Associated with Sleep Problems

A February **2022** study found that having more self-reported sleep problems was associated with a **54%** increased risk of **heart disease**.²³

When a sleep monitoring device (actigraph*) was added as part of a combination assessment, sleep problems were associated with a startling **141%** *higher* risk of **heart disease**.²³

These data suggest that **heart disease** is correlated with sleep problems, including poor quality sleep. This helps identify sleep **quality** as an underappreciated **risk factor** associated with **heart disease**.²³

The *Harvard Heart Letter* reported on this study in August **2022**.²⁴

Although additional studies are needed to confirm correlation and cause, these data suggest that **cardiologists** should inquire about patient **sleep quality** in addition to other cardiovascular risk factors.

* An actigraphic device looks like a wristwatch, and measures changes in movement which are correlated with sleep parameters.

Sleep-Disordered Breathing

A May **2023** study published in the journal **Neurology** showed that severe **sleep apnea** markedly accelerates **aging**.¹¹

What surprised me is the impact of even small reductions in deep (slow-wave) sleep. In an interview, the authors of this study said a mere 10% <u>decline</u> in deep (slow-wave) **sleep** is equivalent to **2.3 years** of **brain aging**.²⁵

Sleep apnea is complete cessation of breathing.

Sleep-disordered breathing refers to a wide spectrum of conditions including increased resistance to airflow in the upper airway, heavy snoring, and marked reduction in airflow.

A March 2023 article published by the American College of Cardiology describes "sleep-disordered breathing" as being linked with obesity, type II diabetes, and premature death.²⁶



The researchers emphasize that this is a growing, but under-recognized **crisis** that provides an opportunity for physicians to reduce cardiovascular disease and improve quality of life by correcting sleep-breathing disorders.

Yale Researchers Concur

A report emanating from **Yale University** in March 2023 describes specific mechanisms by which poor sleep contributes to diabetes and obesity.27

They point out that **sleep deprivation** creates an imbalance in hormones that regulate appetite (ghrelin and leptin).

Leptin helps induce satiety (feeling full) while ghrelin makes people hungry.

During sleep leptin typically rises. With insufficient sleep, leptin levels decrease, making one feel hungrier and more likely to excessively eat and gain weight.

Sleep disruptions of any kind can increase ghrelin, which makes people hungrier for more calories.

This 2023 Yale report points out that people who are more sleep-deprived tend to gain weight and develop type II diabetes.

This Yale report concludes by stating:

"Sleep, obesity, and diabetes are all linked, and improvements to one aspect can benefit others. For example, significant weight loss can treat and, in some cases, eliminate sleep apnea, a disruptive sleep disorder in which breathing stops and starts at night."27

Defying Conventional Wisdom

Traditional factors such as excess calorie intake and lack of physical activity do not fully explain today's high prevalence of unwanted body fat, metabolic syndrome, and obesity.

Insufficient sleep and poor-quality sleep promote weight gain and predispose people to metabolic disorders like type II diabetes.28

A February 2023 report describes a growing recognition that insufficient sleep, misalignment of sleep/ wake cycles, and altered feeding contributes to a constellation of factors behind today's obesity epidemic. The authors conclude that:

"Efforts are needed to highlight the importance of optimal sleep and circadian health in the maintenance of metabolic health and body weight regulation."29



Sleep Well and Reduce Dementia Risk

People who slept six hours or less per night in mid-life are **30**% more likely to develop **dementia** as they age. Those who sleep less than five hours have been shown to double their **dementia risk** in later life.³⁰

The adverse impact of **sleep deprivation** is no longer hidden. Numerous published studies show increased risks of:

- Alzheimer's³¹⁻³³
- Parkinson's^{34,35}
- Multiple sclerosis³⁶
- Stroke^{21,22}
- Frequency of epileptic seizures^{37,38}
- Behavioral changes in Autism Spectrum Disorder^{39,40}
- Progression of glioma⁴¹
- Pain (neuropathic)^{42,43}

The problem is that nearly **50%** of older adults have some kind of **sleep disturbance**, and no single, complete solution exists for many of them.⁴⁴

All validated lifestyle methods shown to improve sleep should be considered by those unable to achieve optimal quantity and quality nightly rest.

In this month's issue...

Researchers isolated two plant extracts that have been shown to improve *every* measured component of the sleep cycle.

Compared to **placebo**, people taking one of these **plant extracts** showed significant sleep enhancements at seven⁴⁵ and 60 days.⁴⁶

Two randomized controlled trials, one for each of these two ingredients, demonstrated improvements in the ability to fall asleep, stay asleep, and perhaps most important, enhance overall **sleep quality**. ^{47,48}

Page 46 of this month's issue describes the science behind this new botanical combination that may provide partial or substantial relief for those not attaining sufficient nightly rest.

You may note that most reports cited in this editorial are published <u>this</u> year (2023).

They provide near-universal consensus that common disorders afflicting aging **humans** may be curtailed in response to healthier **sleep** patterns.

For longer life,

William Faloon, Co-Founder,

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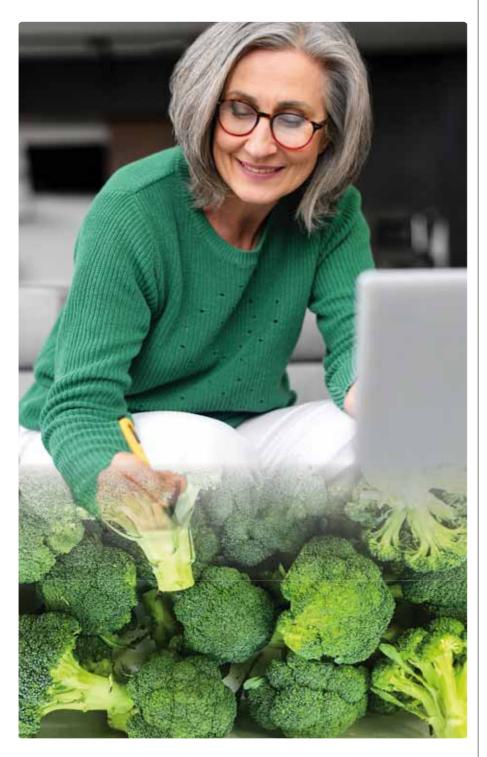




Caution: Temporary flushing, itching, rash, or gastric disturbances may occur.

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

In the News



Consuming More Flavonols, Like Broccoli, May **Slow Cognitive Decline**

Consuming more flavonols was associated with a slower rate of cognitive decline among older men and women, according to a clinical study published in Neurology®, the medical journal of the American Academy of Neurology.*

When individual flavonols were evaluated, participants with the highest intake of kaempferol and quercetin exhibited slower rates of cognitive decline, compared to people with the lowest intake. Kaempferol, found in significant amounts in kale, beans, tea, spinach and broccoli, was associated with the greatest benefit.

Global cognitive test scores of those whose intake of flavonols was among the highest 20% of participants indicated a slower rate of decline during follow-up than participants whose intake was among the lowest 20%.

Editor's Note: There were 961 participants in the study, enrolled in the Rush Memory and Aging Project, average age 81, with no dementia. They responded to yearly dietary questionnaires administered during a 6.9year average follow-up period, providing information about flavonol intake and completed annual cognitive and memory tests.

* Neurology®. 2023 Feb 14;100(7):e694-e702.

Higher Omega-3 Levels Linked with Better Lung Health

A study reported in the American Journal of Respiratory and Critical Care Medicine suggests that people with higher levels of omega-3 may have a better chance of maintaining lung function over time.*

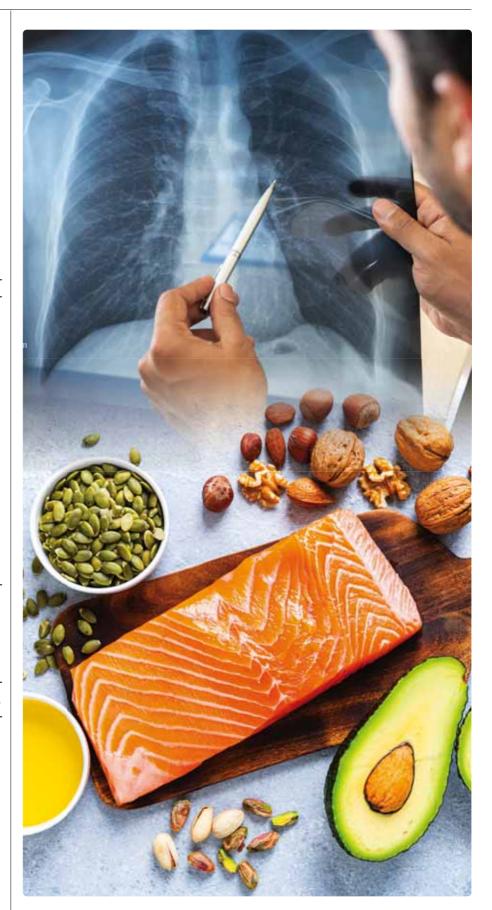
"Inflammation contributes to lung function decline and the development of chronic obstructive pulmonary disease. Omega-3 fatty acids have anti-inflammatory properties and may benefit lung health," the researchers stated as the rationale for the study.

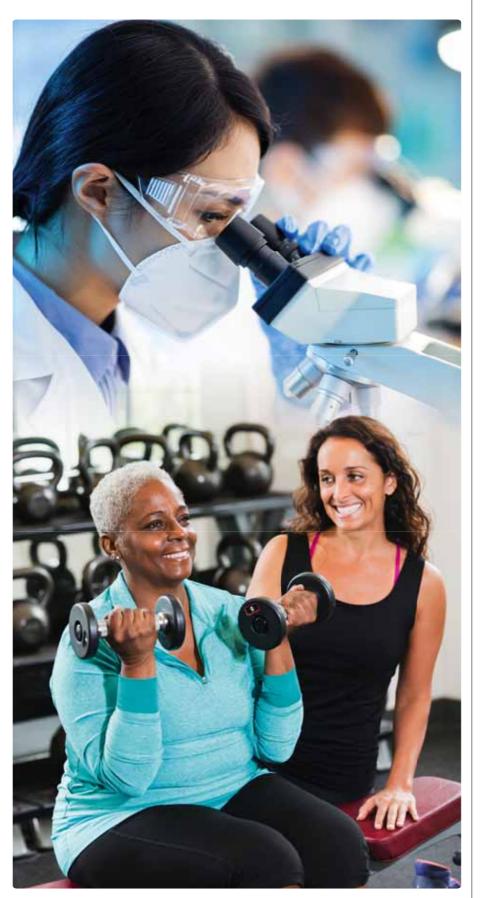
Participants were 15,063 healthy men and women enrolled in the National Heart, Lung, and Blood Institute (NHLBI) Pooled Cohorts Study. They were followed for up to 20 years, during which repeated measures of lung function were obtained. Genetic data were also collected from more than half a million UK Biobank participants to investigate potential associations between genetically predicted omega-3 levels and lung function.

The results showed that people with higher plasma omega-3 fatty acid levels had a lower risk of declining lung function during follow-up. Those with higher genetically predicted omega-3 fatty acid levels also had better lung function over time.

Editor's Note: The study also found that the omega-3 fatty acid DHA appeared to be the most protective.

