



The Science of a Healthier Life®

LifeExtension.com

July 2022

FEATURE ARTICLES

- 7 Strategy for Higher-Dose Melatonin
- 32 Mushrooms that Boost Immunity
- 42 Improve Your Sleep
- 50 Vitamin K and Heart Health
- 58 Systemic Effects of N-Acetyl-L-Cysteine
- 65 Pregnenolone and Brain Function

A New Way to Enjoy MELATONIN



PLUS: Page 71
Dangerous Pet Foods

VOTED #1 MULTIVITAMIN

"Covers all the bases."

Brian
VERIFIED
CUSTOMER
REVIEW



Compare **Two-Per-Day Multivitamin** to the Leading Brand **Centrum®**

The **Two-Per-Day** multinutrient formula is superior to commercial multivitamins because it provides vastly **higher** potencies of **vitamins, minerals and plant extracts.**



#1 Rated
Multivitamins
9 Time Winner!*

**Compared to Centrum®
Two-Per-Day Provides:**

- 50 TIMES THE VITAMIN B1**
- 25 TIMES THE VITAMIN B6**
- 12 TIMES THE VITAMIN B12**
- 10 TIMES THE BIOTIN**
- 10 TIMES THE SELENIUM**
- 8 TIMES THE VITAMIN C**
- 3 TIMES THE VITAMIN E**
- 2.5 TIMES THE VITAMIN B3**
- 2 TIMES THE VITAMIN D**
- 2 TIMES THE ZINC**

Alpha lipoic acid, quercetin and plant extracts lacking in most commercial multivitamins.



**Centrum®
Can't
Compete**

Two-Per-Day Multivitamin Capsules

Item #02314 • 120 capsules (two-month supply)
1 bottle \$19.13 • 4 bottles \$17 each

Two-Per-Day Multivitamin Tablets

Item #02315 • 120 tablets (two-month supply)
1 bottle \$18.38 • 4 bottles \$16.25 each

For full product description and to order
TWO-PER-DAY MULTIVITAMIN,
call **1-800-544-4440** or
visit **www.Life Extension.com**



Lycored LycoBeads® is a registered trademark of Lycored; Orange, New Jersey. SelenoExcell® is a registered trademark of Cypress Systems Inc. L-OptiZinc® and logo are trademarks of Lonza or its affiliates. Crominex® 3+, Capros® and PrimaVie® are registered trademarks of Natreon, Inc. *Ratings based on results of the 2022 ConsumerLab.com Survey of Supplement Users. More information at www.consumerlab.com/survey

REPORTS

42 ON THE COVER

**NEW WAY TO
ENJOY MELATONIN**

People often crave something tasty to chew on before bedtime. A **sugar-free** strawberry-flavored gummy enables individuals to dose their **melatonin** based on how many gummies they ingest at bedtime.



42



32



50



58



65

32 MUSHROOMS AND IMMUNE FUNCTION

Mushrooms contain **beta glucans** and other compounds known to *activate* critical immune functions.

50 VITAMIN K AND HEART HEALTH

Older adults with the *highest* **vitamin K2** intake had a sharply *lower* risk of death from coronary heart disease.

58 SYSTEMIC EFFECTS OF N-ACETYL-L-CYSTEINE

NAC (N-acetyl-L-cysteine) boosts **glutathione** levels in cells throughout the body and may help resolve a host of common disorders.

65 WHAT IS PREGNENOLONE?

Pregnenolone, the “mother of all hormones” has been shown to improve cognitive functions and boost mood.

DEPARTMENTS

7 A CASE FOR HIGHER-DOSE MELATONIN

Emerging data indicate that **melatonin** may help protect against cancer, improve immune function, and reduce inflammation.

25 IN THE NEWS

Curcumin improves diabetic kidney disease; fish oil lowers risk of liver cancer; zinc supplements decrease risk of Alzheimer’s; collagen peptides boost bone health.

71 ASK THE DOCTOR

Veterinarian Dr. Gary Richter explains why standard dry and canned food is so harmful for your pet. He details the best foods to support your pets’ overall health.

75 SUPER FOODS

Bok choy, ranked the sixth most nutrient-dense food, is a cruciferous vegetable linked to a lower risk of numerous types of cancer, including lung, prostate, and colon.



7



71



25



75



MY LIFE EXTENSION OFFERS

- Custom product recommendations
- All your offers—in one place
- Reorder reminders ...and more!

LifeExtension.com/MyLifeExtension



Visit the **Life Extension Health & Wellness Market**

- 400+ Life Extension® supplements
- Health foods & fresh produce
- Good to Go Juice Bar & Cafe
- In-store wellness workshops and lab testing

900 North Federal Highway
Fort Lauderdale, FL 33304
954-766-8144
Monday-Friday 9 AM-8 PM
Saturday 9 AM-6 PM • Sunday 11 AM-5 PM



#1 Rated
Catalog/Internet Merchant
6 Time Winner*

* Ratings based on results of the 2021 ConsumerLab.com survey of supplement users.
More information at www.ConsumerLab.com/survey.

Editorial

Editor-in-Chief • Philip Smith
Executive Managing Editor • Renee Vermeulen
Medical Editor • Hernando Latorre, MD, MSc
Senior Editor • Dan Jewel
Senior Staff Writer • Michael Downey
Department Editor • Laurie Mathena
Associate Editor • Rivka Rosenberger, EdD
Creative Director • Robert Vergara
Art Director • Alexandra Maldonado

Chief Medical Officer

Steven Joyal, MD

Chief Scientific Officer

Andrew Swick, MS, PhD

Scientific Advisory Board

Richard Black, DO • John Boik, PhD • Aubrey de Grey, PhD
Deborah F. Harding, MD • Steven B. Harris, MD • Sandra C. Kaufmann, MD
Peter H. Langsjoen, MD, FACC • Dipnarine Maharaj, MD
L. Ray Matthews, MD, FACS • Ralph W. Moss, PhD
Michael D. Ozner, MD, FACC • Jonathan V. Wright, MD • Xiaoxi Wei, PhD

Contributors

Michael Downey • Laurie Mathena
Anthony Payne, NMD, PhD, MD • Gary Richter, DVM

Advertising

Vice President of Marketing • 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

Life Extension Magazine® values your opinion and welcomes feedback.

Please mail your comments to *Life Extension Magazine*, Attn:
Letters to the Editor, PO Box 407198, Fort Lauderdale, FL 33340
or email us: LEmagazine@LifeExtension.com

BOOST YOUR FREE

TESTOSTERONE

Testosterone builds muscle, maintains sexual health, supports cardiac function, strengthens bones, and nourishes brain cells.^{1,2}

Testosterone Elite helps maintain healthy testosterone levels.†

- A clinical trial showed that **pomegranate** and **cacao** elevated **free testosterone** levels **48%** in just eight weeks.³
- **Luteolin** increases a protein for testosterone synthesis and inhibits aromatase, an enzyme that breaks down testosterone.⁴⁻⁶
- Just one capsule a day.

"Interest in intimacy has been heightened since beginning this supplement."

Larry

VERIFIED CUSTOMER REVIEW

**PLANT-BASED
NUTRIENTS**

Item #02500 • 30 vegetarian capsules

1 bottle \$42 • 4 bottles \$37.50 each



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.

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

† This product is intended to support testosterone levels but does not contain testosterone. Tesnor® is a trademark of Laila Nutra and Gencor.



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

MEDICAL ADVISORY BOARD

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, DO, 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 anti-aging 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.

Garry F. Gordon, MD, DO, is a Payson, Arizona-based researcher of alternative approaches to medical problems that are unresponsive to traditional therapies. He is president of the International College of Advanced Longevity Medicine.

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 Montepulciano 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, DO, 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 anti-aging medicine and has worked for many years as flight surgeon at the European Space Agency. He is a pioneer in functional and anti-aging 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 humans.



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.

Dipnarine Maharaj MD, MB, ChB, FRCP (Glasgow), FRCP (Edinburgh), FRCPath., FACP, is the Medical Director of the Maharaj Institute of Immune Regenerative Medicine, and is regarded as one of the world's foremost experts on adult stem cells. He received his medical degree in 1978 from the University of Glasgow Medical School, Scotland. He completed his internship and residency in Internal Medicine and Hematology at the University's Royal Infirmary.



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.



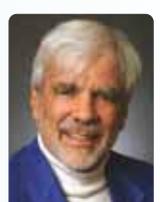
Ralph W. Moss, PhD, is the author of books such as *Antioxidants Against Cancer*, *Cancer Therapy, Questioning Chemotherapy*, and *The Cancer Industry*, as well as the award-winning PBS documentary *The Cancer War*. Dr. Moss has independently evaluated the claims of various cancer treatments and currently 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.



Whole- Body Support

Everything good
takes time.

Magnesium is essential for a healthy heart and sturdy bones; it's even great for your mood. But, most of us don't get enough from our diets.

Our innovative formula delivers both immediate and extended-release magnesium, so you get the maximum benefits—for the long haul.



Item #02107

60 250 mg vegetarian capsules

1 bottle \$9.75 • 4 bottles \$8.75 each



**#1 Rated
Magnesium
Products***

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

*Ratings based on results of the 2022 ConsumerLab.com Survey of Supplement Users. More information at www.consumerlab.com/survey

"For overall health for bones.
Great product."

Roniele

VERIFIED CUSTOMER REVIEW

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

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

A Case for Higher-Dose Melatonin



WILLIAM FALOON

On February 1, 2022, the *Journal of the American Medical Association (JAMA)* published a report showing that **melatonin** consumption “**significantly increased**” from **1999** to **2018** in the United States.¹

The authors point to this trend of “**self-administered**” melatonin as a reason to raise “**safety concerns**” about the lack of long-term clinical data. They make insinuations about the **poor quality** of melatonin supplements sold by certain commercial companies.

Concerns were also raised about insufficient study of people taking **melatonin** in nightly doses above **5 mg**.

It was **30 years** ago when our **Life Extension** group introduced the world to **melatonin**. We provided purified melatonin to researchers for **human** studies, and to our supporters.

We’ve had interactions with thousands of people who have used a wide range of melatonin potencies since we launched it in **1992**.

Rather than defend our long-term observed safe use of melatonin, this article will provide a rationale for some people to consider **higher** doses. I’ve self-experimented with these higher potencies for the last **two years** without experiencing adverse reactions.

The main reason I increased my nightly melatonin dose is the potential for **immune** benefits.²

In reviewing evidence about **higher-dose** melatonin, I recalled our **40-year** history of erring on the side of **safety** when introducing health-promoting compounds.

Below are examples of **dosage increases** of nutrients that **Life Extension** helped pioneer over the decades:

<u>Ingredient</u>	<u>Initial Dose</u>	<u>Current Average Dose</u>
CoQ10	10-30 mg	100-200 mg
Vitamin D	400-800 IU	2,000-5,000 IU
Resveratrol	20 mg	100-250 mg
Vitamin K	45-65 mcg	2,000-45,000 mcg
NAD⁺ precursor (nicotinamide riboside)	100 mg	300 mg

These **higher** potencies are made practical by price reductions for ingredients like **CoQ10** and **resveratrol**.

CoQ10 costs a fraction of what it did when **Life Extension** introduced it in **1983**, as does **resveratrol** that we launched in **2003**.

Given our history of using published data to increase suggested doses, I decided to try **50 mg** of **melatonin** each night and found some **sleep improvement**.

I’ve since lowered my overall melatonin **dose** to incorporate more **sustained-release** formulas, so my average nightly dose is now around **20 mg**.

This article describes what researchers are finding as it relates to additional benefits that may be achieved using a wide range of **melatonin** doses.

The phrase “*sleep like a baby*” refers to tranquil, deep sleep patterns like those young children typically enjoy.

What few people know is that nighttime **blood levels** of **melatonin** in **children** ages **1 to 3 years** are very **high** and then progressively **drop by 80%** during the remainder of childhood.³

Total melatonin secretion further declines with increasing **age**, beginning perhaps as early as the third decade of life.^{4,5}

Data like these prompted some physician-scientists to hypothesize that adults might benefit from **higher** potencies of melatonin when dealing with serious illnesses.

While many studies support some **sleep-enhancing** properties of **low-** and **moderate-dose** melatonin,^{6,7} lacking are tightly controlled human studies measuring the nocturnal effects of **high-dose** melatonin.

What are not missing are an abundant number of studies describing the potential of **melatonin** to help prevent and combat **cancer**.

Melatonin and Cancer

In the early 1990s, I went on national TV talk shows to announce the **lifesaving** benefits of **melatonin**. The data back then showed that melatonin improved **immunity** and might prevent and/or help fight certain **cancers**.^{8,9}

Move forward to **2022**, and there are over 3,000 published studies investigating the potential of **melatonin** to be **useful** in **cancer prevention** or as an **adjuvant** agent in therapy for **cancer patients**.

Data demonstrating **anti-cancer** or other beneficial effects of melatonin in patients are still limited, but results are encouraging.