* Am J Respir Crit Care Med. 2023 Jul 20.





Nicotinamide Boosts Muscle Cells' Energy Production

In a clinical study involving adult twins, a form of vitamin B3 known as nicotinamide riboside (NR) was found to increase the number and density of energy-producing mitochondria within muscle cells.*

Nicotinamide riboside is a precursor of NAD+, a coenzyme found in every cell that supports cellular energy production. NAD+ declines with aging.

For the study 20 sets of twins were recruited to receive NR or a placebo. The NR dosage was 250 mg at the beginning of the study and gradually increased to 1,000 mg per day for five months. Blood, muscle tissue, and other samples were obtained from all participants at the beginning and end of the trial.

At the end of the trial NR improved systemic NAD+ metabolism, muscle mitochondrial number, myoblast differentiation, and gut microbiota composition as compared to the placebo group.

Editor's Note: "NR supplementation is a potential treatment option to be tested in individuals with decreased muscle mitochondrial biogenesis and dysbiosis," the authors stated.

* Sci Adv. 2023 Jan 13;9(2):eadd5163.

Old Drug May Offer New Hope for People with ALS

An FDA-approved medication may be repurposed to aid in the management of amyotrophic lateral sclerosis (ALS), a neurodegenerative disorder, a preclinical study found.*

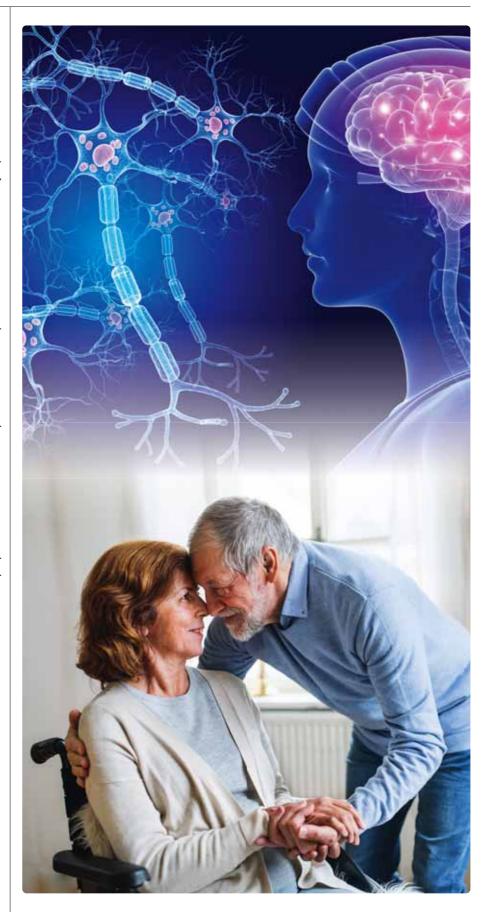
Terazosin is an alpha-blocker drug that has been around for decades, mostly used to treat high blood pressure and the symptoms of an enlarged prostate. Recently, researchers discovered that terazosin also binds to the enzyme PGK1 and increases its activity.

The metabolic pathway that PGK1 is part of is dysfunctional in ALS, and typically causes the progressive death of motor neurons in both the brain and spinal cord—causing paralysis.

Scientists utilized multiple models of ALS—both in cell culture and in various animal models—to show that treatment with terazosin was neuroprotective, defending motor neuron cells from the typical changes and cell death that would otherwise occur.

Editor's Note: "Repurposing terazosin therefore has the potential to increase the limited therapeutic options across all forms of ALS, irrespective of disease cause," the authors of the study stated.

* EBioMedicine. 2022 Sep;83:104202.





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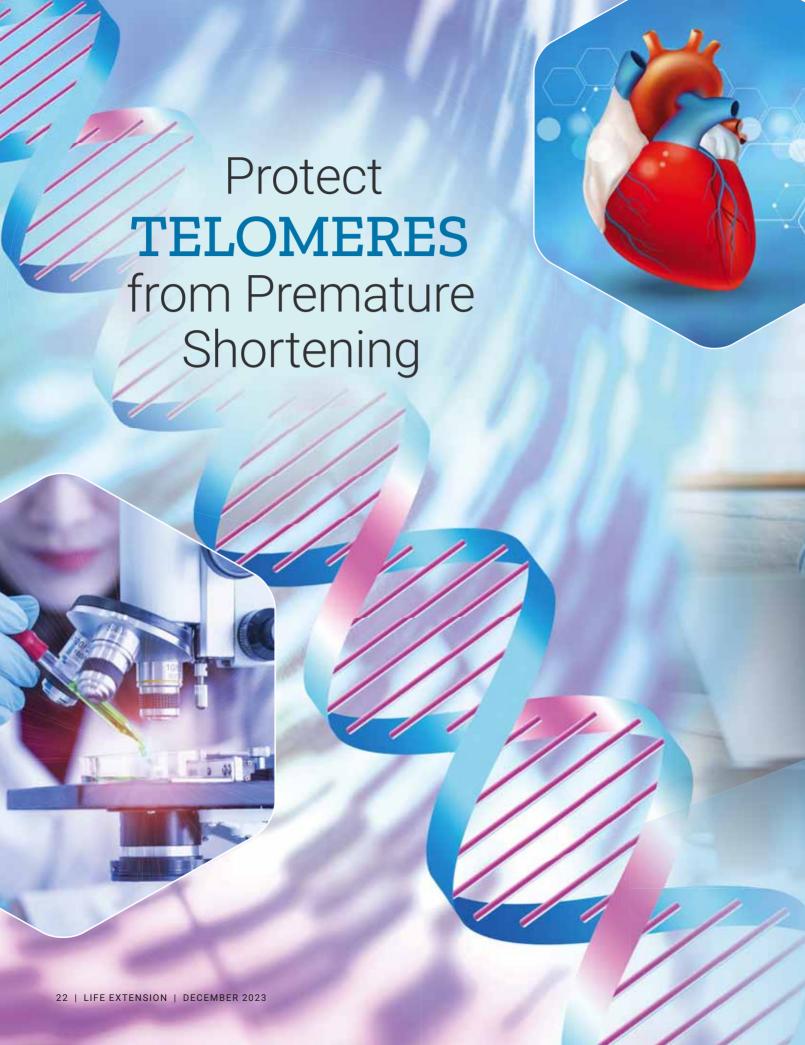
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1. Akay Internal Study. Liposomal hydrogel vitamin C pharmacokinetics. Data on file. 2021.







reported on a study showing that people over age 60 with **shorter telomeres** were three times more likely to die from heart disease and eight times more likely to die from infections 1

Shortened telomeres are associated with accelerated aging and higher risk of all-cause mortality.2

For decades, scientists have searched for ways to slow the shortening of telomeres.

An easy way to reduce the progression of telomere shortening has now been discovered.

Results of a clinical study showed that, in those who took a selenium-CoO10 combination for four years, there was a

to cardiovascular causes compared to placebo.3

A recent sub-study utilizing data from these participants was published in the medical journal Nutrients. Scientists found that the combination of selenium and coenzyme Q10 significantly reduced the attrition of telomeres in subjects' cells.4

This is a potentially game-changing development and adds evidence to the benefits of selenium and coenzyme Q10. Halting telomere shortening, on top of the known benefits, would be huge.

Most readers of this magazine have supplemented with CoQ10 and selenium for many decades.

What Are Telomeres?

Telomeres are protective caps for your genetic material. Every **chromosome**—long, elaborately folded strings of DNA found in every cell-has telomeres on both ends. They help shield the DNA structure and keep the genetic material stable.^{2,5}

Early in life, telomeres tend to be long and healthy. But with time, as cells age, telomeres shorten. When they become too short, the chromosomes are prone to damage and dysfunction. This causes cells to age and eventually die.5,6

Scientists have shown that longer, intact telomeres are associated with excellent cellular health, and may be associated with longevity. On the other hand, shortening of telomeres is associated with aging and chronic disease.^{2,6,7}

For these reasons, the prevention of telomere **shortening** is a major interest of **anti-aging** research.

Selenium and CoQ10

Selenium is a trace mineral and is essential to the proper function of certain enzymes, specifically those involved in defense against oxidative stress and the damage it causes to proteins and cellular DNA.

Many older adults have low selenium levels.8 Observational studies have shown low levels of selenium are associated with increased risk of cardiovascular disease.9

Coenzyme Q10 (CoQ10) is a lipid-soluble antioxidant naturally found in every cell of our body. It is

critical to the health of mitochondria, cellular powerhouses that supply the energy cells need to survive and function. 10. After age 20, production of CoQ10 begins to drop, and older people often suffer from inadequate levels. 10,11

Although selenium and CoQ10 play distinct roles in promoting health, they have an intimate connection. In other words, they are better together.

As CoQ10 provides energy to the body, it becomes inactive. One of the enzymes that can convert the inactive CoQ10 back to the active form-called ubiquinol—requires selenium.10

At the same time, CoQ10 is required for selenium to be properly incorporated into essential body proteins. 12

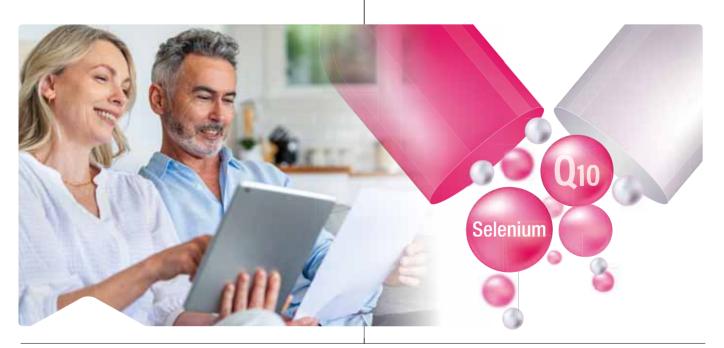
Impede Telomere Shortening

Several trials in the past have assessed the impact of selenium and CoQ10 on mitochondrial, cardiovascular. and metabolic health.

One such trial was of 675 older adults with low selenium levels who were randomized to receive either a placebo or a combination of 200 mcg of selenium and 200 mg of coenzyme Q10 for four years. A significant reduction in cardiovascular mortality was seen in the treatment group as compared to placebo.¹¹

A recent sub-study of this trial was conducted, and telomere length of those in the earlier study evaluated.4

In the **selenium-CoQ10** group, the rate of **telomere** shortening was significantly reduced compared to placebo.



While telomeres in the placebo group continued to shorten, the average length in selenium-CoQ10 users was stable or even slightly increased.

The ability to halt telomere shortening over a four-year period in elderly adults is an extraordinary finding. Even more impressive is that, in this study, shorter telomeres were associated with more cardiovascular disease and a shorter life, while selenium and CoQ10 supplementation preserved telomere length and resulted in less cardiovascular death.

Better Heart Health

A clinical trial found that older people who took a combination of selenium and coenzyme Q10 for a period of four years experienced a lower rate of death due to cardiovascular causes (including heart attack, stroke, and heart failure), which was reduced by more than half.12

Researchers continued to collect data from participants, and results of two subsequent sub-studies have been consistent in regard to cardiovascular mortality.

Ten years after the end of this trial, the selenium-CoQ10 group was still 49% less likely to die from cardiovascular causes.11

Even 12 years after the end of the treatment period, the benefit persisted. A 41% lower risk in the active treatment group, as compared to placebo, was found in the second follow-up analysis.¹³ These benefits remained when looking at subgroups who had preexisting conditions, including heart disease, diabetes, and high blood pressure.

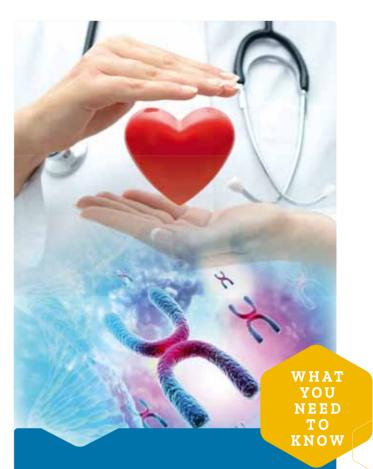
Summary

A study of elderly adults has demonstrated that taking selenium and coenzyme Q10 can impede telomere shortening.

Telomeres protect genetic material in cells. Their shortening is associated with increased risk of disease and death.

Protection against telomere shortening in those receiving the selenium-CoQ10 was accompanied by lower rates of death due to cardiovascular causes during follow-up of up to 12 years. This was true even in those with preexisting conditions. •

If you have any questions on the scientific content of this article, please call a Life Extension Wellness Specialist at 1-866-864-3027.

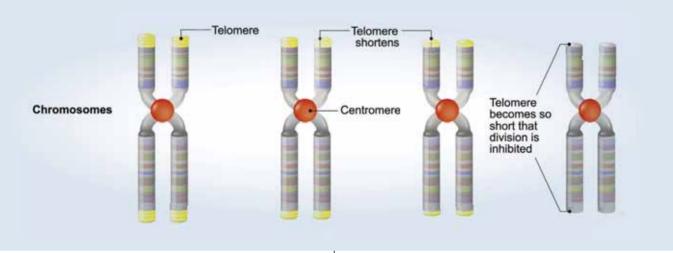


Preserve Telomeres and Reduce Cardiovascular Death

- **Telomeres** protect the genetic material in every human cell. With aging, they tend to shorten, and this change is associated with increased risk for chronic disease
- A study in older adults with low selenium found that oral intake of selenium and coenzyme Q10 (CoQ10) could slow or stop the shortening of telomeres over a four-year study period.
- Those receiving the treatment had significantly lower rates of death due to cardiovascular causes during a follow-up period of 12 years.

THE WALL STREET JOURNAL. March 12, 20231

- The **WSJ** cited several studies associating **telomere length** with health outcomes in older people.
- Shorter telomeres were associated with depression and **cognitive** problems in people aged 60-79.
- People over 60 with shorter telomeres were three times more likely to die from heart disease and eight times more likely to die from infections.
- "Smoking, excessive drinking, pollution, stress, social isolation and eating processed foods...causes telomeres to shorten faster."



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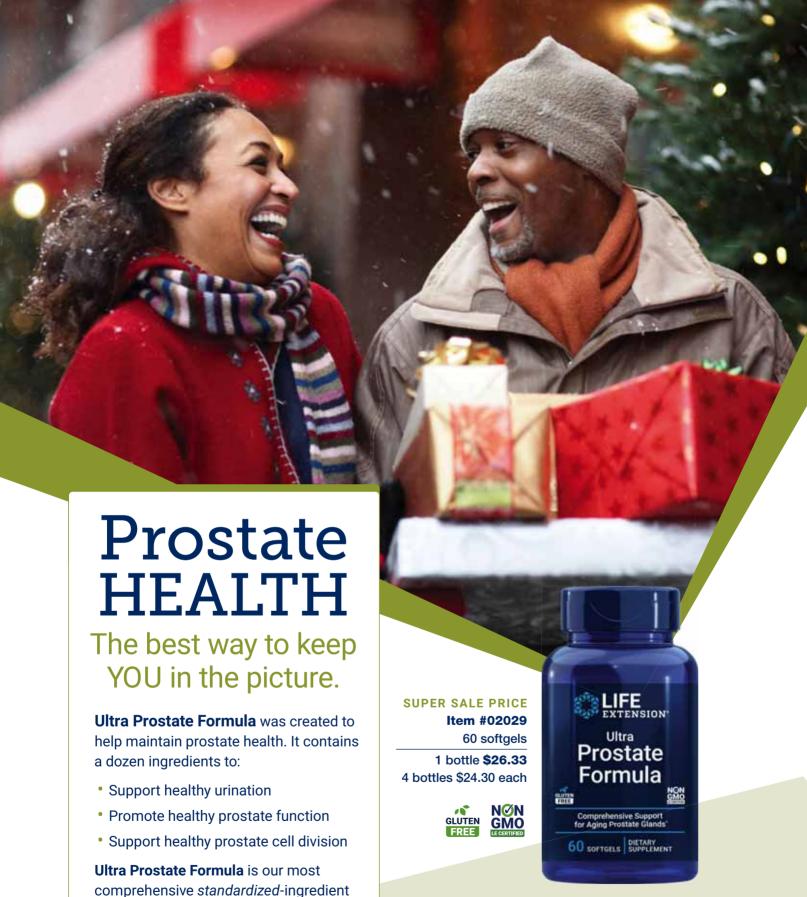
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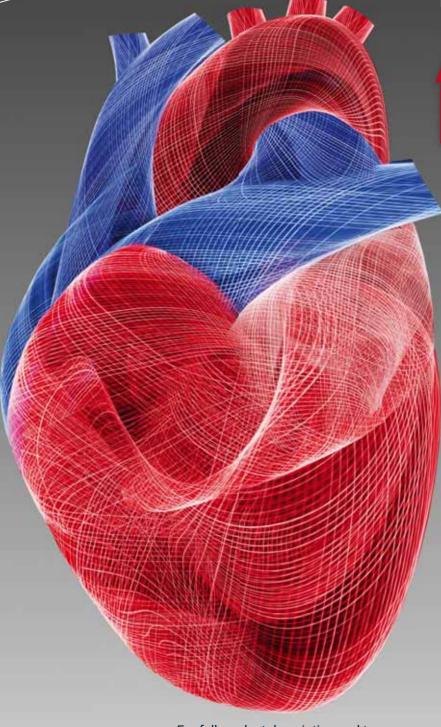
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* Int Angiol. 2014 Feb;33(1):20-6.

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With this innovation, it is thought that resveratrol can better combat the effects of aging.

Activating Anti-Aging Processes

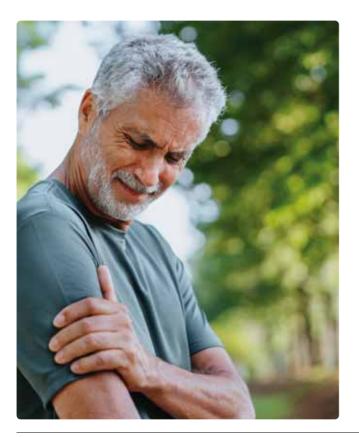
Resveratrol is a polyphenol compound found in red grapes, some berries, and several other plants.

Preclinical studies have shown that resveratrol activates multiple anti-aging processes. 1-3,5

Some of the protective mechanisms demonstrated by resveratrol include:

- Anti-inflammatory support,
- · Increased activity of sirtuins, cellular protector proteins linked to longer life,
- · Improvements in insulin sensitivity and other areas of metabolic health,
- Preventing harmful changes to DNA associated with cellular dysfunction,
- Improved function of energy-generating mitochondria,
- · Activating autophagy, cellular "housekeeping," and
- · Promoting a healthy mix of microorganisms to improve gut health.

Resveratrol has demonstrated beneficial effects on all the above anti-aging factors. 1-3,5



Extending Life

Resveratrol can exert body-wide protection to help protect the heart, muscles, bones, and kidneys.

It has also been shown to prolong overall life. In numerous studies of organisms from yeast to mice, resveratrol extends lifespan.^{2,3,9}

For example, giving resveratrol to short-lived flies resulted in mean lifespan extension of up to 29%.9,10 In honeybees, it increased the maximum lifespan by 38%.11

Because of the long lifespan of humans, it is difficult to evaluate a nutrient's ability to extend life in clinical trials. However, human studies do indicate that resveratrol can reduce major contributors to premature aging.

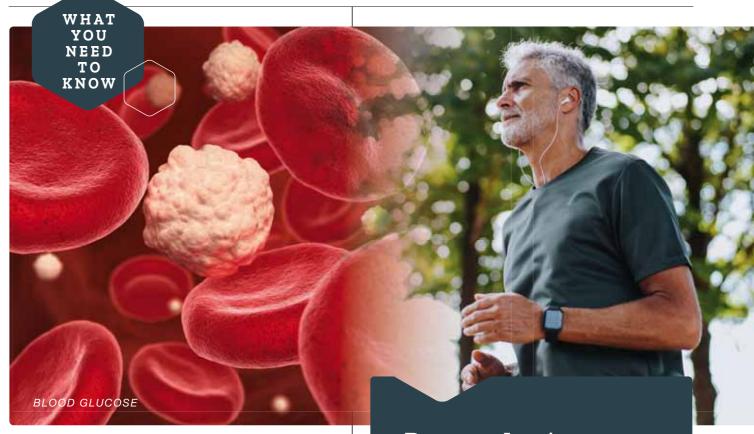
Fighting Metabolic Disease

Low insulin sensitivity and poor glucose control are major contributors to the aging process. They can lead to type II diabetes and increased risk for cardiovascular disease, cancer, and dementia.

Human trials show that resveratrol intake benefits metabolic health in adults with diabetes or other signs of metabolic disease. Doses from 150 to 1,500 mg daily led to improvements in markers of healthy aging, including:12

- · Increased insulin sensitivity and improvements in a marker of insulin function, 12-18
- Better blood glucose control,¹⁹ including lower levels of fasting glucose, post-meal glucose,14,18,20 and glycated hemoglobin HbA1c (a marker of long-term blood sugar control), 12,15-19,21
- Reduction in markers of nonalcoholic fatty liver disease,17,20
- Improved cholesterol levels, 16,21
- Reduction in signs of oxidative stress^{13,22} and markers of inflammation, 17,23,24
- Increased sirtuin activity,¹²
- Lower blood pressure, 12,16,21 and
- · Reduction in body weight, waist circumference, and body mass index.¹⁵

Being overweight or obese is associated with metabolic disease and contributes to rapid aging and risk for disease.



In a clinical trial of diabetics (type II) participants on oral blood sugar medications were recruited. One group received 200 mg of resveratrol daily for 24 weeks and another received a placebo. At the end of the trial, the resveratrol recipients had reductions in glucose and insulin, as well as reduced insulin resistance, compared to the beginning, and to the placebo group.²⁴

In a double-blinded crossover trial of healthy obese men, with a four-week washout period, taking 150 mg of resveratrol daily for 30 days resulted in beneficial changes to fat tissue, including decreasing the size of fat cells. 17,25

One human placebo-controlled study found that 1 gram of resveratrol per day for 45 days, compared to a placebo, provided antidiabetic effects in patients with type I diabetes, a lifelong condition with no cure.²²

Not only did resveratrol improve metabolic health, but it also helped guard against complications of metabolic disease in a clinical trial of diabetics with foot ulcers.