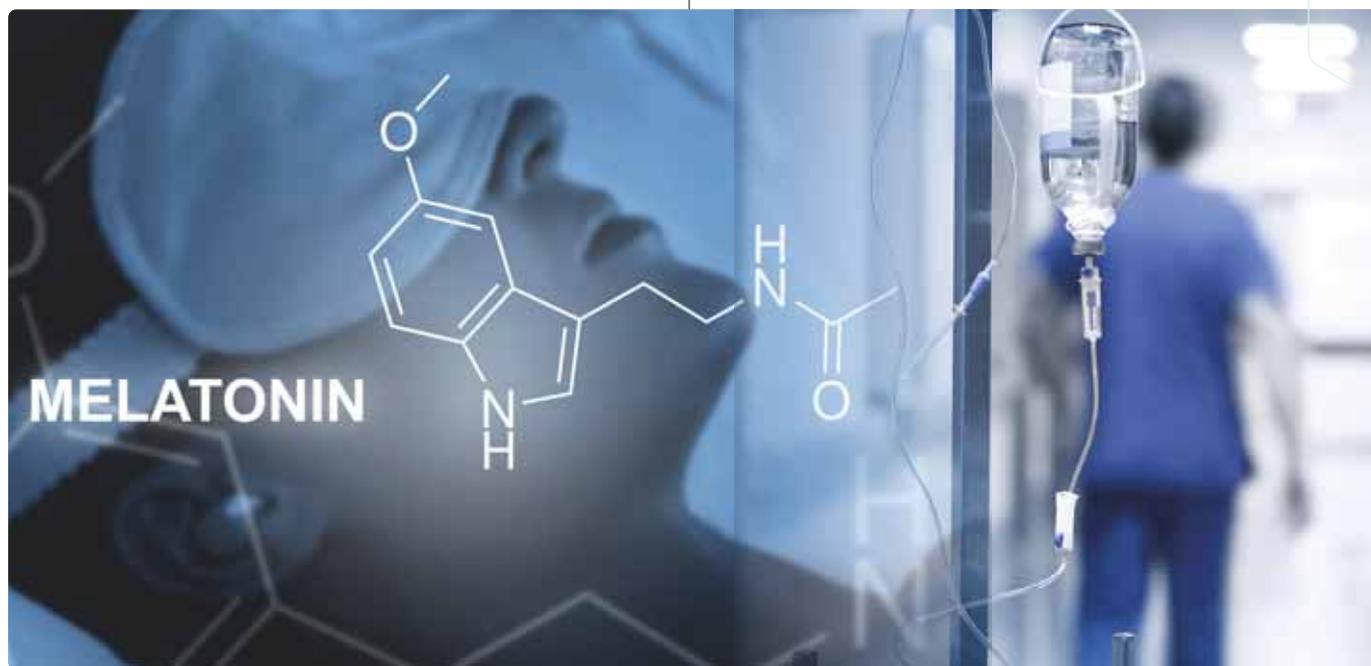
In a handful of completed **clinical trials** in patients with primary brain tumors, colorectal cancer, non-small-cell lung cancer, breast cancer, and brain metastasis, researchers found that **melatonin**, in doses up to **40 mg daily**, worked well with **conventional treatments**.

Researchers also noted improved **quality of life** in cancer patients when no other treatment was available.¹⁰⁻¹⁶

In two separate reviews of clinical trials assessing the use of melatonin during **chemotherapy** or **radiation** for the treatment of solid tumors, **melatonin** was found to **decrease** negative side effects such as fatigue and low platelet counts, **improve** response to treatment, and **increase** one-year survival.^{17,18}

You can access study abstracts about “**melatonin and cancer**” for free on the **National Library of Medicine** website at www.PubMed.gov

At the end of this editorial there is a summary of studies excerpted from the **National Library of Medicine** website about the role of **melatonin** in reducing cancer **incidence** and **mortality**.





Melatonin Use in Rheumatoid Arthritis

By enhancing certain **immune** functions, some early preclinical research suggests melatonin may increase the severity of **rheumatoid arthritis**, which is an auto-immune disease.³³⁻³⁵

This is in contradiction to beneficial effects of melatonin in other **autoimmune** inflammatory diseases.³⁶

Evidence from clinical studies indicates that low-dose melatonin (≤ 10 mg) does not seem to cause harmful effects in subjects with autoimmune diseases, such as multiple sclerosis, ulcerative colitis, lupus, and inflammatory bowel disease.³⁷⁻⁴³

In the past decade, some studies demonstrated that melatonin can alleviate rheumatoid arthritis through the inhibition of specific inflammatory factors.⁴⁴⁻⁴⁸

In fact, a **2021** study found that treatment with **6 mg** of melatonin daily for 12 weeks improved many markers of disease in rheumatoid arthritis patients.⁴⁹

The use of melatonin at doses under **10 mg** in rheumatoid arthritis patients may need consideration by treating physicians.

It is unknown whether high-dose melatonin ≥ 50 mg may exert any harmful effects in those with autoimmune diseases, especially in rheumatoid arthritis patients.



Preclinical Studies on Low- and High-Dose Melatonin

In seeking to ascertain the effects of **high-dose** melatonin we came across some interesting findings suggesting benefits with *higher* dosing. Summaries from these studies are copied below:

- In a mouse model of **amyotrophic lateral sclerosis** (ALS), a **high-dose** oral melatonin delayed disease progression and extended survival.¹⁹
- High-dose melatonin administered intraperitoneally before **myocardial** (heart) injury offered protection against cardiac ischemia-reperfusion injury in Sprague-Dawley rats.²⁰
- High-dose melatonin injected intraperitoneally for 56 days reduced myocardial hypertrophy and preserved **cardiac function** in diabetic Wistar rats.²¹
- High-dose melatonin (human equivalent of **55 mg** a day for 30 days) in **senescence-prone** mice showed that age-related increases in markers of inflammation, oxidative stress and apoptosis were effectively reduced by both low- and high-melatonin doses studied.²²
- Two additional studies with almost identical experimental designs found protective effects of high-dose melatonin on **heart** and **lung** tissue alterations in a mouse model of aging.^{23,24}

Human Studies of High-Dose Melatonin

In a clinical safety study of **ALS** (also called Lou Gehrig's disease) patients, a chronic high dose (**300 mg/day**) of enteral melatonin was well tolerated for up to two years. In this study, a surrogate marker for oxidative stress that is elevated in **ALS** patients was normalized by melatonin treatment. This implies a neuroprotective effect through reduction of oxidative stress.¹⁹

A crossover clinical study including 12 healthy male volunteers investigated the effects of high-dose (**100 mg**) intravenous melatonin and found no adverse effects. This study did not find a greater sedative effect with the **100 mg** intravenous melatonin relative to a **10 mg** dose.²⁵

Indole melatonin (**50 mg**) administered intravenously to three male narcoleptics dramatically increased the amount of REM sleep and decreased REM sleep latency.²⁶

At doses ranging from **10** to **40 mg** daily, melatonin in combination with IL-2 immunotherapy has been shown to improve outcomes in patients being treated for metastatic cancer.²⁷⁻³⁰

A **20 mg** daily oral dose of melatonin, divided into two **10 mg** doses, administered to septic newborns, improved their clinical outcomes after 24 and 48 hours and prevented death. All the newborns treated with melatonin survived, while three of the 10 babies in the non-melatonin group died.³¹

Currently, a clinical trial of antioxidant therapy in adult patients critically ill with septic shock is evaluating the efficacy of a **50 mg** nighttime dose of melatonin. Results are pending (NCT03557229).³²

Short-Term Studies Using High-Dose Melatonin in Humans

A surprising number of **human** studies have been done using varying melatonin doses without serious side effects being found.

In an analysis of 50 studies evaluating the efficacy of oral melatonin supplementation (**1-20 mg**), less than half the studies reported adverse events, which were typically minor and transient. Fatigue was seen most often in studies in which melatonin was taken during daytime hours.⁵⁰

A double-blind, placebo-controlled study evaluating the utility of **5-20 mg** of sublingual melatonin in patients undergoing gynecological surgical procedures reported neither dose-dependent nor dose-independent adverse events.⁵¹

General Safety Data on High-Dose Melatonin

A member of our scientific team did a comprehensive search of the published medical literature. Below is an Executive Summary of this literature review:

Executive Summary: Safety of High-Dose Melatonin

Based on a thorough and comprehensive evaluation of the most up-to-date scientific evidence from reputable sources, the conclusions of our review on efficacy and toxicity/safety of high-dose melatonin are as follows:

-- High-dose melatonin (doses **50 mg** and above) has been used in preclinical and clinical settings, and data collectively show that melatonin even at high doses has a good safety profile and is beneficial, improving disease outcomes.

However, at this time preclinical as well as clinical evidence does not clearly demonstrate that increasing the dose of melatonin is accelerating and/or amplifying melatonin benefits. That is because studies specifically addressing dose-dependent effects of melatonin in various settings are lacking.

-- There are no clinical data showing whether high-dose **50 mg** melatonin may exert any harmful effects in patients with autoimmune diseases, especially rheumatoid arthritis.

-- There is currently no compelling clinical evidence clearly showing that high-dose melatonin (**50 mg** and above) supplementation may interact with prescription drugs and decrease their effectiveness when taken concomitantly.

Oral administration of **1,000 mg a day** of melatonin to five adults for 25 to 30 days resulted in drowsiness being noted as an adverse effect. There were no severe and/or irreversible impacts on clinical parameters (blood pressure, heart rate, ECG, serum chemistry, urine analysis) in these people taking a massive **1,000 mg** dose of melatonin each night for 25 to 30 days.⁵²

Three separate studies did not report adverse side effects using the following **high doses** of melatonin:

- **90 mg**, on average, intravenously administered to healthy patients as well as individuals with seizure disorder and Parkinson's disease,⁵³
- **10 mg** per kilogram (intravenous) in preterm infants and septic neonates,⁵⁴ and
- **100 mg** (intravenous) in healthy subjects.²⁵

These findings suggest that extremely high doses of oral melatonin (**1,000 mg/day**), enteral melatonin (**300 mg/day**) and intravenous melatonin (**1-100 mg**) are safe and do not cause clinically significant side effects.

I am not recommending these high doses, just reporting on what's already been studied in people.

The studies reported in this section were short term and not the long-term, rigorous human trials that the authors of the February 2022 published **JAMA** report¹ and we at **Life Extension** would like to see conducted.

The dilemma is who is going to pay for a multimillion-dollar, long-term clinical trial using high-dose melatonin when it has been available as a low-cost dietary supplement for the last 30 years?

High-Dose Melatonin and Prescription Drugs

There is currently no compelling clinical evidence clearly showing that high-dose melatonin (**30-50 mg**) supplementation will interact with prescription drugs and decrease their effectiveness when taken concomitantly.

The comprehensive 2019 review of 50 studies described earlier including 17 studies in which participants were taking a variety of common medications or receiving treatment for cancer, did not find reports of apparent drug interactions.⁵⁰

The caveat, however, is that there are relatively little human data enabling us to know this for certain.



My only concern is for those with a propensity for low blood pressure, especially because blood pressure normally drops lower at night.

Melatonin has beneficial blood pressure-lowering effects.⁵⁵⁻⁵⁷

Those with **high blood pressure** often take their **anti-hypertensive drug(s)** at night for maximal efficacy. Melatonin may provide additional blood pressure-reducing effects, especially for those challenged to achieve optimal blood pressure levels.

Those concerned with **blood pressure** dropping too low, but who still want to try *higher*-dose melatonin, may consider starting with perhaps **6-10 mg** a night, using an at-home monitor to **self-assess blood pressure**, and adjusting the melatonin dose upwards if **blood pressure** does not drop too low.

I hope every one of our readers has an **at-home blood pressure monitor**, whose prices continue to drop to an affordable range.

The **30-50 mg** nightly doses of **melatonin** I have taken over the past two years have not caused any apparent side effects in me.

Some of you who do not rapidly metabolize melatonin will likely face next-day grogginess and may not want to take this **high** melatonin dose.

Melatonin Put Life Extension® on the Map

When **Life Extension®** introduced **melatonin** to the world in **1992**, virtually no one had ever heard the term. It's now a household name liberally described in the mainstream media as facilitating better sleep.

When the **New York Academy of Sciences** published a book on the multiple benefits of **melatonin**, the media picked up on it and I became a guest on some of the most popular talk shows in America.

The **JAMA** report (**February 1, 2022**) warns about unknown risks of long-term “self-administered” melatonin. **JAMA** is the **American Medical Association’s** most widely read journal.

Contrary to the position taken in the **JAMA** report, I present published data in this editorial as to why I am self-experimenting with *higher-dose melatonin*.

In particular, I am intrigued by the consistency of data indicating that melatonin may reduce **cancer risk** and improve outcomes of cancer patients treated with conventional therapy. These findings, which you can read for yourself at www.PubMed.gov, provide a compelling reason for most aging humans to supplement with at least a few milligrams of melatonin each night.

Copied at the end of this article are the results of a recent database search using the terms “**melatonin and cancer**.”

Those who self-experiment as I do may consider trying **10 mg** or more of melatonin about 30 minutes before bedtime. I started off with **10 mg** and added some sustained-release melatonin so as not to wake up too early. My average nightly melatonin dose now is around **20 mg**.

In this month’s issue...

The world has woken up to the fact that normal **aging** is accompanied by loss of **immune** functions. The article on page 32 describes the immune enhancing properties of specific **mushrooms**.

Vitamin K helps maintain **bone density** and protect against soft tissue calcification. The article on page 50 reviews research showing how vitamin K can improve **heart** health.

Other articles this month describe the *systemic* effects of **N-aceyl-L-cysteine** and a popular way people today are taking their nightly **melatonin**.

For longer life,



William Faloon, Co-Founder
Life Extension®



Our Ongoing Support of Biomedical Research

Life Extension® donates supplements to physician-scientists who use them in **clinical trials** to ascertain efficacy against a wide range of degenerative disorders.

In **2021**, a study was published using **20 mg melatonin** capsules that **Life Extension®** specially formulated to study on non-small-cell **lung cancer** patients. We also provided identical-looking **placebo** capsules for this outside research group.

The data below highlight the **improved survival** in those receiving **20 mg of melatonin** compared to **placebo**:

DAILY EVENING MELATONIN PROLONGS SURVIVAL AMONG PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER¹⁰

- **20 mg** melatonin as an adjunctive to standard chemo treatment.
- Evening supplementation of melatonin reduced risk of death by **39%**.
- Individuals with normal baseline sleep had a median survival of **17.6 months** with evening **melatonin** compared to **10.4 months** in the **placebo** group.

Acknowledgments: We would like to thank William Faloon of **Life Extension** for providing melatonin and placebo for this study.

Biological Rhythm Research. 2021:1-15.

National Library of Medicine Titles and Descriptions of Published Studies About Melatonin and Cancer

These pages contain titles and brief descriptions of studies that were published in **2021** and **2022**, listed on the federal government's National Library of Medicine's data base (www.pubmed.gov).

What we reprinted is only a small portion of the hundreds of studies about "**melatonin and cancer**" one can easily access by logging on to www.PubMed.gov

Melatonin in Cancer Treatment: Current Knowledge and Future Opportunities.

Talib WH, Alsayed AR, Abuawad A, Daoud S, Mahmud AI.

Molecules. 2021 Apr 25;26(9):2506. doi: 10.3390/molecules26092506.PMID: 33923028 **Free PMC article**. [Review](#).

Epidemiological and experimental studies have documented that melatonin could inhibit different types of cancer in vitro and in vivo. ...Studies discussed in this review will provide a solid foundation for researchers and physicians to design and develop new...

Melatonin-A New Prospect in Prostate and Breast Cancer Management.

Anim-Koranteng C, Shah HE, Bhawnani N, Ethirajulu A, Alkasabera A, Onyali CB, Mostafa JA.

Cureus. 2021 Sep 20;13(9):e18124. doi: 10.7759/cureus.18124. eCollection 2021 Sep.PMID: 34692334 **Free PMC article**. [Review](#).

Melatonin exerts its oncostatic effect by inhibiting angiogenesis, preventing cancer spread and growth, and improving the sensitivity of cancer cells to radiation and chemotherapy in both prostate and breast cancer. This review aims to highlight some...

Circadian Rhythm and Concentration of Melatonin in Breast Cancer Patients.

Ahabrach H, El Mlili N, Errami M, Cauli O.

Endocr Metab Immune Disord Drug Targets. 2021;21(10):1869-1881. doi: 10.2174/1871530320666201201110807.PMID: 33261546 [Review](#).

Melatonin has also been shown to display anti-proliferative effects on breast cancer growth and proliferation. ...CONCLUSION: Circadian rhythm and the concentration of melatonin in the blood are altered in patients with breast cancers, and it can...

Melatonin and Pathological Cell Interactions: Mitochondrial Glucose Processing in Cancer Cells.

Reiter RJ, Sharma R, Rosales-Corral S, Manucha W, Chuffa LGA, Zuccari DAPC.

Int J Mol Sci. 2021 Nov 19;22(22):12494. doi: 10.3390/ijms222212494.PMID: 34830375 **Free PMC article**. [Review](#).

Melatonin is synthesized in the pineal gland at night. Since melatonin is produced in the mitochondria of all other cells in a non-circadian manner, the amount synthesized by the pineal gland is less than 5% of the total. Melatonin produced in mitochondria in ...

Usefulness of Melatonin and Other Compounds as Antioxidants and Epidrugs in the Treatment of Head and Neck Cancer.

Guerra J, Devesa J.

Antioxidants (Basel). 2021 Dec 24;11(1):35. doi: 10.3390/antiox11010035.PMID: 35052539 **Free PMC article**. [Review](#).

Along with genetic mutations, aberrant epigenetic alterations are the initiators of head and neck cancer carcinogenesis. Currently, several drugs are being developed to correct these epigenetic alterations, known as epidrugs. ...The objective of this review is to describe ...

Sleep disorders and cancer: State of the art and future perspectives.

Mogavero MP, DelRosso LM, Fanfulla F, Bruni O, Ferri R.

Sleep Med Rev. 2021 Apr;56:101409. doi: 10.1016/j.smrv.2020.101409. Epub 2020 Nov 28.PMID: 33333427 [Review](#).

A bidirectional connection between sleep and cancer exists; however, the specific associations between individual sleep disorders and particular tumors are not very clear. An accurate assessment of sleep disorders in cancer patients is necessary to improve patient ...

Involvement of NRF2 in Breast Cancer and Possible Therapeutical Role of Polyphenols and Melatonin.

Tascioglu Aliyev A, Panieri E, Stepanić V, Gurer-Orhan H, Saso L.

Molecules. 2021 Mar 25;26(7):1853. doi: 10.3390/molecules26071853.PMID: 33805996 **Free PMC article**. [Review](#).

Due to its regulatory role in the expression of numerous cytoprotective genes involved in the antioxidant and anti-inflammatory responses, the modulation of NRF2 seems to be a promising approach in the prevention ...

Role and Therapeutic Potential of Melatonin in Various Type of Cancers.

Gurunathan S, Qasim M, Kang MH, Kim JH.

Onco Targets Ther. 2021 Mar 18;14:2019-2052. doi: 10.2147/OTT.S298512. eCollection 2021. PMID: 33776451 Free PMC article. Review.

Lung, prostate, colorectal, stomach, and liver cancers are the most common types of cancer in men, whereas breast, colorectal, lung, cervical, and thyroid cancers are the most common among women. ...The combination of melatonin with conventional drugs ...

The effect of melatonin on sleep quality and insomnia in patients with cancer: a systematic review study.

Jafari-Koulaee A, Bagheri-Nesami M.

Sleep Med. 2021 Jun;82:96-103. doi: 10.1016/j.sleep.2021.03.040. Epub 2021 Apr 25. PMID: 33910162 Review.

Therefore, the aim of the present systematic review was to investigate effect of melatonin on sleep quality and insomnia in patients with cancer. METHODS: The present systematic review was conducted in 2021. ...CONCLUSIONS: The present review study showed that melatonin may be ...

Pan-cancer analyses reveal genomics and clinical characteristics of the melatonergic regulators in cancer.

Zhang J, Jiang H, Du K, Xie T, Wang B, Chen C, Reiter RJ, Cen B, Yuan Y.

J Pineal Res. 2021 Oct;71(3):e12758. doi: 10.1111/jpi.12758. Epub 2021 Sep 5. PMID: 34289167

Melatonin, an endogenous hormone, plays protective roles in cancer. ...In the present study, we performed a comprehensive characterization of melatonin regulators in 9,125 tumor samples across 33 cancer types using multi-omic data from The Cancer Genome Atlas ...

Melatonin inhibits proliferation and viability and promotes apoptosis in colorectal cancer cells via upregulation of the microRNA-34a/449a cluster.

Ji G, Zhou W, Li X, Du J, Li X, Hao H.

Mol Med Rep. 2021 Mar;23(3):187. doi: 10.3892/mmr.2021.11826. Epub 2021 Jan 5. PMID: 33398374 Free PMC article.

Melatonin exerts anticarcinogenic effects via various mechanisms; however, the identified underlying molecular mechanisms do not explain the full breadth of anti-CRC effects mediated by melatonin. ...Therefore, melatonin may serve as a potential therapeutic ...

A New Paradigm in the Relationship between Melatonin and Breast Cancer: Gut Microbiota Identified as a Potential Regulatory Agent.

Laborda-Illanes A, Sánchez-Alcoholado L, Boutriq S, Plaza-Andrades I, Peralta-Linero J, Alba E, González-González A, Queipo-Ortuño MI.

Cancers (Basel). 2021 Jun 23;13(13):3141. doi: 10.3390/cancers13133141. PMID: 34201776 Free PMC article. Review.

In this review we summarize a possible connection between gut microbiota, melatonin production, and breast cancer. An imbalance in gut bacterial population composition (dysbiosis), or changes in the production of melatonin (circadian disruption) alters ...

The Intricate Relationship between Melatonin and Breast Cancer: A Short Review.

Pistioli L, Katsarelis D, Audisio RA, Olofsson Bagge R.

Chirurgia (Bucur). 2021 Mar-Apr;116(2 Suppl):24-34. PMID: 33963691 Free article.

There is ongoing research investigating the deterrent relationship between melatonin and malignancies and in particular breast cancer. The aim of this article is to review some of the most important findings concerning the effect of melatonin on cancer ...

Melatonin and its derivative disrupt cancer stem-like phenotypes of lung cancer cells via AKT downregulation.

Phiboonchaiyanan PP, Puthongking P, Chawjarean V, Harikarnpakdee S, Sukprasansap M, Chanvorachote P, Pripem A, Govitrapong P.

Clin Exp Pharmacol Physiol. 2021 Dec;48(12):1712-1723. doi: 10.1111/1440-1681.13572. Epub 2021 Aug 31. PMID: 34396568

Cancer stem cells (CSCs), a small subpopulation of tumour cells, have properties of self-renewal and multipotency, which drive cancer progression and resistance to current treatments. Compounds potentially targeting CSCs have been recently developed. This study show ...

Melatonin and Cancer: A Polyhedral Network Where the Source Matters.

Bonmati-Carrion MA, Tomas-Loba A.

Antioxidants (Basel). 2021 Feb 1;10(2):210. doi: 10.3390/antiox10020210. PMID: 33535472 Free PMC article. Review.

Indeed, this activity has been demonstrated to be mediated by interfering with various **cancer** hallmarks, and different epidemiological studies have also linked light at night (**melatonin** suppression) with a higher incidence of different types of **cancer**.

Melatonin interrupts osteoclast functioning and suppresses tumor-secreted RANKL expression: implications for bone metastases.

Liu PI, Chang AC, Lai JL, Lin TH, Tsai CH, Chen PC, Jiang YJ, Lin LW, Huang WC, Yang SF, Tang CH.

Oncogene. 2021 Feb;40(8):1503-1515. doi: 10.1038/s41388-020-01613-4. Epub 2021 Jan 15. PMID: 33452455

We also observed that melatonin inhibits RANKL production in lung and prostate cancer cells by downregulating the p38 MAPK pathway, which in turn prevents cancer-associated osteoclast differentiation. ...These findings show promise for melatonin in the ...

Melatonin inhibits lung cancer development by reversing the Warburg effect via stimulating the SIRT3/PDH axis.

Chen X, Hao B, Li D, Reiter RJ, Bai Y, Abay B, Chen G, Lin S, Zheng T, Ren Y, Xu X, Li M, Fan L.

J Pineal Res. 2021 Sep;71(2):e12755. doi: 10.1111/jpi.12755. Epub 2021 Jul 30. PMID: 34214200

Recently, the morbidity and mortality from lung cancer have continued to increase. Mitochondrial dysfunction plays a key role in apoptosis, proliferation, and the bioenergetic reprogramming of cancer cells, especially for energy metabolism. Herein, we investigated ...

Effects of melatonin and doxorubicin on primary tumor and metastasis in breast cancer model.

Tanriover G, Dilmac S, Aytac G, Farooqi AA, Sindel M.

Anticancer Agents Med Chem. 2021 Dec 12. doi: 10.2174/1871520621666211213094258. Online ahead of print. PMID: 34961467

BACKGROUND: Melatonin exerts oncostatic effects on breast cancer via immunomodulation and anti-oxidation. ...Based on these results, melatonin is a promising candidate for combinatory use with conventional chemotherapeutics for breast cancer treatment. ...

MT1 and MT2 melatonin receptors play opposite roles in brain cancer progression.

Kinker GS, Ostrowski LH, Ribeiro PAC, Chanoch R, Muxel SM, Tirosch I, Spadoni G, Rivara S, Martins VR, Santos TG, Markus RP, Fernandes PA.

J Mol Med (Berl). 2021 Feb;99(2):289-301. doi: 10.1007/s00109-020-02023-5. Epub 2021 Jan 3. PMID: 33392634

Primary brain tumors remain among the deadliest of all cancers. Glioma grade IV (glioblastoma), the most common and malignant type of brain cancer, is associated with a 5-year survival rate of < 5%. ...However, our understanding of the specific effects mediated ...

Melatonin inhibits gallbladder cancer cell migration and invasion via ERK-mediated induction of epithelial-to-mesenchymal transition.

Tang H, Shi X, Zhu P, Guo W, Li J, Yan B, Zhang S.

Oncol Lett. 2021 Aug;22(2):609. doi: 10.3892/ol.2021.12870. Epub 2021 Jun 15. PMID: 34188711 Free PMC article.

However, little is known regarding the effects of melatonin on gallbladder cancer (GBC) cells. The present study aimed to investigate the role of melatonin on the prevention of GBC cell invasion. ...Thus, melatonin may be used as a potential novel ...

Melatonin indirectly decreases gastric cancer cell proliferation and invasion via effects on cancer-associated fibroblasts.

Liu D, Shi K, Fu M, Chen F.

Life Sci. 2021 Jul 15;277:119497. doi: 10.1016/j.lfs.2021.119497. Epub 2021 Apr 18. PMID: 33864820

Recent studies have revealed the potential value of melatonin in cancer therapy, but its role in gastric cancer and CAFs requires further exploration. ...SIGNIFICANCE: This study provides insights into the role of melatonin in the tumor microenvironment ...

Alcohol and melatonin.

Kurhaluk N.

Chronobiol Int. 2021 Jun;38(6):785-800. doi: 10.1080/07420528.2021.1899198. Epub 2021 Mar 24. PMID: 33761823 Review.

It discusses the main clinical effects of melatonin on alcohol injury and the main targets as a therapy for alcohol disorders. Chronobiological effects of ethanol are related to melatonin suppression that has been associated with, among others, cancer risk ...

Melatonin reduces proliferation and promotes apoptosis of bladder cancer cells by suppressing O-GlcNAcylation of cyclin-dependent-like kinase 5.

Wu J, Tan Z, Li H, Lin M, Jiang Y, Liang L, Ma Q, Gou J, Ning L, Li X, Guan F.

J Pineal Res. 2021 Oct;71(3):e12765. doi: 10.1111/jpi.12765. Epub 2021 Sep 18. PMID: 34487576

Dysregulated glycosylation, particularly O-GlcNAcylation, is often a biomarker of cancer cells. In this study, elevated O-GlcNAc level in bladder cancer was inhibited by melatonin treatment. Melatonin treatment inhibited proliferation and migration and ...

Associations between artificial light at night and risk for thyroid cancer: A large US cohort study.

Zhang D, Jones RR, James P, Kitahara CM, Xiao Q.

Cancer. 2021 May 1;127(9):1448-1458. doi: 10.1002/cncr.33392. Epub 2021 Feb 8. PMID: 33554351

BACKGROUND: Light at night (LAN) inhibits nighttime secretion of melatonin and may cause circadian disruption, which may be a risk factor for cancer. Recent studies have linked high LAN exposure with elevated breast cancer risk. Given that breast cancer ...

Melatonin Targets Metabolism in Head and Neck Cancer Cells by Regulating Mitochondrial Structure and Function.

Guerra-Librero A, Fernandez-Gil BI, Florido J, Martinez-Ruiz L, Rodríguez-Santana C, Shen YQ, García-Verdugo JM, López-Rodríguez A, Rusanova I, Quiñones-Hinojosa A, Acuña-Castroviejo D, Marruecos J, De Haro T, Escames G.

Antioxidants (Basel). 2021 Apr 14;10(4):603. doi: 10.3390/antiox10040603. PMID: 33919790 Free PMC article.

In this study, we aim to investigate the role of melatonin in mitochondrial metabolism and its functional consequences in head and neck cancer. ...Our findings highlight new molecular pathways involved in melatonin's oncostatic activity, suggesting ...

Melatonin Inhibits Migration and Invasion in LPS-Stimulated and -Unstimulated Prostate Cancer Cells Through Blocking Multiple EMT-Relative Pathways.

Tian QX, Zhang ZH, Ye QL, Xu S, Hong Q, Xing WY, Chen L, Yu DX, Xu DX, Xie DD.

J Inflamm Res. 2021 May 25;14:2253-2265. doi: 10.2147/JIR.S305450. eCollection 2021. PMID: 34079331 Free PMC article.