For example, nonhealing foot ulcers are a frequent problem in those with type II diabetes. Resveratrol increased the healing rate. In a clinical trial of diabetics with foot ulcers 50 mg of resveratrol two times per day for 60 days promoted reduction in foot ulcer size in the treatment group as compared to placebo.²⁶

Protect Against **Accelerated Aging**

- Resveratrol is a polyphenol found in red grapes and other plants. It helps defend cells against accelerated aging and risk for disease.
- In animal models and cell experiments, resveratrol was capable of significantly extending lifespan.
- In human trials, resveratrol countered many factors associated with rapid aging, including reducing oxidative stress and chronic inflammation, improving insulin sensitivity and glucose control, and enhancing heart function.
- Encasing resveratrol in a hydrogel of plant-derived fiber boosts its bioavailability by more than 10 times.

In another trial, diabetics suffering from chronic **gum** and **tooth disease** who took **480 mg** resveratrol **per day for** four weeks had a significant improvement in periodontal status along with improved insulin sensitivity as compared to the **placebo**.²⁷

Cardiovascular Benefits

Preliminary studies have shown that resveratrol can support metabolic health associated with cardiovascular disease risk. And it may protect against the development of **atherosclerosis** (buildup of plaque in arteries) and other **heart disease**. Now, clinical studies are confirming these findings.

One clinical trial published in **2023** included 80 patients with high blood pressure who were randomized to receive either **400 mg** resveratrol or placebo for six months. Results showed that resveratrol protected the heart against **remodeling** (harmful changes in size and shape that affect cardiac functioning), while also protecting against left ventricular function **fibrosis** (scarring).²⁸

In a double-blind, placebo-controlled trial, 40 heart attack patients were randomized to receive a **10 mg** resveratrol capsule daily for three months or a placebo. After three months the resveratrol group showed improved heart function, blood vessel function, and LDL cholesterol levels as compared to placebo.²⁹ Platelet aggregation, which can lead to abnormal blood clotting, was also reduced.

Better Bioavailability

Many researchers have long believed that resveratrol's effectiveness is limited by its poor **bioavailability**. The body's metabolism of unformulated resveratrol causes it to be rapidly cleared from the bloodstream and eliminated.

Scientists have discovered that encasing resveratrol in a **hydrogel** made of indigestible plant-derived fiber called **galactomannans** shields it from this process and makes it more bioavailable.

In a **human trial**, this hydrogel boosted the bioavailability of resveratrol by more than **10 times** compared to that of standard resveratrol.⁸ That means **10 times** more resveratrol stayed in the bloodstream to get delivered to cells.

It also stayed in the bloodstream longer, with a **four-fold** greater half-life than standard resveratrol.

That may help resveratrol to fully achieve its many benefits throughout the body.

Summary

Resveratrol counters many of the factors that contribute to accelerated aging and risk for disease.

Animal models have shown that it **extends life** and reduces risk of disease.

Human trials have found that resveratrol improves insulin sensitivity, reduces chronic inflammation, helps protect the heart, and more.

Encasing resveratrol in a **hydrogel** of plant-derived fiber improves the **bioavailability** of this nutrient. •



If you have any questions on the scientific content of this article, please call a Life Extension Wellness Specialist at 1-866-864-3027.

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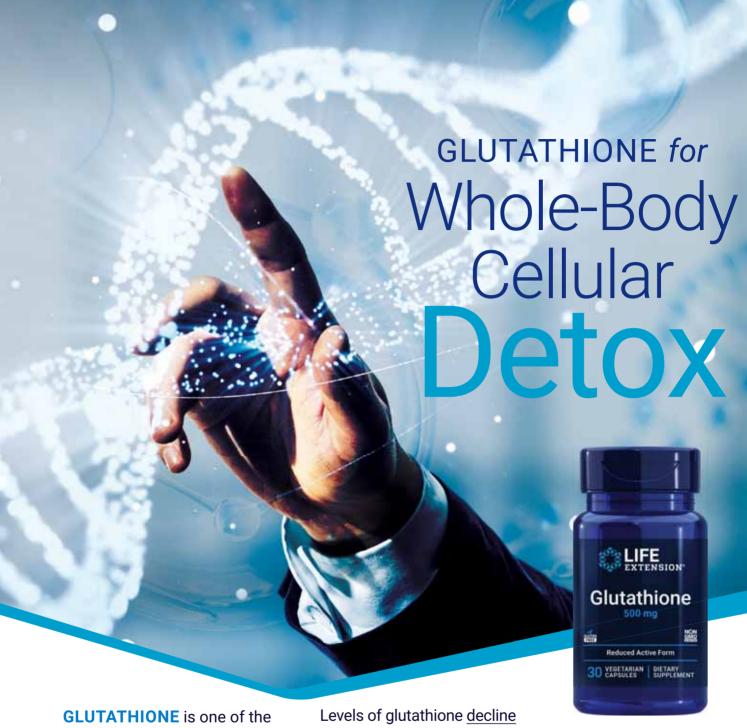




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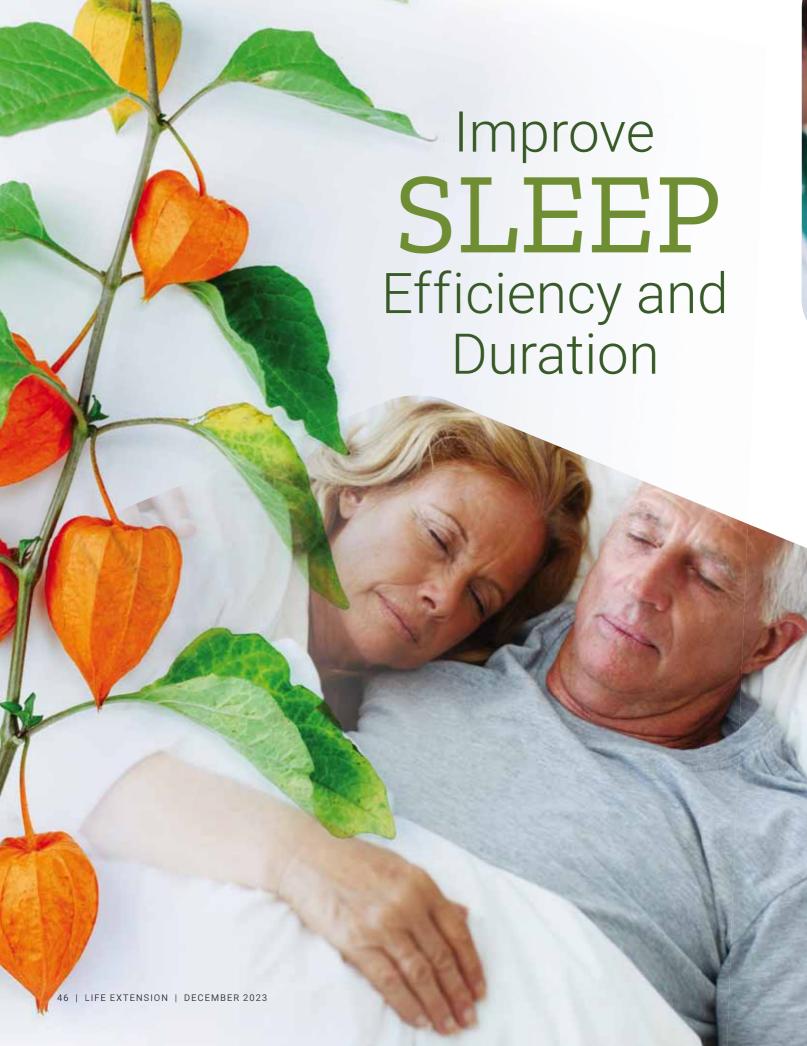
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BY MICHAEL DOWNEY

Nearly a third of U.S. adults get less sleep than they should.1

Those who rely on medications confront tolerance whereby even higher doses fail to enable restorative sleep.

In an effort to improve sleep without drugs, researchers conducted randomized clinical trials on plant-derived extracts used in traditional medicine.

One of these extracts improved **sleep efficiency** by 74%,2 while another enhanced restorative sleep measures by 72%.3

This article describes findings from placebocontrolled studies in sleep-challenged humans.

Sleep Deprivation and Human Longevity

Experts recommend that adults get **seven or more hours** of sleep each night.^{1,4}

Yet around **40**% of elderly adults suffer from some form of sleep problem.⁵

For every **one-hour** <u>reduction</u> in sleep per night, there's about a **6**% <u>increase</u> in risk of **death** from any cause.⁶

Effects of Plant Extracts

Two extracts have been individually tested in randomized placebo-controlled clinical trials to promote deep, **restorative sleep**:

 Black cumin is an herb long used in Indian and Arab traditional medicine. Its health properties come from the seed oil, which contains the active compound thymoquinone.⁷

Scientists developed a **black cumin seed extract** standardized to **5% thymoquinone**, higher than other cumin extracts.

In a small pilot study of healthy subjects with sleep disturbances, it improved **sleep quality** and **duration**, and relieved stress and anxiety.⁷ This result was confirmed in a larger trial in healthy people with self-reported unsatisfactory sleep (discussed later).²

2) Ashwagandha is an herb used for thousands of years in traditional Indian medicine that has been shown to have anxiety-reducing effects.⁸⁻¹⁰ Its roots and leaves contain active compounds called withanolide glycosides.⁹ One clinical trial showed that an extract standardized to **35% withanolide glycosides** lowered the stress hormone **cortisol**, which may help promote sleep.¹¹

Clinical Trials with Black Cumin

A study published in **2023** enlisted healthy volunteers who reported **non-refreshing sleep**. This included waking multiple times nightly or being unable to achieve sound sleep.

Participants were given a placebo or **200 mg** of **black cumin extract** nightly, 20-30 minutes before bedtime. All subjects refrained from caffeine, alcohol, and tobacco.²

Beneficial effects were reported by **62**% of the black cumin group after a *single dose*. This rose to an astonishing **88**% on day 90.

After **90 days**, compared to placebo, the **black cumin** users were evaluated using a validated self-reported sleep questionnaire. They reported not only better, longer sleep but also improved functioning during the day.

Researchers reported the following <u>improvements</u> of sleep parameters:²

- 74% in sleep efficiency (time asleep out of total time in bed),
- **56**% in sleep latency (time needed to fall asleep after going to bed),
- 49% in sleep quality,
- 45% in daytime function,
- 22% in sleep disturbance, and







Unlike those using prescription sleep meds, these people performed better the next day without drowsiness.

In a second trial, subjects with non-refreshing sleep took a placebo or **200 mg** of **black cumin** extract nightly, 10-30 minutes before bedtime. 12

All participants wore an actigraphy wristwatch sensor that monitors rest/activity, a validated objective evaluation of sleep quality and duration.

After **just seven days**, extract users had meaningfully improved their sleep duration, efficiency, and time to fall asleep, as evaluated by the objective actigraphy sensor. Compared to the placebo group, researchers reported improvements of sleep parameters:12

- 69% in restorative sleep,
- 35% in sleep latency, (amount of time to fall asleep),
- 23% in time spent awake after sleep onset, (wakefulness time after defined sleep onset),
- 19% in total sleep time, (from an average 6.4 hours to >7 hours, as recommended by the CDC), and
- 8% in sleep efficiency (time asleep out of total time in bed).