PURPOSE: Gram-negative bacteria are usually found in prostate cancer (PCa) tissues. This study aims to investigate the role of lipopolysaccharide (LPS), a glycolipid compound found in the outer membrane of gram-negative bacteria, on the migration and invasion of PCa cells, ...



References

- Li J, Somers VK, Xu H, et al. Trends in Use of Melatonin Supplements Among US Adults, 1999-2018. *JAMA.* 2022 Feb 1;327(5):483-5.
- Bondy SC, Campbell A. Melatonin and Regulation of Immune Function: Impact on Numerous Diseases. *Curr Aging Sci.* 2020;13(2):92-101.
- Waldhauser F, Kovacs J, Reiter E. Age-related changes in melatonin levels in humans and its potential consequences for sleep disorders. *Exp Gerontol.* 1998 Nov-Dec;33(7-8):759-72.
- Kennaway DJ, Lushington K, Dawson D, et al. Urinary 6-sulfatoxymelatonin excretion and aging: new results and a critical review of the literature. *J Pineal Res.* 1999 Nov;27(4):210-20.
- Zhou JN, Liu RY, van Heerikhuizen J, et al. Alterations in the circadian rhythm of salivary melatonin begin during middle-age. *J Pineal Res.* 2003 Jan;34(1):11-6.
- Ferracioli-Oda E, Qawasmi A, Bloch MH. Meta-analysis: melatonin for the treatment of primary sleep disorders. *PLoS One.* 2013;8(5):e63773.
- van Geijlswijk IM, Korzilius HP, Smits MG. The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis. *Sleep.* 2010 Dec;33(12):1605-14.
- Lissoni P, Barni S, Cazzaniga M, et al. Efficacy of the concomitant administration of the pineal hormone melatonin in cancer immunotherapy with low-dose IL-2 in patients with advanced solid tumors who had progressed on IL-2 alone. *Oncology.* 1994 Jul-Aug;51(4):344-7.
- Conti A, Maestroni GJ. The clinical neuroimmunotherapeutic role of melatonin in oncology. *J Pineal Res.* 1995 Oct;19(3):103-10.
- Hrushesky WJM, Lis CG, Levin RD, et al. Daily evening melatonin prolongs survival among patients with advanced non-small-cell lung cancer. *Biological Rhythm Research.* 2021:1-15.
- Lissoni P, Barni S, Mandala M, et al. Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumour patients with poor clinical status. *Eur J Cancer.* 1999 Nov;35(12):1688-92.
- Lissoni P, Paolorossi F, Tancini G, et al. A phase II study of tamoxifen plus melatonin in metastatic solid tumour patients. *Br J Cancer.* 1996 Nov;74(9):1466-8.
- Lissoni P, Barni S, Meregalli S, et al. Modulation of cancer endocrine therapy by melatonin: a phase II study of tamoxifen plus melatonin in metastatic breast cancer patients progressing under tamoxifen alone. *Br J Cancer.* 1995 Apr;71(4):854-6.
- Lissoni P, Barni S, Ardizzoia A, et al. A randomized study with the pineal hormone melatonin versus supportive care alone in patients with brain metastases due to solid neoplasms. *Cancer.* 1994 Feb 1;73(3):699-701.
- Lissoni P, Barni S, Cattaneo G, et al. Clinical results with the pineal hormone melatonin in advanced cancer resistant to standard antitumor therapies. *Oncology.* 1991;48(6):448-50.

(References continued on page 18.)

National Library of Medicine

Back in the **1980s**, finding **medical studies** was an arduous task.

To uncover published data, our group spent days in **medical libraries** using an archaic paper system (Index Medicus) to find relevant medical journals.

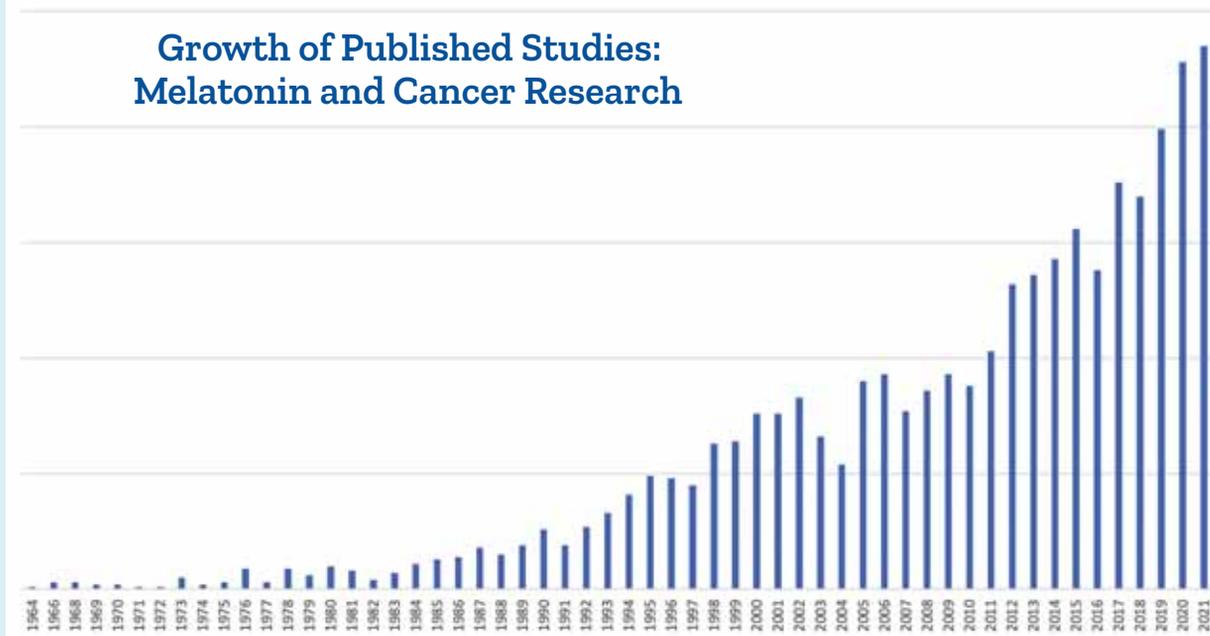
We then had to hope the library subscribed to that journal, photocopy relevant articles, bring them back to our office and mail information to others for further analysis.

In the early **1990s**, a subscription service became available whereby I received four large floppy disks with new medical studies every Saturday. I would load the disks onto my computer and search items of interest. This was a huge **improvement** compared to spending days at a **medical library**.

Then in **1997** the **National Library of Medicine** offered **free** public access to medical articles dating back to the late 1970s. The **National Library of Medicine** is operated by the United States government and is the world's largest medical library.

This free service not only makes my work more efficient but enables anyone who reads **Life Extension Magazine®** to check out studies we write about and find out as many details as they'd like.

Growth of Published Studies: Melatonin and Cancer Research



This chart shows the surging numbers of published studies at www.PubMed.gov when entering the search phrase: **"melatonin and cancer"**

16. Barni S, Lissoni P, Paolorossi F, et al. A study of the pineal hormone melatonin as a second line therapy in metastatic colorectal cancer resistant to fluorouracil plus folates. *Tumori*. 1990 Feb 28;76(1):58-60.
17. Seely D, Wu P, Fritz H, et al. Melatonin as adjuvant cancer care with and without chemotherapy: a systematic review and meta-analysis of randomized trials. *Integr Cancer Ther*. 2012 Dec;11(4):293-303.
18. Wang YM, Jin BZ, Ai F, et al. The efficacy and safety of melatonin in concurrent chemotherapy or radiotherapy for solid tumors: a meta-analysis of randomized controlled trials. *Cancer Chemother Pharmacol*. 2012 May;69(5):1213-20.
19. Weishaupt JH, Bartels C, Polking E, et al. Reduced oxidative damage in ALS by high-dose enteral melatonin treatment. *J Pineal Res*. 2006 Nov;41(4):313-23.
20. Ceyran H, Narin F, Narin N, et al. The effect of high dose melatonin on cardiac ischemia- reperfusion Injury. *Yonsei Med J*. 2008 Oct 31;49(5):735-41.
21. Kandemir YB, Tosun V, Guntekin U. Melatonin protects against streptozotocin-induced diabetic cardiomyopathy through the mammalian target of rapamycin (mTOR) signaling pathway. *Adv Clin Exp Med*. 2019 Sep;28(9):1171-7.
22. Cuesta S, Kireev R, Garcia C, et al. Beneficial effect of melatonin treatment on inflammation, apoptosis and oxidative stress on pancreas of a senescence accelerated mice model. *Mech Ageing Dev*. 2011 Nov-Dec;132(11-12):573-82.
23. Puig A, Rancan L, Paredes SD, et al. Melatonin decreases the expression of inflammation and apoptosis markers in the lung of a senescence-accelerated mice model. *Exp Gerontol*. 2016 Mar;75:1-7.
24. Forman K, Vara E, Garcia C, et al. Beneficial effects of melatonin on cardiometabolic alterations in a murine model of accelerated aging. *J Pineal Res*. 2010 Oct;49(3):312-20.
25. Andersen LP, Werner MU, Rosenkilde MM, et al. Pharmacokinetics of high-dose intravenous melatonin in humans. *J Clin Pharmacol*. 2016 Mar;56(3):324-9.
26. Pavel S, Goldstein R, Petrescu M. Vasotocin, melatonin and narcolepsy: possible involvement of the pineal gland in its patho-physiological mechanism. *Peptides*. 1980 Winter;1(4):281-4.
27. Barni S, Lissoni P, Cazzaniga M, et al. A randomized study of low-dose subcutaneous interleukin-2 plus melatonin versus supportive care alone in metastatic colorectal cancer patients progressing under 5-fluorouracil and folates. *Oncology*. 1995 May-Jun;52(3):243-5.
28. Lissoni P, Brivio F, Fumagalli L, et al. Neuroimmunomodulation in medical oncology: application of psychoneuroimmunology with subcutaneous low-dose IL-2 and the pineal hormone melatonin in patients with untreatable metastatic solid tumors. *Anticancer Res*. 2008 Mar-Apr;28(2B):1377-81.
29. Lissoni P, Barni S, Fossati V, et al. A randomized study of neuroimmunotherapy with low-dose subcutaneous interleukin-2 plus melatonin compared to supportive care alone in patients with untreatable metastatic solid tumour. *Support Care Cancer*. 1995 May;3(3):194-7.
30. Lissoni P, Tisi E, Barni S, et al. Biological and clinical results of a neuroimmunotherapy with interleukin-2 and the pineal hormone melatonin as a first line treatment in advanced non-small cell lung cancer. *Br J Cancer*. 1992 Jul;66(1):155-8.
31. Gitto E, Karbownik M, Reiter RJ, et al. Effects of melatonin treatment in septic newborns. *Pediatr Res*. 2001 Dec;50(6):756-60.
32. Available at: <https://clinicaltrials.gov/ct2/show/NCT03557229>. Accessed March 24, 2022.
33. Hansson I, Holmdahl R, Mattsson R. The pineal hormone melatonin exaggerates development of collagen-induced arthritis in mice. *J Neuroimmunol*. 1992 Jul;39(1-2):23-30.
34. Bang J, Chang HW, Jung HR, et al. Melatonin attenuates clock gene cryptochrome1, which may aggravate mouse anti-type II collagen antibody-induced arthritis. *Rheumatol Int*. 2012 Feb;32(2):379-85.
35. Jimenez-Caliani AJ, Jimenez-Jorge S, Molinero P, et al. Dual effect of melatonin as proinflammatory and antioxidant in collagen-induced arthritis in rats. *J Pineal Res*. 2005 Mar;38(2):93-9.
36. Zhao CN, Wang P, Mao YM, et al. Potential role of melatonin in autoimmune diseases. *Cytokine Growth Factor Rev*. 2019 Aug;48:1-10.
37. Nabatian-Asl M, Ghorbanihaghjo A, Malek Mahdavi A, et al. Effects of melatonin supplementation on serum oxidative stress markers and disease activity in systemic lupus erythematosus patients: A randomised, double-blind, placebo-controlled trial. *Int J Clin Pract*. 2021 Jul;75(7):e14246.
38. Adamczyk-Sowa M, Sowa P, Adamczyk J, et al. Effect of melatonin supplementation on plasma lipid hydroperoxides, homocysteine concentration and chronic fatigue syndrome in multiple sclerosis patients treated with interferons-beta and mitoxantrone. *J Physiol Pharmacol*. 2016 Apr;67(2):235-42.
39. Adamczyk-Sowa M, Pierzchala K, Sowa P, et al. Influence of melatonin supplementation on serum antioxidative properties and impact of the quality of life in multiple sclerosis patients. *J Physiol Pharmacol*. 2014 Aug;65(4):543-50.
40. Mozaffari S, Abdollahi M. Melatonin, a promising supplement in inflammatory bowel disease: a comprehensive review of evidences. *Curr Pharm Des*. 2011 Dec;17(38):4372-8.
41. Chojnacki C, Wisniewska-Jarosinska M, Walecka-Kapica E, et al. Evaluation of melatonin effectiveness in the adjuvant treatment of ulcerative colitis. *J Physiol Pharmacol*. 2011 Jun;62(3):327-34.
42. Sanchez-Barcelo EJ, Mediavilla MD, Tan DX, et al. Clinical uses of melatonin: evaluation of human trials. *Curr Med Chem*. 2010;17(19):2070-95.
43. Todisco M. Effectiveness of a treatment based on melatonin in five patients with systemic sclerosis. *Am J Ther*. 2006 Jan-Feb;13(1):84-7.
44. Forrest CM, Mackay GM, Stoy N, et al. Inflammatory status and kynurenine metabolism in rheumatoid arthritis treated with melatonin. *Br J Clin Pharmacol*. 2007 Oct;64(4):517-26.
45. Huang CC, Chiou CH, Liu SC, et al. Melatonin attenuates TNF-alpha and IL-1beta expression in synovial fibroblasts and diminishes cartilage degradation: Implications for the treatment of rheumatoid arthritis. *J Pineal Res*. 2019 Apr;66(3):e12560.
46. Nah SS, Won HJ, Park HJ, et al. Melatonin inhibits human fibroblast-like synoviocyte proliferation via extracellular signal-regulated protein kinase/P21(CIP1)/P27(KIP1) pathways. *J Pineal Res*. 2009 Aug;47(1):70-4.
47. Rudra DS, Pal U, Maiti NC, et al. Melatonin inhibits matrix metalloproteinase-9 activity by binding to its active site. *J Pineal Res*. 2013 May;54(4):398-405.
48. MacDonald IJ, Huang CC, Liu SC, et al. Reconsidering the Role of Melatonin in Rheumatoid Arthritis. *Int J Mol Sci*. 2020 Apr 20;21(8).
49. Esalatmanesh K, Loghman A, Esalatmanesh R, et al. Effects of melatonin supplementation on disease activity, oxidative stress, inflammatory, and metabolic parameters in patients with rheumatoid arthritis: a randomized double-blind placebo-controlled trial. *Clin Rheumatol*. 2021 Sep;40(9):3591-7.
50. Foley HM, Steel AE. Adverse events associated with oral administration of melatonin: A critical systematic review of clinical evidence. *Complement Ther Med*. 2019 Feb;42:65-81.
51. Naguib M, Samarkandi AH. Premedication with melatonin: a double-blind, placebo-controlled comparison with midazolam. *Br J Anaesth*. 1999 Jun;82(6):875-80.
52. Nordlund JJ, Lerner AB. The effects of oral melatonin on skin color and on the release of pituitary hormones. *J Clin Endocrinol Metab*. 1977 Oct;45(4):768-74.
53. Anton-Tay F, Diaz JL, Fernandez-Guardiola A. On the effect of melatonin upon human brain. Its possible therapeutic implications. *Life Sci*. 1971 Aug 1;10(15):841-50.
54. Gitto E, Reiter RJ, Cordaro SP, et al. Oxidative and inflammatory parameters in respiratory distress syndrome of preterm newborns: beneficial effects of melatonin. *Am J Perinatol*. 2004 May;21(4):209-16.
55. Grossman E. Should melatonin be used to lower blood pressure? *Hypertens Res*. 2013 Aug;36(8):682-3.
56. Grossman E, Laudon M, Zisapel N. Effect of melatonin on nocturnal blood pressure: meta-analysis of randomized controlled trials. *Vasc Health Risk Manag*. 2011;7:577-84.
57. Brzezinski A. Melatonin in humans. *N Engl J Med*. 1997 Jan 16;336(3):186-95.