Compared to the baseline there was 75% improvement in **restorative** sleep in the group that received the extract. This specific black cumin seed extract, standardized to 5% thymoguinone, safely promoted deeper, more healthful sleep.

Get Deep, Stress-Free Sleep

- Over a third of Americans get insufficient or poor-quality sleep. This increases the risk of many chronic diseases, including heart disease, dementia, and some cancers, and of all-cause mortality.
- Clinical studies show that two plant extracts safely promote high-quality sleep and reduce stress and anxiety. without compromising daytime functioning.
- A **black cumin seed extract** improved sleep efficiency by **74%** and reduced the time needed to fall asleep by **56%**.
- An **ashwagandha extract** improved restorative sleep by 72%, reduced stress by 62%, and lowered levels of cortisol (the "stress hormone") by 67%.
- Together, these extracts offer a **melatonin-free** choice for those seeking stress relief and a deeper, more restorative sleep.

Clinical Trials with Standardized Ashwagandha

To test an **ashwagandha extract** standardized to **35% withanolide glycosides**, scientists enlisted 150 volunteers suffering from non-restorative sleep. Half the subjects took a **placebo** and half took **120 mg** of **ashwagandha** each night for six weeks.³

All participants wore an **actigraphy** wristwatch that monitors rest/activity and evaluates sleep duration, efficiency, and latency.

Those taking ashwagandha had improvements of:3

- 72% in restorative sleep,
- 27% in sleep latency,
- 15% in time spent awake after sleep onset,
- 5% in total sleep time, and
- 5% in sleep efficiency.

A second clinical study enlisted volunteers with moderate **anxiety** and elevated **cortisol**, which can lead to sleep issues. Participants were randomized to receive either ashwagandha **60 mg** or **120 mg**, or a placebo. Thay were evaluated at baseline and after 15, 30, 45 and 60 days.¹³

After 60 days, those taking **120 mg** of **ashwagandha** had:¹³

- 67% reduced cortisol levels,
- 59% reduced anxiety, and
- 62% reduced stress.

Standardized to **35% withanolide glycosides**, this novel **ashwagandha extract** safely lowered anxiety and promoted more restful sleep.

Black cumin and ashwagandha extracts have been shown to improve parameters of **restorative sleep**.

Summary

Many Americans turn to medications to cope with poor sleep, but they come with side effects.

Two plant extracts have been shown to improve sleep onset, efficiency, and **total sleep time**, and reduce **anxiety** without compromising daytime function.

In clinical studies, a **black cumin seed extract** improved sleep efficiency by **74**% and perceived stress by **44**% – leading to improved daytime functioning.

An **ashwagandha extract** improved restorative sleep by **72%** and lowered stress by **62%**.

These **plant extracts** together provide an opportunity for more Americans to achieve healthy **restorative sleep**. •

If you have any questions on the scientific content of this article, please call a **Life Extension**Wellness Specialist at 1-866-864-3027.

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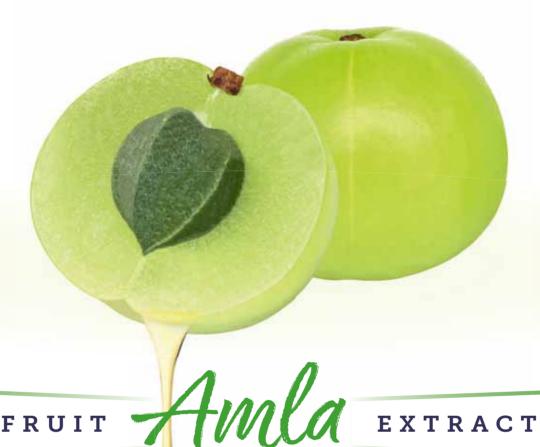






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measures of restorative sleep.3 reduced stress measures,3 and maintained healthy levels of the stress hormone cortisol.4

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- 1. Front Nutr. 2023;10:1152680.
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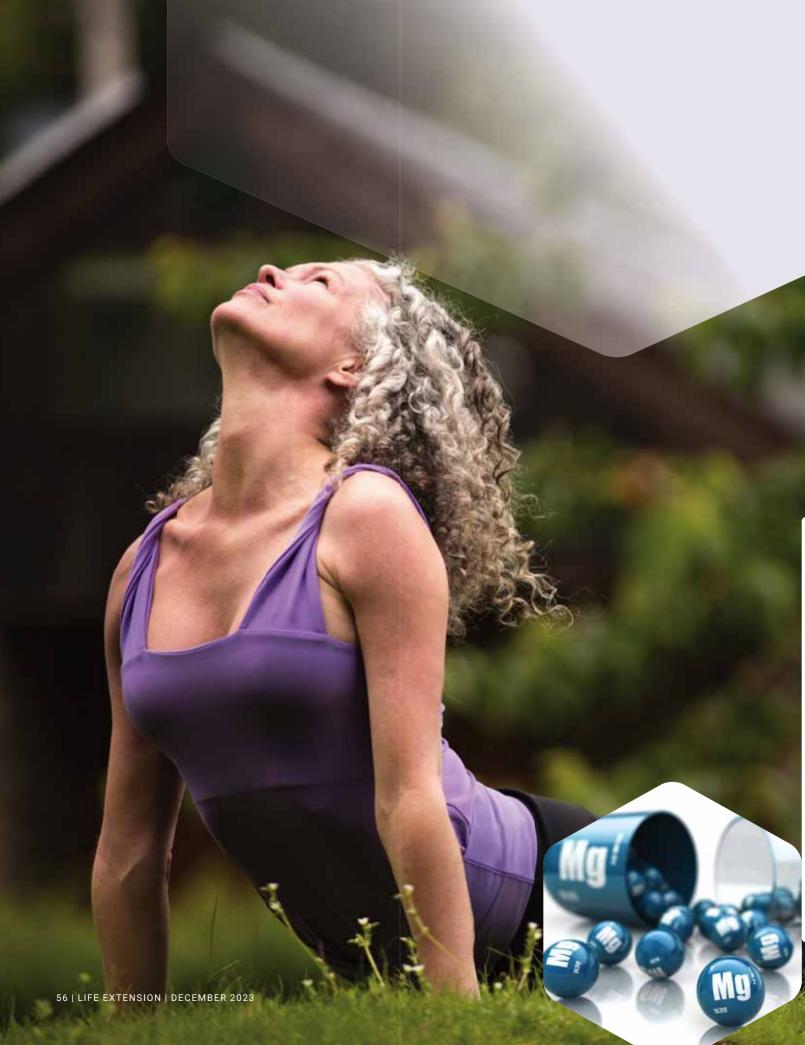


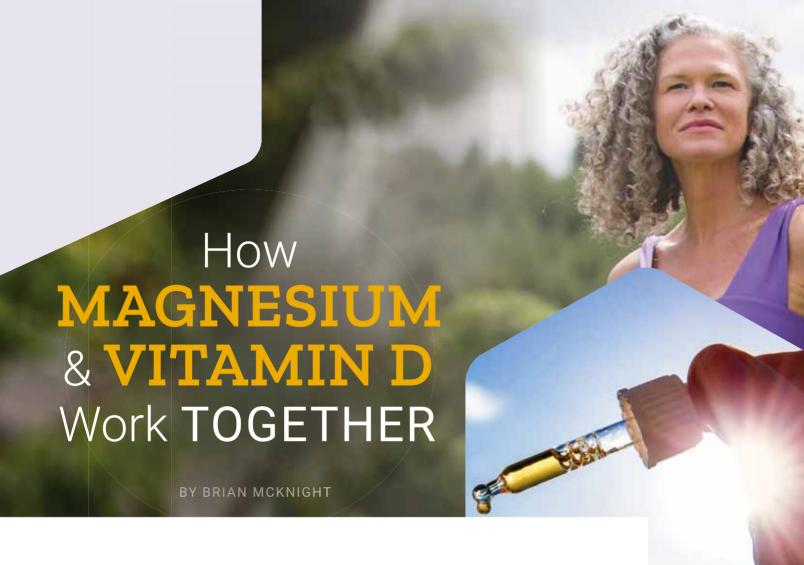


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Magnesium^{1,2} and **vitamin D**³⁻⁵ are vital to overall health.

But if you're taking either one *alone*, you're not getting the full benefits.

Research has shown that these two nutrients rely on each other to provide systemic benefits.⁶

Magnesium is critical for converting vitamin D to its *active* form in the body and aids its transport in the blood.⁷

At the same time vitamin D promotes magnesium *absorption* in the intestines.^{6,7}

Given their inter-reliance, taking them together is a sound nutritional strategy.

Observational studies show that both vitamin D and magnesium intake is associated with improved protection against insulin resistance, type II diabetes, and even death from any cause.

In **clinical studies**, taking both vitamin D and magnesium led to lower blood pressure, improved strength and muscle function, and reduced markers of **inflammation**.

Whole-Body Health

Magnesium is required for the function of 300-600 *enzymes* in the body.^{1,6}

Magnesium deficiency has been tied to many common health conditions, including osteoporosis, high blood pressure, 1,8 risk for cardiovascular disease, 1,8 metabolic disease, 1,2,8 cognitive decline, 8 and dementia.8

Vitamin D impacts a range of bodily functions. People with low levels of vitamin D have been found to have higher rates of cardiovascular disease,^{3,5} dementia,⁴ cancer,³ bone thinning,^{4,5} and more.³⁻⁵

Recent estimates show that as many as **50**% of all adults may have suboptimal **magnesium** levels⁹ and over **40**% of adolescents and adults in the U.S. have low **vitamin D** levels.¹⁰

Working Together

These two nutrients are *not* independent. Inadequate intake of one can impact the levels and function of the other.

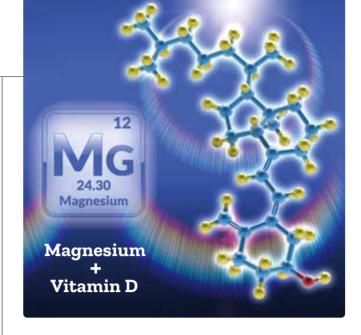
Here's how:6,7

- Vitamin D supports intestinal magnesium absorption. Vitamin D supports optimal absorption of magnesium in the intestines.
 If you consume oral magnesium but don't get enough vitamin D, your magnesium levels may remain low.
- Magnesium is required for vitamin D activation. Whether consumed or obtained by exposure to sunlight, vitamin D must be modified into its active form in the body to exert its beneficial effects. The enzymes that convert vitamin D to its active form require magnesium to function.
- Vitamin D transport and delivery rely on magnesium. Almost all vitamin D in the blood is transported and delivered to tissues by a protein called the vitamin D-binding protein. This protein also requires magnesium to function.

In short, inadequate magnesium compromises vitamin D activation and delivery.

And inadequate vitamin D compromises magnesium absorption and can contribute to low magnesium status.

If either nutrient is lacking, the other suffers as well. It's vital to get enough of *both*.