Broccoli

THE TREE OF LIFE

Just one daily **Optimized Broccoli and Cruciferous Blend** tablet provides cell-protective compounds found in fresh vegetables.

For maximum absorption each **enteric coated** tablet contains two layers:

- **Myrosinase** to release **sulforaphane** in the small intestine, in one layer, and
- **DIM** (3, 3-diindolymethane) to promote healthy estrogen balance, and
- **Glucoraphanin** from broccoli, watercress, cabbage and rosemary (sulforaphane precursors), in the other layer.

"I feel this has made the difference! My hormones seem to be falling into place."

MJ

VERIFIED CUSTOMER REVIEW



Item #02368 • 30 enteric coated vegetarian tablets

1 bottle \$28.50 • 4 bottles \$26.50 each

For full product description and to order **Optimized Broccoli and Cruciferous Blend**, call 1-800-544-4440 or visit www.LifeExtension.com

TrueBroc® Produced under US patents 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC; TrueBroc® is a trademark of Brassica Protection Products LLC. BroccoVital® Myrosinase is a registered trademark of Berg Imports, LLC.



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

HIGHLY ABSORBABLE

ASTAXANTHIN

SUPPORTS
HEART
HEALTH

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

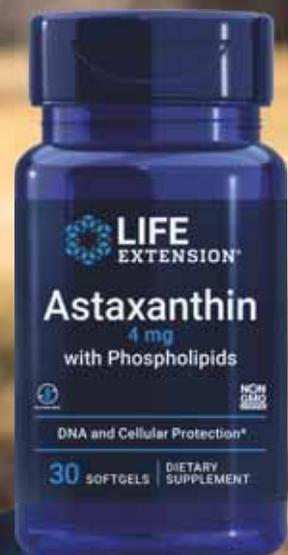
Found naturally in seafood and algae, as little as **50%** of **astaxanthin** is normally **absorbed** in the blood-stream.^{2,3}

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.

For full product description and to order **ASTAXANTHIN 4 mg with Phospholipids**, call **1-800-544-4440** or visit www.LifeExtension.com



Item #01923 • 30 softgels

1 bottle \$12

4 bottles \$10.50 each



HIGHLY PURIFIED

Fish Oil

Super Omega-3 provides components found in **Mediterranean diets**, including **sesame lignans** to extend the stability of **DHA** in the blood.



SUPER OMEGA-3 PLUS
EPA/DHA Fish Oil, Sesame Lignans,
Olive Extract, Krill & Astaxanthin
(2,520 mg of EPA + DHA in four softgels)

Item #01988 • 120 softgels
1 bottle **\$34.50**
4 bottles \$32 each



SUPER OMEGA-3*
EPA/DHA Fish Oil,
Sesame Lignans & Olive Extract
(2,400 mg of EPA + DHA in four softgels)

Item #01982 • 120 softgels
1 bottle **\$24.75**
4 bottles \$22 each

For full product description and to order **Super Omega-3**, or **Super Omega-3 Plus**, call 1-800-544-4440 or visit www.LifeExtension.com

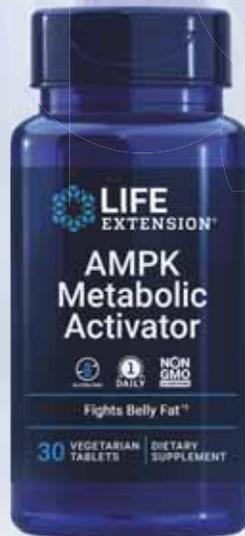
* Highest Independent 5-star rating, International Fish Oil Society For Over Nine Years.
IFOS™ certification mark is a registered trademark of Nutrasource Diagnostics, Inc.



CAUTION: If you are taking anti-coagulant or anti-platelet medications, or have a bleeding disorder, consult your healthcare provider before taking this product.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

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

1 bottle **\$28.50** • 4 bottles \$24 each

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

Actiponin® is a trademark of TG Biotech Co., Ltd.



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.

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

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

Sweet DREAMS



Choose the Melatonin That's Right For You

Healthy sleep is one of the best ways to feel revitalized and maintain optimal health.

While many people find **melatonin** helps improve sleep, others take it nightly for its **immune** protection effects.

People often try a range of doses before bedtime to assess what potency works best for them.

Caution: Do not consume alcohol, drive or operate machinery after taking this product.

MicroActive® Melatonin is a registered trademark of Bioactives LLC.



Lower-Potency Melatonin IR/XR

60 capsules

1.5 mg of combined immediate-release and extended-release melatonin in each capsule.

Item #02201
PRICE: \$9



Higher-Potency Melatonin 10 mg

60 vegetarian capsules

10 mg of melatonin in each vegetarian capsule.

Item #00331
PRICE: \$21



Melatonin 3 mg

60 vegetarian capsules

3 mg of melatonin in each vegetarian capsule.

Item #00330
PRICE: \$6



Liquid Melatonin

(Fast-Acting Liquid)
Citrus Vanilla • 2 fl. oz

3 mg of melatonin per 1 mL dropper (approximately 20 drops).

Item #02234
PRICE: \$9



GLUTEN FREE



NON-GMO
LE CERTIFIED



Melatonin Gummy

60 vegetarian gummies

3 mg of melatonin in each sugar-free vegetarian gummy.

Item #02503
PRICE: \$16.50

For full product description and to order any of these premium-grade **Melatonin supplements**, call 1-800-544-4440 or visit www.LifeExtension.com

2 WAYS TO SAVE



PREMIER REWARDS

Get 4% Back on Every Purchase
Earn LE Dollars you can use on any Life Extension® product & lab services!

Unlimited Free Shipping
No matter how big or small the order, U.S. shipping is always free.

Exclusive Savings
Get sneak peeks into sales & special pricing.

Premium Content
Exclusive webinars, plus a free subscription to *Life Extension Magazine*®.

Rewards Galore
Earn rewards for taking surveys, plus get rewarded on your birthday month.

Costs \$49.95 a year...Instant \$50 sign-up credit means zero cost to enroll!

LifeExtension.com/YourPremier



AUTOSHIP & SAVE

Save an average of 16% on your supplements!*

Free Shipping
We ship to any address in the United States (including Alaska and Hawaii) regardless of order size.

Lowest Prices
Always pay the lowest price for your favorite Life Extension® products.

Newest Formulations
Always receive the latest version of our innovative formulas.

Complimentary program! Cancel any time
LifeExtension.com/AutoShip

Call 1-855-867-9361
Please use code **REWARDS**

*Average savings based on the average AutoShip discount across all products.



Premier service expires 12 months after date of purchase or renewal and can only be renewed 6 months after Premier purchase or renewal. Includes FREE standard delivery (3 to 5 business days) to any mailing address within the United States, excluding U.S. territories. Discounts on non-standard and international shipping also available. International customers pay \$59.95 for Premier. During checkout, redeem LE Dollars (one is equal to \$1 U.S. Dollar) to purchase products, blood tests, sale items, and shipping fees.

In the News



Fish Oil Lowers Risk of Liver Cancer

A study published in *Frontiers in Nutrition* found a significantly lower risk of liver cancer among people who supplemented with fish oil, compared to those who didn't.*

The study included 434,584 middle-aged and older men and women enrolled in the UK Biobank who were cancer free on enrollment.

The median follow-up period of this large study group was **7.8 years**.

Compared to people who did not use **fish oil**, those who supplemented with fish oil had a **44% lower** risk of liver cancer, a **52%** lower risk of hepatocellular carcinoma, and a **40%** lower risk of intrahepatic cholangiocarcinoma.

Editor's Note: "The inverse association of fish-oil use with the risk of total liver cancer did not vary by baseline age, sex, smoking status, or diabetes of the participants," the researchers stated.

* *Front Nutr.* 2021 Dec 31;8:771984.

Curcumin Can Help People with Diabetic Kidney Disease

Diabetic kidney disease is a common microvascular complication of diabetes.

A study published in the journal *Evidence-Based Complementary and Alternative Medicine* reported an **improvement** in response to **curcumin** supplementation.*

People with kidney disease have a *higher* risk for cardiovascular morbidity and mortality, which are closely associated with risk factors such as hypertension and chronic inflammation.

A meta-analysis of five randomized, double-blind, placebo-controlled clinical trials, including 290 individuals with diabetic kidney disease, concluded that **curcumin** supplementation was associated with improved **creatinine** (a marker of kidney function), cholesterol, glucose and systolic blood pressure, compared to a **placebo**.

Editor's Note: "Up to 40% of patients with type II diabetes develop DKD, and DKD is currently the leading cause of end-stage renal disease worldwide," the authors stated.

* *Evid Based Complement Alternat Med.*
2021 Dec 2;2021:6109406.





Supplementing with Zinc Linked to Lower Risk of Alzheimer's Disease

A study published in the *Journal of Neuroscience* found an association between **zinc** supplementation and a decreased risk of Alzheimer's disease as well as a reduction in the progression of cognitive decline in Alzheimer's disease patients.*

Researchers utilized data from the Alzheimer's Disease Neuroimaging Initiative database, which included 1,631 individuals who were cognitively normal or diagnosed with mild cognitive impairment or early Alzheimer's disease.

Subjects were evaluated upon enrollment, at six and 12 months, and yearly thereafter, during up to 10 years of follow-up.

Among those who reported supplementing with zinc, **6%** were diagnosed with Alzheimer's disease compared to **26%** of those who reported no zinc supplement use.

Editor's Note: "Here we provide epidemiological evidence suggesting that zinc supplementation was associated with reduced risk and slower cognitive decline in people with Alzheimer's disease and mild cognitive impairment," the authors stated.

* *J Neurosci.* 2021 Mar 31;41(13):3025-3038.

Better Bone Health with Collagen Peptides

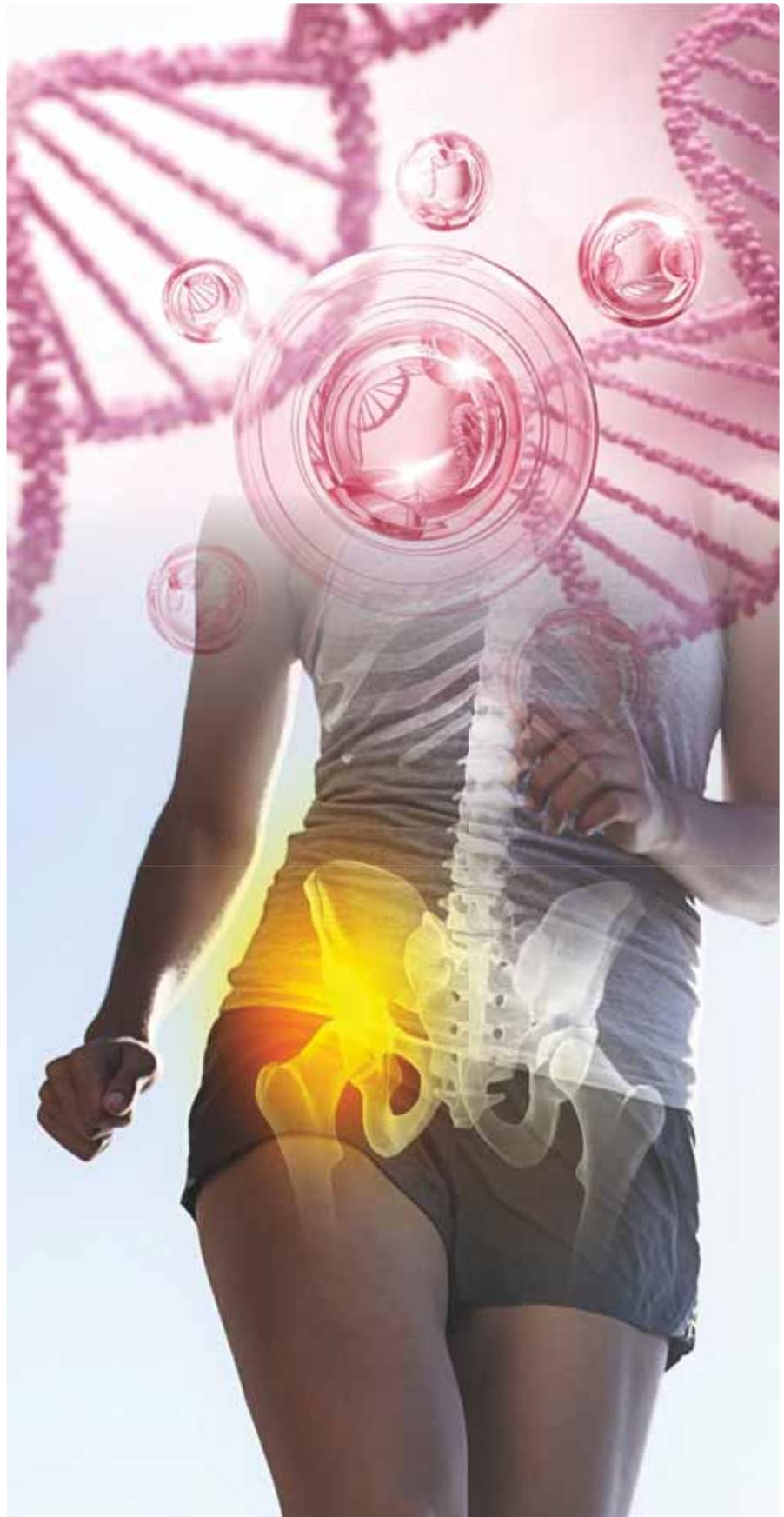
The addition of collagen peptides, the building blocks of collagen, to a bone-supporting regimen of calcium and vitamin D was associated with greater improvements in measures of bone health compared to calcium and vitamin D alone, according to a study published in the *Journal of Clinical Densitometry*.*

The study included 51 postmenopausal women with osteopenia, a condition of lower-than-normal bone mineral density that is associated with an increased risk of developing osteoporosis. All participants received **500 mg** of calcium and **400 IU** of vitamin D3 daily for one year. Twenty-three women also received **5 grams** of collagen peptides.

After one year, women who received **collagen** peptides had a significant increase in bone mineral content and volumetric bone mineral density in trabecular (porous) bone tissue of the tibia, compared to values measured at the beginning of the study, and compared to participants who received calcium and vitamin D alone.

Editor's Note: Volumetric bone mineral density also improved in cortical (more solid) bone among collagen peptides-supplemented participants in comparison with those who did not receive collagen.

* *J Clin Densitom.* 2021 Nov 25;S1094-6950(21)00099-8.



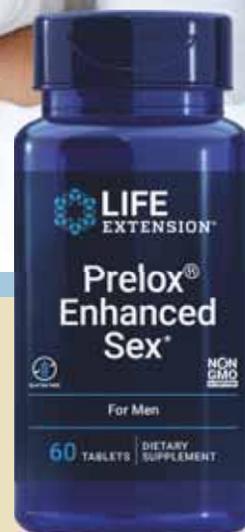
Take Your **SEXUAL** Performance to the **MAX**



Prelox® Enhanced Sex promotes
blood flow where you need it most.

For full product description and to order
Prelox® Enhanced Sex, call **1-800-544-4440**
or visit www.LifeExtension.com

Item #01373 • 60 tablets
1 bottle **\$39**
4 bottles \$36 each



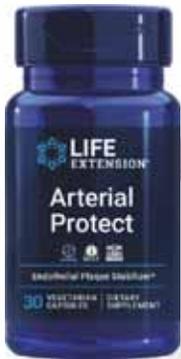
Prelox® and Pycnogenol® are registered trademarks of Horphag Research Ltd.



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

THE VERSATILE BENEFITS OF PYCNOGENOL®

Pycnogenol® is a plant extract derived from French maritime pine bark. Its benefits are available in these three formulations:



*ARTERIAL PROTECT

Item #02004 • 30 vegetarian capsules
1 bottle **\$33**



4 bottles \$29 each



†**VENOFLOW™

Item #02102 • 30 vegetarian capsules
1 bottle **\$39**



4 bottles \$36 each



†PYCNOGENOL®

French Maritime Pine Bark Extract

Item #01637 • 60 vegetarian capsules
1 bottle **\$48**

4 bottles \$45 each

ARTERIAL PROTECT

Provides Pycnogenol® and standardized gotu kola leaf extract to help stabilize endothelial plaque and promote healthy blood flow throughout the body.

VENOFLOW™

For those who sit for long periods while traveling or in the office, this proprietary blend of Pycnogenol® and nattokinase promotes healthy venous blood flow.

PYCNOGENOL®

Numerous published studies describe how concentrated extracts in Pycnogenol® help protect against multiple factors related to normal aging.

For full product descriptions and to order **PYCNOGENOL®**, **ARTERIAL PROTECT**, or **VENOFLOW™**, call **1-800-544-4440** or visit **www.LifeExtension.com**



*Pycnogenol® and Centellicum® are registered trademarks of Horphag Research. Use of this product may be protected by one or more U.S. patents and other international patents.

†Pycnogenol® is a registered trademark of Horphag Research, Ltd.

**CAUTION: Consult your healthcare provider before use of Venoflow™ if taking medication (especially those affecting blood coagulation or blood pressure), being treated for a medical condition (especially bleeding disorders), under the age of 18, pregnant, or lactating.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

45 Times Greater Bioavailability CURCUMIN



Patented **turmeric** and **fenugreek blend** (500 mg) results in **45 times** greater bioavailability of free **curcuminoids**.

Item #02407

500 mg, 60 vegetarian capsules

1 bottle **\$24** • 4 bottles \$22 each

Same 500 mg potency of patented **turmeric** and **fenugreek blend** with added benefits of **ginger** and other **turmeric** actives.

Item #02324

500 mg curcumin + gingerol, 30 softgels

1 bottle **\$20** • 4 bottles \$18 each

For full product description and to order **Curcumin Elite™** or **Advanced Curcumin Elite™**, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.



MUSHROOMS

That *Boost*

IMMUNE FUNCTION

BY MICHAEL DOWNEY

Mushrooms have been used medicinally for *thousands* of years.¹

Modern science has pinpointed a primary reason:

They contain beneficial compounds called **beta glucans** that *boost immune function*.²⁻⁵

On their own, **beta glucans** deliver **antiviral** and **immunity-strengthening** properties.²⁻⁵

In **human** studies, taking **beta glucans** reduces the length and severity of **upper respiratory tract infections** such as the common **cold** and **flu**.⁶⁻¹¹

Combining beta glucans with medicinal mushrooms may supercharge a variety of **immune functions**.

What Are Beta Glucans?

Beta glucans are a group of polysaccharides found in the cell walls of **mushrooms**, seaweed, and whole grains.⁷

Beta glucans derived from yeast and fungi are known for their **immunomodulating** properties.⁷

They also help nourish the gut microbiota and augment the action of **immune cells**.^{3,12-15}

Key Immune-Supportive Mushrooms

There are hundreds of strains of mushrooms. **Three** that most effectively support the immune system are **shiitake**, **maitake**, and **chaga**.

SHIITAKE

Shiitake mushrooms have long been used in traditional Asian medicine.¹⁶ They *increase* the number of immune cells, including **T-cells**, which fight specific kinds of viruses, and **NK (natural killer) cells**, which kill a variety of virally infected cells and tumors.¹⁷

In cell studies **shiitake extract** was able to directly inactivate several types of **viruses** and block viral replication.¹⁸⁻²⁰

In an animal model of severe **bacterial lung infection**, shiitake mushrooms significantly *decreased* the number of bacteria in the lungs and improved the animals' condition.²¹

Shiitake also boosts secretion of **antibodies** that protect the digestive tract and reduces **C-reactive protein**, a marker of **inflammation**.¹⁷

MAITAKE

Commonly used in cuisine, **maitake** mushrooms were shown in preclinical studies to activate some of the *first* immune cells to fight an infection, including **NK cells** and **macrophages**.^{22,23}

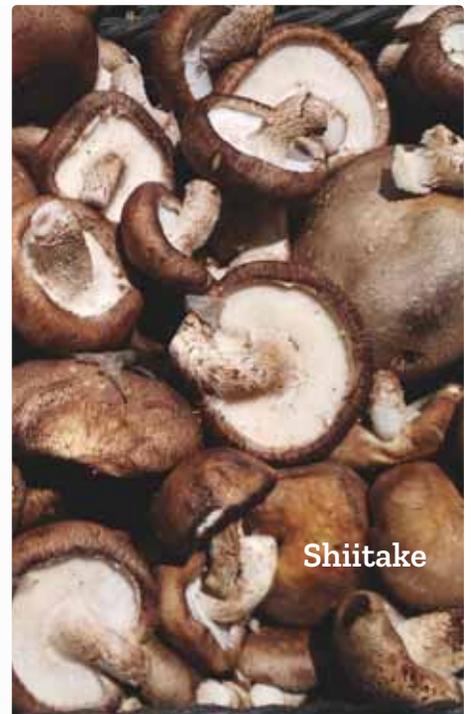
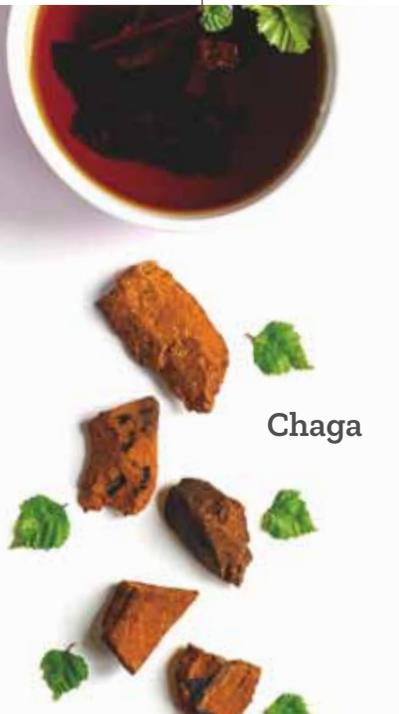
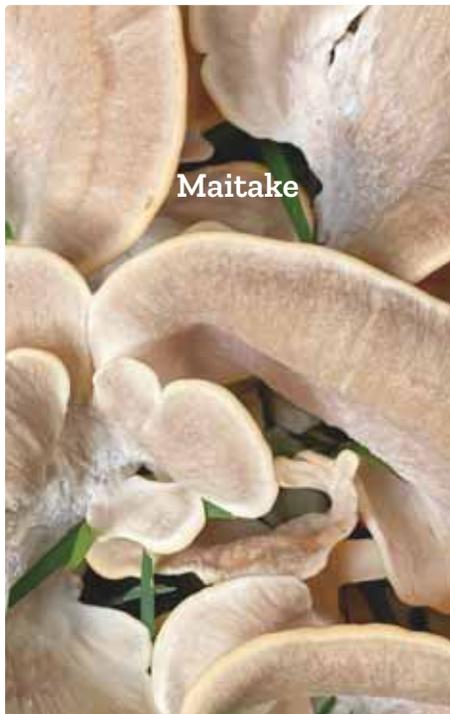
Extracts of maitake also induce the secretion of **interferons**, proteins that improve the body's ability to defend against infection.²³

CHAGA

Chaga mushrooms, which grow on alder, beech, birch, and various other hardwood trees, are powerful **immuno-modulators**.

When scientists treated mice with a drug that *inhibits* **immune system** activity, chaga extract returned levels of immune cells almost back to normal. It also kept down levels of **tumor necrosis factor**, a marker of inflammation.²⁴

In preclinical studies, chaga demonstrated **antiviral** activity against a wide range of viruses, including influenza, herpes, hepatitis C, HIV, and others.²⁵





WHAT
YOU
NEED
TO
KNOW

Mushrooms and Beta Glucans Boost Immunity

Activating the Immune System

Mushrooms contain numerous health-promoting compounds. But perhaps the most powerful and bioactive immune supporters are **beta glucans**.

Beta glucans bind to receptors found on an assortment of cells important for **immunity**.^{3,26} This boosts the function of these cells, helping them defend against infection and other threats.

Immune responses can be divided into two types:²⁷

- **Innate immunity**, which forms the body's first line of defense, is accomplished by immune cells including macrophages, neutrophils, and NK cells.
- **Adaptive immunity** cells include lymphocytes, such as B-cells and T-cells. These are the specialists brought in later to fight off *specific* threats, like a particular bacteria or virus. Adaptive immunity helps the body develop **long-term immunity** to a pathogen.

Beta glucans activate and stimulate **both** systems.^{3,4,17,28,29}

- **Mushrooms** have long been used for medicinal properties. **Shiitake**, **maitake**, and **chaga** mushrooms help support the immune system, activating immune cells.
- **Beta glucans**, compounds found in the cell walls of mushrooms, contribute to these **immune** benefits.
- Oral intake of **beta glucans** can boost the immune system's ability to prevent and fend off **infections** (including the common cold and flu), and support a healthy gut microbiota, and it may reverse age-related weakening of the immune system.
- Blending **beta glucans** with **shiitake**, **maitake**, and **chaga** mushrooms may help optimize healthy immune function.



Results of Human Tests

To validate these benefits in **humans**, scientists conducted a number of different trials. Volunteers were randomized to receive either a **placebo** or **beta glucans**. Most of these studies used a **250 mg** dose of beta-glucans.⁶⁻¹¹

Beta glucans demonstrated infection-fighting effects, particularly in **upper respiratory tract infections** such as the common **cold** and **flu**.

Participants who received **beta glucans** had:⁶⁻¹¹

- Fewer symptomatic days,
- Less severe infection symptoms,
- Fewer workdays lost to illness,
- Increased numbers of immune cells in the blood,
- Higher levels of interferon secretion, and
- Increased secretion of **antibodies** in the saliva, a defense against digestive tract and respiratory tract infections.

Higher Mushroom Intake Associated with Reduced Mortality

In September 2021, scientists with the College of Medicine at **Pennsylvania State University** published results from a meta-analysis of prospective studies that included over 600,000 individuals, on the relationship between **mushroom intake** and **mortality**.³⁴

They found that *higher* mushroom consumption correlated with a *lower* risk of **death from any cause**.

This study had several major strengths, including the facts that it involved a very comprehensive meta-analysis and it employed a sample that was nationally representative of the American adult population.