Benefits of Combined Intake

Over the last decade, *observational studies* have documented this interdependent relationship between **magnesium** and **vitamin D**, including how it relates to several common chronic diseases of aging.¹¹⁻¹⁴

For example, *higher* **vitamin D** levels in the body are associated with a *lower* likelihood of insulin resistance, pancreas dysfunction, type II diabetes, high blood pressure, and **overall mortality**. ¹¹⁻¹⁵

Higher intake of **magnesium** has been shown to improve vitamin D levels. ¹⁶ It appears that magnesium may also allow the body to properly utilize vitamin D in order to protect against these chronic conditions.

In one large, observational study, those with *higher* levels of **vitamin D** had *lower* risk for **insulin resistance**, a condition that often leads to type II diabetes. **Magnesium** intake supports this association. That suggests that people with *higher* vitamin D levels and higher magnesium intake may have the *greatest protection* against insulin resistance.¹⁵

In a separate analysis of that same observational dataset, vitamin D was associated with better pancreatic beta-cell function, and magnesium helped strengthen this effect.¹²

An analysis of data from another large observational cohort (over 10,000 participants), showed that high magnesium intake was associated with a modest reduction in incidence of type II diabetes, compared to low magnesium intake. The analysis also found that better vitamin D levels helped strengthen this association.¹⁴

Another observational study found that elevated systolic **blood pressure** was associated with lower vitamin D levels. Higher intake of magnesium strengthens the protective effect of vitamin D against high blood pressure.¹³

Clinical Trials

Clinical trials have further confirmed the link between magnesium and vitamin D.

In one randomized controlled trial, oral magnesium supplementation successfully raised vitamin D levels in subjects with *low* blood vitamin D concentrations.¹⁷

Another double-blind, controlled trial in obese or overweight individuals found that the combination of both magnesium and vitamin D resulted in greater increases in blood levels of vitamin D compared to those who took vitamin D alone.¹⁸

In a similar study, healthy postmenopausal women were randomized to receive either **500 mg** of **magnesium** daily or a placebo.¹⁶ At baseline, over **80%** of these women were vitamin D deficient. Taking magnesium resulted in a significant *increase* in **vitamin D** levels.

Placebo-controlled clinical studies have also explored how taking <u>both</u> **magnesium** and **vitamin D** can affect various areas of health, including:

 High blood pressure. In a study referenced above, in obese or overweight adults with elevated systolic blood pressure at baseline, taking 360 mg of magnesium with 1,000 IU vitamin D resulted in greater serum concentrations of vitamin D.

- Mental health. Magnesium and vitamin D have each been shown to benefit mental health, including anxiety and depression.¹⁹⁻²¹
- Muscle strength and function. In a clinical study, 83 healthy, middle-aged, vitamin D-deficient women were randomized to receive a combination of 50,000 IU of vitamin D weekly and 250 mg of magnesium daily for eight weeks, or placebo. Results showed that the vitamin D and magnesium group had a significant increase in handgrip strength and overall mobility, compared to the placebo group. The treatment group also had a decrease in an important inflammatory marker, compared to the beginning of the study.²²

Magnesium and Vitamin D Need Each Other

WHAT YOU NEED TO KNOW

- Getting enough magnesium and vitamin D is critical to overall health. A deficiency in either is associated with increased risk for a wide range of chronic health conditions.
- Magnesium and vitamin D rely on each other. Studies have found that adequate levels of either one are necessary for the other to function properly and to reach optimal levels.
- In observational studies, taking <u>both</u>
 vitamin D and magnesium is associated
 with increased protection against insulin
 resistance, and better metabolic health.
- In clinical studies, taking <u>both</u> **vitamin D** and **magnesium** is associated with improved mental health, muscle strength, and blood pressure.



Together with a wealth of observational studies, these trials show the benefits of ensuring adequate intake of both vitamin D and magnesium.

Summary

Magnesium and **vitamin D** are inextricably linked. The levels of one impact the levels and function of the other.

The body needs magnesium to activate and transport vitamin D. In return, vitamin D can *enhance* magnesium absorption and retention.

Working together, **magnesium** and **vitamin D** can benefit musculoskeletal, metabolic, and heart health. •

If you have any questions on the scientific content of this article, please call a **Life Extension**Wellnes Specialist at 1-866-864-3027.

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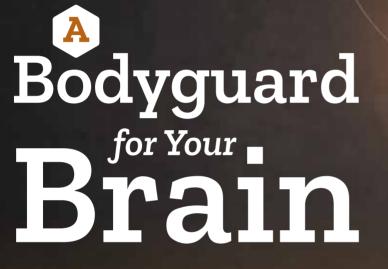






For full product description and to order **Super K**, call **1-800-544-4440** or visit **www.LifeExtension.com**





People tend to live longer in areas where lithium is abundant in the drinking water.*

Lithium is a low-cost mineral that functions in several ways to support cognition and overall brain health.

Protect healthy cognition with lithium—it's like a bodyguard for your brain!

For full product description or to order **Lithium**, call **1-800-544-4440** or visit **www.LifeExtension.com**

(1,000 mcg of lithium per tiny cap)

SUPER SALE PRICE Item #02403

100 vegetarian capsules

1 bottle **\$10.80** 4 bottles **\$9.45** each

Each bottle lasts 100 days.

LIFE
EXTENSION

Lithium
1000 mcg

Essential Mineral for
Brain and Body Health

100 VEGETARIAN DETARY
SUPPLEMENT



*European Journal of Nutrition, 2011:50(5):387-389

C₆H₆MgO₇ MgO

"I love that it's extend release."

Carol

VERIFIED CUSTOMER REVIEW

Immediate Uptake. Extended Release. Up to 6 Hours of Support.

Magnesium is terrific for head-to-toe, in-and-out wellness. Extend-Release Magnesium is clinically formulated to:

- Deliver magnesium citrate for immediate uptake
- Deliver magnesium oxide for extended release
- Support heart and bone health
- Encourage metabolic health

SUPER SALE PRICE

Item #02107

60 250 mg vegetarian capsules

1 bottle **\$8.78** 4 bottles \$7.88 each

CAUTION: If taken in high doses, magnesium may have a laxative effect. If this occurs, divide dosing, reduce intake, or discontinue product.

ZümXR® is a registered trademark and protected by patents. See www.ZümXR.com





For full product description and to order Extend-Release Magnesium, call 1-800-544-4440 or visit www.LifeExtension.com



Feed Your Brain

Cognitex® Elite Pregnenolone

SUPER SALE PRICE

Item #02397 • 60 vegetarian tablets (with pregnenolone)

1 bottle **\$39.15**

4 bottles \$36 each

Cognitex® Elite

SUPER SALE PRICE

Item #02396 • 60 vegetarian tablets (without pregnenolone)

1 bottle **\$37.80**

4 bottles \$34.20 each







Do not use if you are of childbearing age, pregnant or planning to become pregnant.

memory performance in healthy, older volunteers.

Cognitex® Elite combines sage with other studied ingredients for brain health:

Sage extract SIBELIUS™: SAGE	333 mg
Proprietary Wildcrafted Blueberry Blend	200 mg
Sensoril® ashwagandha extract	125 mg
Phosphatidylserine	100 mg
Uridine-5'-monophosphate, disodium	50 mg
Vinpocetine	20 mg

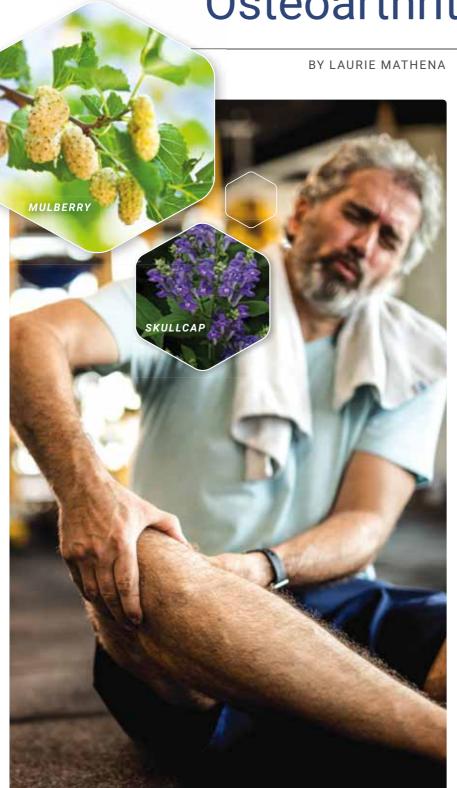
Cognitex® Elite Pregnenolone contains these same powerful ingredients but with 50 mg of pregnenolone added.

For a full product description and to order Cognitex® Elite or Cognitex® Elite Pregnenolone, call 1-800-544-4440 or visit www.LifeExtension.com

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Reduce Cartilage Loss in





Osteoarthritis is the most common cause of joint pain, affecting more than 30 million adults in the U.S.1

Most standard approaches address its symptoms,2,3 such as pain and stiffness.

But osteoarthritis damages and ultimately destroys the cartilage that allows the joint to function.1

Targeting only the pain and stiffness risks letting cartilage damage and joint degeneration continue unabated.

A novel solution may address not only pain and stiffness, but also underlying damage and destruction.

In two animal models, three botanical extracts demonstrated the ability to relieve pain and swelling and reduce damage to cartilage.4,5

Human studies have demonstrated that these plant extracts can provide symptomatic relief as well as benefits for joint structure. 6,7

How They Work

Pain relief is the immediate goal of anyone suffering from osteoarthritis and the limitations it imposes.

But protecting against joint damage and improving joint structure is iust as important.

Separate studies have shown that a combination of Chinese skullcap. cutch tree, and white mulberry tree extracts makes it possible to support both.

All three extracts help fight inflammation and maintain comfortable joints.

Cutch trees are rich in catechins,8 compounds that inhibit proinflammatory signaling molecules. They suppress major pro-inflammatory molecules, such as COX-2, 5-LOX, and "master inflammatory promoter" nuclear factor-kappa B (NF-kB).7,9

The root and bark of the mulberry tree are similarly rich in compounds with anti-inflammatory properties. 10,11

Chinese skullcap (Scutellaria baicalensis) is rich in a compound called baicalin, with known antiinflammatory properties that complement those in cutch tree.4,12

Reduced Joint Damage

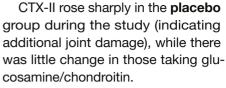
Researchers conducted a randomized controlled clinical trial to compare two non-drug treatments to placebo.

This study enrolled 135 subjects aged 35-75 with mild to moderate knee osteoarthritis. Subjects had to have had symptoms for at least six months before the start of the study, and for at least 15 out of the previous 30 days at admission. They received one of three treatments for 12 weeks: 7

- 1. Cutch tree and white mulberry extracts (400 mg/day),
- 2. Glucosamine (1,500 mg/day) and chondroitin (1,200 mg/ day), or
- 3. Placebo.

The botanical extracts appeared to protect against joint damage and potentially stop the progression of the disease.

This was seen by measuring urinary levels of C-terminal crosslinking telopeptide (CTX-II), a urinary biomarker of cartilage breakdown. Higher CTX-II levels in urine indicate more joint damage.



In the group taking cutch tree and white mulberry, there was a significant decrease in CTX-II levels.