An earlier study by the same team, with **15,546** participants followed for an average of nearly 20 years, from the Third National Health and Nutrition Examination Survey (NHANES III), found an even stronger correlation between mushroom intake and **lower all-cause mortality**.³⁵

In a different meta-analysis, researchers found that higher mushroom consumption was associated with a *lower* risk of **cancer**.³⁶

When site-specific cancer was studied, a significant association was observed with reduced **breast cancer** risk and greater mushroom consumption.³⁶

Beta glucans can improve immune responses to *other* challenges as well. One study looked at **ragweed allergy** sufferers who received either a placebo or **250 mg of beta glucans**.³⁰

After four weeks, those receiving **beta glucans** had significant *reductions* in total allergy symptoms and severity. Measures of mood, energy, vigor, sleep, and overall quality of life were all improved.³⁰

Reversing Immune Senescence

The elderly become more susceptible to infectious diseases and cancer due to a deterioration of immune function known as **immunosenescence**.³¹

In animal models of aging, intake of **beta glucans** can help *prevent* or even *reverse* this weakening of the immune system.^{28,32}

In one mouse study, **beta glucans** boosted the numbers of immune cells, *and* improved their function, which had a **rejuvenating effect** on immune system responses.³²

Stronger Gut Defenses

The **gut microbiota** is made up of the trillions of microorganisms in the digestive tract. Beneficial populations of these microorganisms are critical to fighting **infections** and maintaining optimal overall health.

Both **mushrooms** and isolated **beta glucans** encourage the growth of healthy microbiota.^{3,13-15}

The benefits don't stop there. When beneficial bacteria consume beta glucans, they produce **short-chain fatty acids** as a byproduct.^{13,15} Among other benefits, these fatty acids:³³

- Reduce harmful **inflammation**,
- Support a healthy gut lining,
- Defend against **cancer**, and
- Help regulate appetite and metabolism.

Combining **beta glucans** with immune-supporting **mushrooms** may help maximize the function of the immune system.

Summary

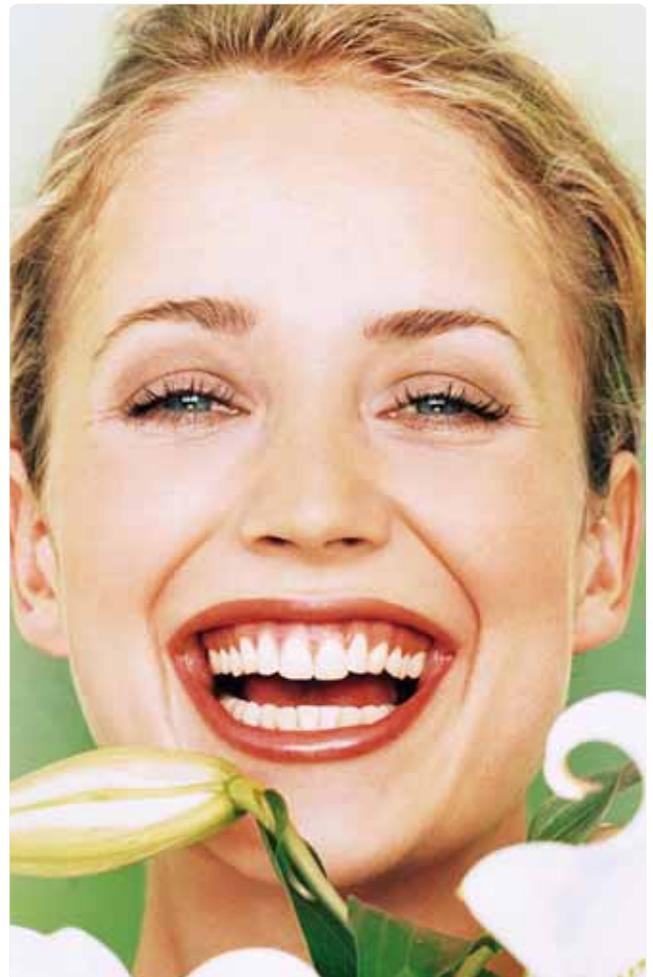
Mushrooms have wide-ranging medicinal properties, including powerful support for the function of the **immune system**.

Beta glucans are compounds found in the cell walls of mushrooms, and in yeast, seaweed, and some grains that are also known to help the immune system.

Beta-glucans have been shown to improve immune responses, helping to:

- Prevent and fight **infections** like the common cold and flu,
- Prevent or reverse immune senescence, and
- Support a healthy gut microbiota.

A carefully formulated blend of **beta glucans** from yeast as well as **shiitake**, **maitake**, and **chaga mushrooms** can help support healthy immune function. •



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

References

1. Stamets P, Zwickey H. Medicinal Mushrooms: Ancient Remedies Meet Modern Science. *Integr Med (Encinitas)*. 2014 Feb;13(1):46-7.
2. Blagodatski A, Yatsunskaya M, Mikhailova V, et al. Medicinal mushrooms as an attractive new source of natural compounds for future cancer therapy. *Oncotarget*. 2018 Jun 26;9(49):29259-74.
3. Ciecierska A, Drywien ME, Hamulka J, et al. Nutraceutical functions of beta-glucans in human nutrition. *Rocz Panstw Zakl Hig*. 2019;70(4):315-24.
4. Jin Y, Li P, Wang F. beta-glucans as potential immunoadjuvants: A review on the adjuvanticity, structure-activity relationship and receptor recognition properties. *Vaccine*. 2018 Aug 23;36(35):5235-44.
5. Zhang M, Zhang Y, Zhang L, et al. Chapter Thirteen - Mushroom polysaccharide lentinan for treating different types of cancers: A review of 12 years clinical studies in China. In: Zhang L, ed. *Progress in Molecular Biology and Translational Science*. Vol 163: Academic Press; 2019:297-328.
6. Carpenter KC, Breslin WL, Davidson T, et al. Baker's yeast beta-glucan supplementation increases monocytes and cytokines post-exercise: implications for infection risk? *Br J Nutr*. 2013 Feb 14;109(3):478-86.
7. Mah E, Kaden VN, Kelley KM, et al. Beverage Containing Dispersible Yeast beta-Glucan Decreases Cold/Flu Symptomatic Days After Intense Exercise: A Randomized Controlled Trial. *J Diet Suppl*. 2020;17(2):200-10.
8. McFarlin BK, Carpenter KC, Davidson T, et al. Baker's yeast beta glucan supplementation increases salivary IgA and decreases cold/flu symptomatic days after intense exercise. *J Diet Suppl*. 2013 Sep;10(3):171-83.
9. McFarlin BK, Venable AS, Carpenter KC, et al. Oral Supplementation with Baker's Yeast Beta Glucan Is Associated with Altered Monocytes, T Cells and Cytokines following a Bout of Strenuous Exercise. *Front Physiol*. 2017;8:786.
10. Talbott S, Talbott J. Effect of BETA 1, 3/1, 6 GLUCAN on Upper Respiratory Tract Infection Symptoms and Mood State in Marathon Athletes. *J Sports Sci Med*. 2009;8(4):509-15.
11. Feldman S, Schwartz H, Kalman D, et al. Randomized Phase II Clinical Trials of Wellmune WGP® for Immune Support During Cold and Flu Season. *J Appl Res*. 2009 01/01;9.
12. Kim HS, Hong JT, Kim Y, et al. Stimulatory Effect of beta-glucans on Immune Cells. *Immune Netw*. 2011 Aug;11(4):191-5.
13. Jayachandran M, Chen J, Chung SSM, et al. A critical review on the impacts of beta-glucans on gut microbiota and human health. *J Nutr Biochem*. 2018 Nov;61:101-10.
14. Jayachandran M, Xiao J, Xu B. A Critical Review on Health Promoting Benefits of Edible Mushrooms through Gut Microbiota. *Int J Mol Sci*. 2017 Sep 8;18(9).
15. Mitsou EK, Saxami G, Stamoulou E, et al. Effects of Rich in Beta-Glucans Edible Mushrooms on Aging Gut Microbiota Characteristics: An In Vitro Study. *Molecules*. 2020 Jun 18;25(12).
16. Choudhury MBK, Rahman T. Shiitake Mushroom: A Tool of Medicine. *Bangladesh Journal of Medical Biochemistry*. 2013 01/20;5(1):24-32.
17. Dai X, Stanilka JM, Rowe CA, et al. Consuming Lentinula edodes (Shiitake) Mushrooms Daily Improves Human Immunity: A Randomized Dietary Intervention in Healthy Young Adults. *J Am Coll Nutr*. 2015;34(6):478-87.
18. Avtonomova AV, Krasnopolskaya LM. [Antiviral properties of basidiomycetes metabolites]. *Antibiot Khimioter*. 2014;59(7-8):41-8.
19. Ren G, Xu L, Lu T, et al. Structural characterization and antiviral activity of lentinan from Lentinus edodes mycelia against infectious hematopoietic necrosis virus. *Int J Biol Macromol*. 2018 Aug;115:1202-10.
20. Rincao VP, Yamamoto KA, Ricardo NM, et al. Polysaccharide and extracts from Lentinula edodes: structural features and antiviral activity. *Virolog J*. 2012 Feb 15;9:37.
21. Masterson CH, Murphy EJ, Gonzalez H, et al. Purified beta-glucans from the Shiitake mushroom ameliorates antibiotic-resistant Klebsiella pneumoniae-induced pulmonary sepsis. *Lett Appl Microbiol*. 2020 Oct;71(4):405-12.
22. Hou L, Meng M, Chen Y, et al. A water-soluble polysaccharide from Grifola frondosa induced macrophages activation via TLR4-MyD88-IKKbeta-NF-kappaB p65 pathways. *Oncotarget*. 2017 Oct 17;8(49):86604-14.
23. Vetvicka V, Vetvickova J. Immune-enhancing effects of Maitake (Grifola frondosa) and Shiitake (Lentinula edodes) extracts. *Ann Transl Med*. 2014 Feb;2(2):14.
24. Kim YR. Immunomodulatory Activity of the Water Extract from Medicinal Mushroom Inonotus obliquus. *Mycobiology*. 2005 Sep;33(3):158-62.
25. Szychowski KA, Skora B, Pomianek T, et al. Inonotus obliquus - from folk medicine to clinical use. *J Tradit Complement Med*. 2021 Jul;11(4):293-302.
26. Ji L, Sun G, Li J, et al. Effect of dietary beta-glucan on growth, survival and regulation of immune processes in rainbow trout (*Oncorhynchus mykiss*) infected by *Aeromonas salmonicida*. *Fish Shellfish Immunol*. 2017 May;64:56-67.
27. Chaplin DD. Overview of the immune response. *J Allergy Clin Immunol*. 2010 Feb;125(2 Suppl 2):S3-23.
28. Song L, Yuan J, Ni S, et al. Enhancement of adaptive immune responses of aged mice by dietary intake of beta-glucans, with special emphasis on anti-aging activity. *Mol Immunol*. 2020 Jan;117:160-7.
29. Zheng X, Zou S, Xu H, et al. The linear structure of beta-glucan from baker's yeast and its activation of macrophage-like RAW264.7 cells. *Carbohydr Polym*. 2016 Sep 5;148:61-8.
30. Talbott SM, Talbott JA, Talbott TL, et al. beta-Glucan supplementation, allergy symptoms, and quality of life in self-described allergy sufferers. *Food Sci Nutr*. 2013 Jan;1(1):90-101.
31. Aiello A, Farzaneh F, Candore G, et al. Immunosenescence and Its Hallmarks: How to Oppose Aging Strategically? A Review of Potential Options for Therapeutic Intervention. *Front Immunol*. 2019;10:2247.
32. Xu X, Yang J, Ning Z, et al. Lentinula edodes-derived polysaccharide rejuvenates mice in terms of immune responses and gut microbiota. *Food Funct*. 2015 Aug;6(8):2653-63.
33. Silva YP, Bernardi A, Frozza RL. The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. *Front Endocrinol (Lausanne)*. 2020 2020-January-31;11:25.
34. Ba DM, Gao X, Al-Shaar L, et al. Prospective study of dietary mushroom intake and risk of mortality: results from continuous National Health and Nutrition Examination Survey (NHANES) 2003-2014 and a meta-analysis. *Nutr J*. 2021 Sep 21;20(1):80.
35. Ba DM, Gao X, Muscat J, et al. Association of mushroom consumption with all-cause and cause-specific mortality among American adults: prospective cohort study findings from NHANES III. *Nutr J*. 2021 Apr 22;20(1):38.
36. Ba DM, Ssentongo P, Beelman RB, et al. Higher Mushroom Consumption Is Associated with Lower Risk of Cancer: A Systematic Review and Meta-Analysis of Observational Studies. *Adv Nutr*. 2021 Oct 1;12(5):1691-704.

Baby *your* Skin

Healthy skin. Comfortable joints. Both rely on collagen. Our **Collagen Peptides for Skin & Joints** formula:

- Stimulates increased production of collagen in the body
- Improves skin elasticity, hydration, smoothness and suppleness
- Supports joint structure, comfort and flexibility
- Protects joint cartilage



Item #02408

343 grams of powder
(0.75 lb or 12 oz)

1 jar **\$27**

4 jars **\$24 each**

**MIX ONE SCOOP WITH WATER
OR BEVERAGE OF CHOICE**



GLUTEN FREE

**NON
GMO
LE CERTIFIED**

For full product description or to order
Collagen Peptides for Skin & Joints, call
1-800-544-4440 or visit www.LifeExtension.com

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



Clean

Your House at the Cellular Level



Ever heard of **cell senescence**?

It's when some of your body's cells no longer function optimally and emit undesirable **compounds** that affect healthy cells.

Senescent cells need to be cleaned out to promote a healthy **inflammatory response** and inhibit **protein-degrading** enzymes to support healthy aging processes.

Senolytic Activator[®] helps your body manage pesky **senescent cells**.

Item #02301 • 36 vegetarian capsules

1 bottle \$19.50 | 4 bottles \$18 each

Each bottle lasts **3 months** based on recommended once per week dosing.



For full product description or to order **Senolytic Activator**[®], call **1-800-544-4440** or visit **www.LifeExtension.com**

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

SUPPORT HEALTHY IMMUNE FUNCTION

Mushroom Immune

with **BETA GLUCANS**

"I can recommend it highly as a failsafe way to revitalize my immune system in a natural way."

Richard

VERIFIED CUSTOMER REVIEW

Once daily **Mushroom Immune** provides a blend of:

- **Shiitake**
- **Maitake**
- **Chaga**
- Plus **250 mg of beta glucans**

Scientific studies show these four nutrients can:

- Promote **innate** immune cell function, the body's first line of defense
- Modulate **adaptive** immune cells, critical for long-term immune protection
- Exert effects that may reverse many factors of **immune senescence**
- Encourage a healthy **gut microbiota**



Item # 02426 30 vegetarian capsules
1 bottle \$19.50 • 4 bottles \$18 each
(Suggested dose is one capsule daily)

For full product description and to order **Mushroom Immune with Beta Glucans**, call **1-800-544-4440** or visit www.LifeExtension.com

Wellmune® is a registered trademark of Kerry Group.