This finding indicates that the plant extracts were protecting the joint against damage and could help reduce osteoarthritis progression over time.7

Clinical Study Shows Pain Relief

A randomized, placebo-controlled 90-day trial in 60 subjects aged 40-75. with symptomatic osteoarthritis of the knee or hip tested the effect of a different herbal combination supplement, made of Chinese skullcap and cutch tree.

The patients were randomized to receive either a placebo, 200 mg/day of the drug celecoxib (Celebrex®), or one of two doses of the combination herbal supplement (250 or 500 mg/day of Chinese skullcap + cutch tree).

Subjects were followed-up for pain, stiffness, functional impairment, and physical function using standard measurement scales.6

Both doses of the dual-ingredient herbal supplement significantly reduced pain scores by the end of the 90 days.

Stiffness and functional impairment were significantly reduced in both herbal dosage groups, compared to baseline, and at all time points. These measures did not significantly improve in the celecoxib or placebo groups.

A measure of **physical function** significantly improved at all time points in the herbal-supplemented groups compared to placebo.6



Cartilage and **Bone Protection**

Animal and laboratory research confirms the results of the clinical trial that showed that the cutch treewhite mulberry combination preserves joint health.

An animal model showed that when used together, cutch tree + white mulberry reduced cartilage breakdown by nearly 55% with a 41% reduction in sensitivity to pain after five weeks.5

A similar animal model showed this same combination (cutch tree + white mulberry) resulted in an improvement in pain and inflammation much like that of a commonly used overthe-counter and pain medication, ibuprofen.13

Comparison to Common Medications

Many people suffering from joint pain turn to nonsteroidal antiinflammatory drugs (NSAIDs).

Unfortunately, this standard care manages only the symptoms,^{2,3} such as pain and stiffness, overlooking damage to cartilage and bone.

A combination of cutch tree and white mulberry extracts was found in an animal study to be similar to ibuprofen in its ability to reduce pain and swelling.14

Chinese skullcap is also rich in anti-inflammatory compounds.

A blend of Chinese skullcap and cutch tree extracts was tested headto-head against the drug celecoxib in people with severe knee osteoarthritis.6

After 90 days, the cutch tree-Chinese skullcap blend was more effective than the drug at relieving pain, reducing stiffness, and improving physical function.

The combination was evaluated in animal and lab studies and has been shown to inhibit production and activity of inflammatory signaling molecules and significantly reduced pain and swelling.4,15-17

Summary

In addition to causing pain, stiffness, and loss of mobility, osteoarthritis causes progressive cartilage damage and joint degradation.

The three herbs-Chinese skullcap, cutch tree, and white mulberry—have been shown to reduce markers of inflammation, joint destruction, and cartilage degradation...indicating their potential to change the osteoarthritis landscape.

Studies indicate that combinations of these extracts are equal or superior to common medications at relieving pain, swelling, and stiffness.

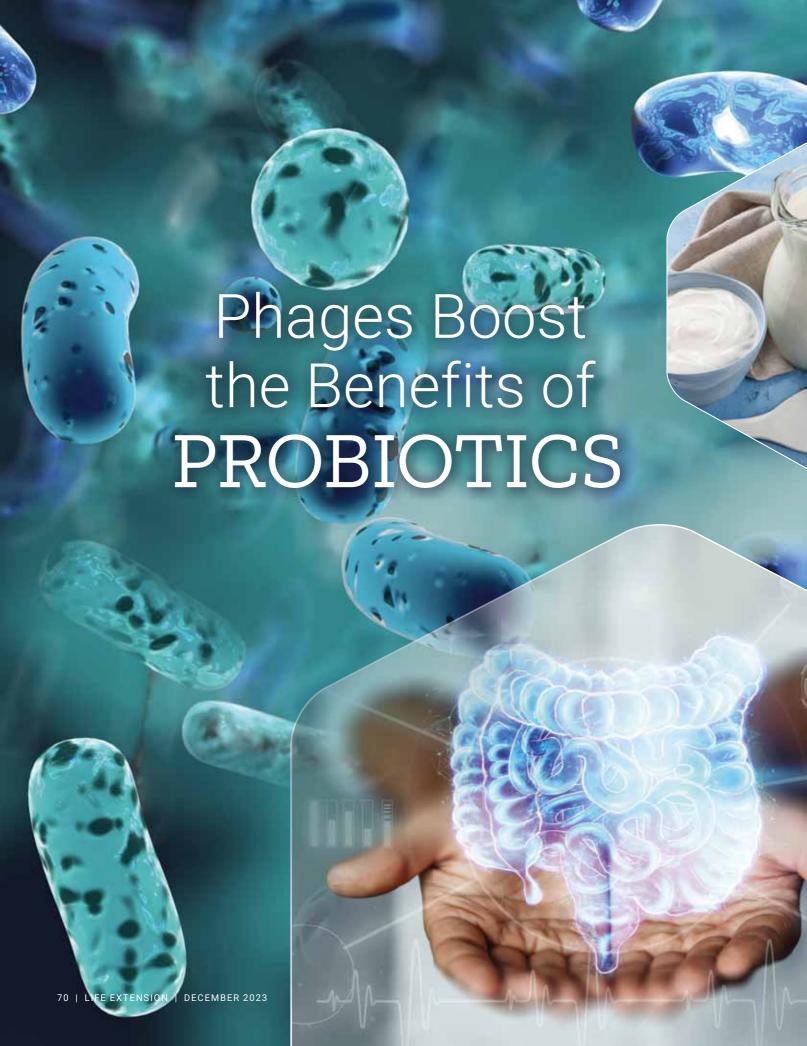
As with any approach that offers prevention and relief of symptoms, the earlier you start, the better the long-term protective effect. •

If you have any questions on the scientific content of this article, please call a **Life Extension** Wellness Specialist at 1-866-864-3027.

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One way to do this employs the <u>combined</u> use of probiotics and bacteriophages or "phages."

Phages are tiny packages of DNA or RNA wrapped in protein.

Each type of phage naturally attacks *only specific* types of bacteria.⁷⁻⁹ By selecting specific phages, it is possible to target specific, potentially harmful bacteria in the digestive tract.

This allows a dual-approach strategy of using **probiotics** for their beneficial effects, while reducing competition from bacteria, of which we want less.

How Gut Health Impacts Overall Health

Gut bacteria affect almost *all* aspects of human health.

Researchers have estimated that a healthy adult individual's intestines host about **160** distinct bacterial species.⁵ The presence or absence of certain species can have dramatic consequences.^{10,11}

An enormous range of gut bacteria is necessary for optimal health. One important health-promoting property of some bacteria in the gut is the ability to produce **short-chain fatty acids**, compounds that have shown anti-inflammatory, immune-supportive, and neuroprotective activity, among other benefits.¹²

Certain factors, including advancing age,¹³ poor diet,¹³ stress,¹³ antibiotic use,¹³ and lack of physical activity,¹⁰ can cause our microbiomes to become **imbalanced**, a state known as **dysbiosis**.¹⁴

This imbalance is associated with worse health.⁴ Scientists have linked dysbiosis to colon infections, antibiotic-associated diarrhea, irritable bowel syndrome, autoimmune disease, allergic conditions, and obesity.^{15,16}



Other harmful microbes in the gut can cause infections, inflammation, and gastrointestinal discomfort, and appear to contribute to the risk for chronic disease. 13,17

Even in otherwise healthy individuals, a gut bacteria imbalance can trigger the development of digestive symptoms like diarrhea, gas, bloating, and abdominal pain.¹⁸

Gut bacteria even appear to play a role in the metabolism of **neurotransmitters** such as serotonin, a moodregulating hormone.¹⁹ That could help explain why people with certain gastrointestinal disorders have a higher risk of mental health conditions like **depression** and **anxiety**.^{1,20}

Shifting the gut microbiota toward a healthy balance can ease digestive issues and improve overall health.

The Benefits of Probiotics and Phages

Research has established the many and varied benefits of taking oral probiotics. *Lactobacillus* and *Bifidobacterium*, two of the most common probiotics, help ease symptoms of certain gastrointestinal diseases.²¹

Bacteriophages are lesser-known tools that help promote **gut** and **overall health**.²²

The term "bacteriophage" literally means "bacteria eater." Phages are selective killers, only targeting and destroying specific bacteria.^{7,9,23}

The phages can allow *beneficial* bacteria to flourish and grow at a greater rate by removing competing harmful species.²⁴

Phages were discovered almost a century ago and were recognized by the FDA as early as 1958 as safe to use to help protect foods against the growth of undesirable bacteria. Because they exclusively target bacteria and not animals or humans, and as suggested by their safety to use in the food supply, phages pose no health threat to humans.

However, research into phages as therapeutic agents in human infections fell out of favor with the discovery of antibiotics.²⁶ Today, as the threat of **antibiotic-resistant infections** and superbugs has become more concerning, medical research is refocusing on the potential of **phage therapy**.

Phages have now been used in numerous human trials and therapeutic settings with **no reports of adverse effects.**²⁷⁻³²

Combining probiotics with phages holds great promise for gut health and other areas impacted by the gut microbiome.

Human Trials

Researchers developed a targeted four-phage blend that can help rapidly decrease intestinal populations of the unfavorable bacteria E. coli, while boosting growth of beneficial bacteria.33,34

In a clinical study, scientists tested the impact of these bacteriophages on the gut microbiome and gastrointestinal inflammation. Healthy adults received either the four-phage blend (LH01-Myoviridae, LL5-Siphoviridae, T4D-Myoviridae, and LL12-Myoviridae) or a placebo daily for 28 days.34

Compared to placebo, the phage blend was associated with:34

- · Increases in beneficial bacteria in the gut,
- Decreases in Escherichia coli (E. coli) bacteria, a common cause of diarrhea and other digestive problems, and
- Decreases in interleukin-4, a marker of inflammation.

This shows that phages can beneficially modify gut bacteria.

In another clinical study, researchers tested whether adding the four-phage blend to a common probiotic bacterium, Bifidobacterium lactis, could enhance the effects of the probiotic.33

Healthy adults received either *B. lactis* or that probiotic with the four-phage blend for four weeks. Compared to the probiotic-only group, the group that consumed B. lactis plus the phage blend had:33

- Improvement in symptoms of gastrointestinal inflammation,
- Reduction in colon pain,
- A six-fold increase in beneficial Lactobacillus bacteria, and
- Decreases in the gastrointestinal tract in the amount of Citrobacter and Desulfovibrio, and a trend toward a decrease of E. coli, intestinal bacteria associated with inflammation, gastrointestinal dysfunction, infections, and other potentially serious health problems.

These observations suggest adding phages to probiotics could support probiotic benefits and aid in the shift toward a more favorable gut microbiome.



Improve the Microbiome with a Phage-Probiotic Blend

- The mix of microbes in our gut has a huge impact on digestive and overall health.
- Taking beneficial bacteria called probiotics can improve the balance of the gut microbiome.
- Bacteriophages, called **phages** for short, are packages of DNA or RNA wrapped in protein. They can selectively kill harmful bacteria, allowing probiotic bacteria to flourish.
- Combining phages with probiotics may boost the beneficial impact of the probiotic.

Summary

An unhealthy imbalance of bacteria in the gut can negatively affect gut and overall health.

Probiotics taken as supplements have helped balance intestinal flora.

Taking an oral combination of **probiotics** and **bacteriophages** may improve the health of the gut microbiome.

Phages show promise in relieving the functional changes caused by gut microbiome imbalance. This may be especially valuable for aging individuals. •

If you have any questions on the scientific content of this article, please call a **Life Extension**Wellness Specialist at 1-866-864-3027.

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We complied and our overall sales quadrupled the month we introduced **Life Extension® Mix™ Powder**.

GNC asked us to ship a case (12 bottles) of Life Extension® Mix™ Powder to every one of their stores.

Back then, we could barely keep up with client demand. We had to turn down **GNC** and other companies who wanted to offer their customers **Life Extension® Mix™ Powder**

51 INGREDIENTS IN ONE POWDER BLEND

What generated so much enthusiasm was the ability of **Life Extension® Mix™ Powder** to deliver a wide range of *higher*-potency **nutrients** at a far <u>lower</u> price than taking them individually.

It also reduced the need for people to swallow so many pills.

Life Extension® Mix™ Powder contains the vitamins and minerals found in multi-nutrient tablets, but at higher concentrations and more effective forms when warranted.

Plant extracts include lutein, lycopene, luteolin, apigenin, silymarin, quercetin and other botanicals people want to ingest as part of a healthy diet.

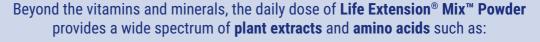
COMPREHENSIVE, CONVENIENT, COST EFFECTIVE

Three scoops of Life Extension® Mix™ Powder deliver meaningful potencies of vitamins, minerals, and plant extracts that would otherwise require swallowing dozens of tablets and capsules.

A one-month supply costs \$54 during the annual **Super Sale**. This price is reduced to **\$48.60** when four bottlers are purchased...a fraction of the cost of taking these standardized **nutrients** separately.

For those seeking to ensure daily intake of healthy fruits and vegetables, along with the higher potencies + better forms of vitamins and minerals, Life Extension® Mix® Powder delivers all this in a comprehensive, convenient, and cost-effective manner.

Life Extension® Mix™ Powder can be combined with smoothies, fruit-vegetable juices, or consumed by itself in water. View the entire Life Extension® Mix™ Powder formula on the next page.



NAC (n-acetyl-cysteine)	600 mg	Pomegranate Extract	85 mg
Broccoli concentrate	525 mg	Cherry Extract	85 mg
Green Tea Extract (decaffeinated)	325 mg	Grape Extract (seed & fruit)	50 mg
Bioflavonoids (citrus)	200 mg	Bilberry Extract	30 mg
Blueberry Extract	150 mg	Olive Fruit Extract	12.5 mg
Dideberry Extraor	roo mg	Onto France Extraot	12.0 mg



Complete LIFE EXTENSION® MIX™ POWDER Formula

Complete Life Extension Mix POWDER For	mula
Vitamin C (as calcium ascorbate, ascorbic acid, ascorbyl palmitate, magnesium ascorbate, niacinamide ascorbate, acerola exi	tract) 970 mg
Vitamin D3 (as cholecalciferol)	2,000 IU
Vitamin A (as beta-carotene and acetate)	5,000 IU
Thiamine (vitamin B1) (as thiamine HCl)	125 mg
Riboflavin (vitamin B2) (as riboflavin, riboflavin 5'-phosphate)	50 mg
Niacin (as 61% niacinamide, 38% niacin, 1% niacinamide ascorbate)	190 mg•
Vitamin B6 [as pyridoxal 5'-phosphate (100 mg), pyridoxine HCI (5 mg)]	105 mg
Folate (as L-5-methyltetrahydrofolate calcium salt)	680 mcg°
Vitamin B12 (as methylcobalamin)	600 mcg
Biotin	3000 mcg
Pantothenic acid (as D-calcium pantothenate with 5 mg pantethine)	600 mg
Vitamin E (as D-alpha tocopheryl succinate, D-alpha tocopherol) (100 IU)	67 mg
Magnesium (as magnesium oxide, citrate, arginate, glycinate, taurinate, ascorbate)	420 mg
Selenium [as sodium selenite, SelenoExcell®4 high selenium yeast, Se-methyl L-selenocysteine]	200 mcg
Zinc (as zinc citrate, L-OptiZinc®3 zinc mono-L-methionine sulfate)	35 mg
Calcium (as Ca ascorbate, D-calcium pantothenate, dicalcium phosphate)	140 mg
lodine (as potassium iodide)	150 mcg
Copper [as copper bisglycinate chelate]	1 mg
Manganese (as manganese citrate, gluconate)	1 mg
Chromium [as Crominex®5 3+ chromium stabilized with Capros® amla extract (fruit), PrimaVie® Shilajit]	500 mcg
Molybdenum (as molybdenum amino acid chelate)	125 mcg
Potassium (as potassium citrate)	35 mg
N-acetyl-L-cysteine (NAC)	600 mg
Taurine	200 mg
Broccoli concentrate blend [broccoli powder, extract (sprout, floret, seed) (providing glucosinolates, sulforaphane)]	525 mg
Green tea extract (leaf-decaffeinated) [std. to 45% epigallocatechin gallate (EGCG)]	325 mg
Acerola extract 4:1 (berry)	300 mg
Inositol	250 mg
Bitter orange citrus bioflavonoids (peel, fruit) [std. to 50% hesperidin]	200 mg
Fruit/berry proprietary blend [European elder, blackberry, blueberry, sweet cherry, cranberry, plum, persimmon (Diospyros kaki) pow	/ders] 200 mg
Wild blueberry anthocyanin extract (fruit)	150 mg
Sensoril®12 Ashwagandha extract (root, leaf) [std. to 32% oligosaccharides, 10% glycoside conjugates]	125 mg
Silymarin [from milk thistle extract (seed)]	100 mg
Trimethylglycine (TMG) (as betaine anhydrous)	100 mg
CherryPure®1 sour cherry (tart cherry) proanthocyanidin powder (skin)	85 mg
POMELLA® pomegranate extract (fruit) [std. to 30% punicalagins]	85 mg
Natural mixed tocopherols (providing gamma, delta, alpha, beta tocopherols)	60 mg
MirtoSelect®11 bilberry extract (fruit)	30 mg
BioVin®7 grape proanthocyanidin extract (whole grape)	25 mg
Leucoselect® grape seed proanthocyanidin extract	25 mg
Bio-Quercetin phytosome (providing 5 mg quercetin	20 1119
[from Japanese sophora concentrate (flower bud)], phosphatidylcholine complex [from sunflower])	15 mg
Bromelain [from pineapple (stem)] (2400 gelatin digestive units/gram)	15 mg
Lutein [from marigold extract (<i>Tagetes erecta</i>) (flower)] (providing 465 mcg <i>trans</i> -zeaxanthin)	15 mg
Olive extract (fruit) (providing polyphenols, hydroxytyrosol, tyrosol, oleuropein)	12.5 mg
Sesame seed lignan extract	10 mg
Luteolin [from Japanese sophora (flower bud)]	8 mg
Apigenin	5 mg
Boron (as boron amino acid chelate)	3 mg
Lycopene [from LycoBeads® natural tomato extract (fruit)]	3 mg
Delphinidins [from Delphinol®2 maqui berry (Aristotelia chilensis) extract (fruit)]	2 mg
Cyanidin-3-glucoside (C3G) [from black current extract (fruit)]	
Cyaniani-3-glacoside (C3G) [Holli black cultaint extract (Hult)]	1.25 mg





For full product description and to order Life Extension® Mix™ Powder call 1-800-544-4440 or visit www.LifeExtension.com

Other ingredients: maltodextrin, natural orange flavor, stevia extract, silica, modified food starch, luo han guo extract. ^RAE (retinol activity equivalents). *DFE (dietary folate equivalents). •NE (niacin equivalents).

- 1. CherryPURE® is a registered trademark of Shoreline Fruit, LLC.
- 2. Delphinol® is a registered trademark of MNL.
- 3. L-OptiZinc® is a Lonza trademark, registered in USA.
- 4. SelenoExcell® is a registered trademark of Cypress Systems Inc.
- 5. Crominex® 3+, Capros® and PrimaVie® are registered trademarks of Natreon, Inc.
- $\mbox{6. Leucoselect} \mbox{$^{\$}$ is a registered trademark of Indena S.p.A.} \label{eq:constraints}$
- 7. BioVin® is a registered trademark of Cyvex Nutrition dba Bioriginal.
- 8. Lycored LycoBeads® is a registered trademark of Lycored; Orange, New Jersey.
- 9. POMELLA® Extract is covered under U.S. Patent 7,638,640 and POMELLA® is a registered trademark of Verdure Sciences, Inc.
- 10. MirtoSelect® is a registered trademark of Indena, S.p.A., Milan, Italy.
- 11. Sensoril® is protected under US Patent No. 7,318,938 and is a registered trademark of Natreon, Inc.
- 12. TRAACS® is a registered trademark of Albion Laboratories, Inc.

SUPER SALE PRICE Item #02356

Life Extension® Mix™ Powder, 12.70 oz

1 bottle **\$54** 4 bottles \$48.60 each (Each bottle lasts 30 days)

A Therapeutic Foot Massage with every step

Wearing Kenkohs daily, even for short periods, can help improve blood circulation, keep your body aligned, relieve pain in the feet, ankles, knees, legs, hips and back, reduce swelling, relieve stress and enhance your overall mood. Kenkoh revitalizes and rejuvenates your whole body!



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Tilt Your Bacteria Ratio

for a Healthy Digestive Tract

Phages target bad intestinal bacteria, allowing beneficial strains to flourish.

FLORASSIST® GI provides a 7-strain blend of **probiotics** in a **dual encapsulation** formula to deliver beneficial bacteria and **phages** where you need them the most.



Dual-Encapsulation Delivery



SUPER SALE PRICE

Item #02125
30 liquid vegetarian capsules

1 bottle **\$22.28** 4 bottles \$20.25 each



For full product description and to order FLORASSIST® GI with Phage Technology, call 1-800-544-4440 or visit www.LifeExtension.com



Vitamin D3

Systemic support for immune function and bone health.

SUPER SALE PRICE Item #01713

125 mcg (5000 IU) 60 softgels

1 bottle **\$6.75** 4 bottles \$5.85 each For full product description and to order Vitamin D3, call 1-800-544-4440 or visit www.LifeExtension.com







CAUTION: Individuals consuming more than 50 mcg (2000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.





Supports Improvement in Overall Cognitive Ability*

With age, **synapses** that connect our brain cells wither.

Formulated by MIT scientists,

Neuro-Mag® Magnesium L-Threonate has
been shown to improve synaptic density and
other structural components of the brain.



SUPER SALE PRICE

Item #01603 • 90 vegetarian capsules

1 bottle \$27.68 • 4 bottles \$24.75 each





SUPER SALE PRICE

Item #02032 • 93.35 grams of powder

1 jar **\$27.68** • 4 jars \$24.75 each

For full product description and to order Neuro-Mag® Magnesium L-Threonate or Neuro-Mag® Magnesium L-Threonate Powder, call 1-800-544-4440 or visit www.LifeExtension.com

* Gerontology. 1996;42(3):170-80.

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IN THIS EDITION OF LIFE EXTENSION MAGAZINE®













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