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





A *NEW* Way to Enjoy **MELATONIN**

BY MICHAEL DOWNEY

Melatonin has helped many people sleep better.¹

But not all those who suffer **sleep issues** derive perceivable **benefits**.

A delicious *new* way to boost **individualized melatonin** levels is available in the form of a vegetarian, *sugar-free gummy*.

This article describes how melatonin functions to improve sleep and how you may better derive these benefits.



The Dangers of Inadequate Sleep

Getting **too little sleep** doesn't just leave people fatigued. **Inadequate sleep** is associated with increased risk of:^{2,3}

- Excess body weight and obesity,
- Type II diabetes,
- Sleep apnea,
- Hypertension,
- Mood disorders (depression, anxiety),
- Pain and disability,
- Stroke, and even
- Premature death.

In addition, people with sleep problems often have a **disrupted circadian rhythm**, the body's internal clock. Misalignment of this sleep/wake cycle disrupts and impairs many psychological and physiological functions, which may increase the risk of metabolic disorders.^{4,5}

It's critical to get sufficient sleep *and* keep your circadian rhythm in tune.

What is Melatonin?

Melatonin is a hormone that regulates circadian rhythm and promotes healthy sleep patterns.¹

Studies have found that the pineal gland's secretion of **melatonin** decreases with age, which can make it more difficult to get quality sleep.^{6,7}

Use of computers, cell phones, tablets, and other devices exposes users to **blue light**, which also decreases melatonin levels.⁸

Melatonin has been shown to **improve** the onset, duration, and quality of sleep.⁹⁻¹¹

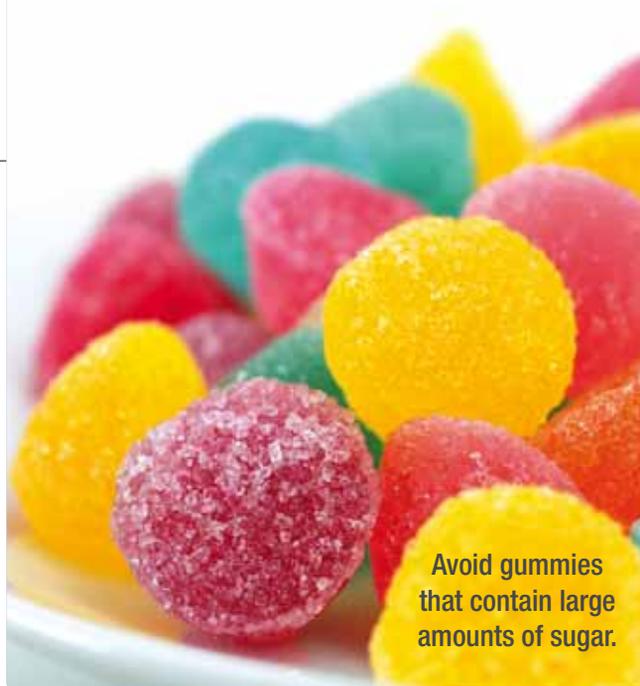
Many Americans today take melatonin before bedtime.¹²

A Sugar-Free Option

Melatonin capsules, tablets, or drops have become part of the nightly regimen for many aging adults.

Scientists have now developed a convenient way to supplement with **melatonin**—a great-tasting, easy-to-chew, vegetarian-friendly **gummy**.

Some people like chewing on something tasty before bedtime, and melatonin **gummies** have become enormously popular.



There are some problems with commercial gummies, however.

Take a look at any gummy label in the store. Many of these gummy supplements contain **high** amounts of **sugar** as the first ingredient.

Sugar inflicts a myriad of deleterious effects, including impeding restorative sleep.¹³

The new gummies are different. Each tasty gummy provides **3 mg** of melatonin and is **100% sugar-free**.

So, you can chew on the number of gummies that provide a low-calorie way of satisfying hunger while individually **dosing** the amount of **melatonin** that works best for you.

Many will find it a delicious way to get ready for bed.

Melatonin Promotes Healthy Sleep in Five Ways

In **human** studies, scientists have demonstrated that **melatonin** improves **five** parameters of sleep.

Clinical studies suggest that taking oral melatonin:⁹⁻¹¹

- *Reduces* **sleep onset latency**, the time between lights out and falling asleep,
- *Increases* **sleep efficiency**, the percentage of time we spend asleep while in bed,
- *Increases* **total sleep time**, time spent asleep after sleep onset,
- *Reduces* **wakefulness after sleep onset**, time spent awake after sleep begins, and
- *Synchronizes* and maintains a healthy **circadian rhythm**, to promote healthy sleep patterns.

In one meta-analysis of **17** studies involving a total of 284 volunteers, researchers found that, on average, **melatonin** use significantly:⁹

- *Reduced* **sleep onset latency** by **4.0 minutes**,
- *Increased* **sleep efficiency** by **2.2%**, and
- *Increased* **total sleep time** by **12.8 minutes**.

Syncing Circadian Rhythm

Nearly *every* cell in our body has an internal “clock” which is governed by a “master clock” in the brain that responds to changes in light exposure and helps create and maintain our **circadian rhythm**.¹⁴

Among other functions, circadian rhythm regulates our **sleep-wake cycle**. The body **increases** melatonin levels as light levels fall in the evening and **lowers** melatonin levels as light levels rise around daybreak.¹⁴

If circadian rhythm becomes *disrupted*, as may happen with age, this cycle can become impaired.

A study from the prestigious journal *Lancet Psychiatry* revealed that disrupted circadian rhythms are associated not only with sleep disturbances, but also with an increased risk of **depression** and **bipolar disorder**.¹⁵

Endogenous **melatonin** plays a critical role in keeping this central clock in sync with the environment, maintaining our circadian rhythm and improving sleep.^{16,17}

Oral melatonin has also been used to help **synchronize** the circadian rhythm in **blind** individuals whose bodies have been unable to synchronize with the day-night cycle.¹⁸

Help for Insomnia Sufferers

Insomnia is defined as difficulty initiating or maintaining refreshing sleep. It can have a drastic effect on daily life and health.

Low melatonin levels have been linked to insomnia, particularly in the elderly. Clinical studies have reported **serum** melatonin levels to be significantly **lower** (and the time of peak melatonin values delayed) in elderly subjects with insomnia compared with age-matched normal controls.¹⁹

A meta-analysis of 14 randomized controlled trials, of which insomnia was the primary diagnosis in 12 studies, found that people with insomnia who took melatonin had reduced **sleep onset latency** (the time it takes to fall asleep).²⁰

Another review found that oral melatonin provided a significant improvement in both **sleep onset latency** and **total sleep time** in those suffering from insomnia.²¹



WHAT
YOU
NEED
TO
KNOW

Get a Better Night's Sleep

- An age-related decline in **melatonin** levels can interfere with falling and staying asleep.
- **Inadequate sleep** is associated with the risk of obesity, type II diabetes, stroke, premature death, and more.
- Taking oral melatonin at night helps people **fall asleep faster** and **stay asleep longer**.
- Melatonin can also improve quality of sleep for patients with **insomnia** and help relieve symptoms of **jet lag**.
- Melatonin is now available in a great-tasting vegetarian **gummy** that is *sugar-free*.



Relief for Jet Lag

The energy-sapping effects of **jet lag** are a symptom of disrupted **circadian rhythm**.²²

Your body doesn't recognize the change when you fly into new time zones. As a result, the body's rhythms are suddenly out of step with the day-night cycle at your destination.

Oral **melatonin** can help to get your circadian rhythm back on schedule.

One review found that oral melatonin, taken close to the target bedtime at the destination (10 pm to midnight), was **remarkably effective** in preventing or reducing jet lag.²³

Similarly, melatonin may help shift workers adjust their sleep timing after a shift rotation.²⁴

These and other benefits make melatonin a safe, effective way to relieve sleep problems and promote optimal sleep.

Summary

Difficulty falling asleep and staying asleep can be caused by an age-related decline in levels of **melatonin**.^{6,7}

Not getting enough **sleep** is associated with a higher risk of obesity, diabetes, cognitive decline, stroke, shortened telomeres, and premature death.^{2,3}

Taking oral melatonin at night has been shown to improve **five** different aspects of sleep, helping to support overall health.⁹⁻¹¹

Scientists have developed a vegetarian, **sugar-free gummy**—a delicious *new* way to boost nighttime melatonin levels. ●

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

References

1. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK534823/>. Accessed March 28, 2022.
2. Available at: <https://www.nichd.nih.gov/health/topics/sleep/conditioninfo/inadequate-sleep>. Accessed March 28, 2022.
3. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK19961/>. Accessed March 28, 2022.
4. Cable J, Schernhammer E, Hanlon EC, et al. Sleep and circadian rhythms: pillars of health—a Keystone Symposia report. *Ann N Y Acad Sci*. 2021 Dec;1506(1):18-34.
5. Potter GD, Skene DJ, Arendt J, et al. Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. *Endocr Rev*. 2016 Dec;37(6):584-608.
6. Kennaway DJ, Lushington K, Dawson D, et al. Urinary 6-sulfatoxymelatonin excretion and aging: new results and a critical review of the literature. *J Pineal Res*. 1999 Nov;27(4):210-20.
7. Zhou JN, Liu RY, van Heerikhuizen J, et al. Alterations in the circadian rhythm of salivary melatonin begin during middle-age. *J Pineal Res*. 2003 Jan;34(1):11-6.
8. Tahkamo L, Partonen T, Pesonen AK. Systematic review of light exposure impact on human circadian rhythm. *Chronobiol Int*. 2019 Feb;36(2):151-70.
9. Brzezinski A, Vangel MG, Wurtman RJ, et al. Effects of exogenous melatonin on sleep: a meta-analysis. *Sleep Med Rev*. 2005 Feb;9(1):41-50.
10. Garfinkel D, Laudon M, Nof D, et al. Improvement of sleep quality in elderly people by controlled-release melatonin. *Lancet*. 1995 Aug 26;346(8974):541-4.
11. Xie Z, Chen F, Li WA, et al. A review of sleep disorders and melatonin. *Neural Res*. 2017 Jun;39(6):559-65.
12. Li J, Somers VK, Xu H, et al. Trends in Use of Melatonin Supplements Among US Adults, 1999-2018. *JAMA*. 2022 Feb 1;327(5):483-5.
13. Available at: <https://www.sleepfoundation.org/physical-health/sleep-and-blood-glucose-levels>. Accessed April 5, 2022.
14. Pandi-Perumal SR, Cardinali DP, Zaki NFW, et al. Timing is everything: circadian rhythms and their role in the control of sleep. *Front Neuroendocrinol*. 2022 Jan 13:100978.
15. Lyall LM, Wyse CA, Graham N, et al. Association of disrupted circadian rhythmicity with mood disorders, subjective wellbeing, and cognitive function: a cross-sectional study of 91 105 participants from the UK Biobank. *Lancet Psychiatry*. 2018 Jun;5(6):507-14.
16. Albrecht U. Timing to perfection: the biology of central and peripheral circadian clocks. *Neuron*. 2012 Apr 26;74(2):246-60.
17. Pevet P. The internal time-giver role of melatonin. A key for our health. *Rev Neurol (Paris)*. 2014 Nov;170(11):646-52.
18. Emens JS, Eastman Cl. Diagnosis and Treatment of Non-24-h Sleep-Wake Disorder in the Blind. *Drugs*. 2017 Apr;77(6):637-50.
19. Cardinali DP, Srinivasan V, Brzezinski A, et al. Melatonin and its analogs in insomnia and depression. *J Pineal Res*. 2012 May;52(4):365-75.
20. Buscemi N, Vandermeer B, Hooton N, et al. The efficacy and safety of exogenous melatonin for primary sleep disorders. A meta-analysis. *J Gen Intern Med*. 2005 Dec;20(12):1151-8.
21. Low TL, Choo FN, Tan SM. The efficacy of melatonin and melatonin agonists in insomnia - An umbrella review. *J Psychiatr Res*. 2020 Feb;121:10-23.
22. Available at: <https://www.mayoclinic.org/diseases-conditions/jet-lag/symptoms-causes/syc-20374027>. Accessed March 29, 2022.
23. Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag. *Cochrane Database Syst Rev*. 2002 (2):CD001520.
24. Sadeghniaat-Haghighi K, Bahrami H, Aminian O, et al. Melatonin therapy in shift workers with difficulty falling asleep: A randomized, double-blind, placebo-controlled crossover field study. *Work*. 2016 Sep 27;55(1):225-30.

LITHIUM
1,000 mcg
12 cents a day!

A
Bodyguard
for Your
Brain

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.

It's like a bodyguard for your brain!

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



LITHIUM

(1000 mcg of lithium per tiny cap)
Item #02403 | 100 vegetarian capsules

1 bottle **\$12** | 4 bottles **\$10.50** each
Each bottle lasts 100 days.

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

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



"Felt a renewed energy from the very first day."

Alan

VERIFIED CUSTOMER REVIEW

Low-Cost Biologically Active

B COMPLEX

Enzymatically Active Vitamins

BioActive Complete B-Complex provides *enzymatically active forms* of meaningful potencies of each B vitamin.

This includes the *pyridoxal 5'-phosphate* form of vitamin B6 shown to protect lipids and proteins against **glycation** and the most biologically active *form* of **folate** called *5-methyltetrahydrofolate (5-MTHF)*, which is up to **7 times more** bioavailable than folic acid.*



Item #01945 • 60 vegetarian capsules

1 bottle \$9 • 4 bottles \$8 each

For full product description and to order **BioActive Complete B-Complex**, call 1-800-544-4440 or visit www.LifeExtension.com

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



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

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

SUGAR-FREE

A DELICIOUS WAY TO IMPROVE SLEEP



Sweet DREAMS



Item #02503 • 60 vegetarian gummies

1 jar **\$16.50**

4 jars \$15 each

People often crave something tasty to chew on before **bedtime**.

A new strawberry-flavored **gummy** lets you dose your **melatonin** based on how many **gummies** you ingest before bedtime.

Clinical studies show that **melatonin** improves revitalizing **sleep** in five ways.¹⁻³

Each **sugar-free gummy** provides **3 mg of melatonin**.

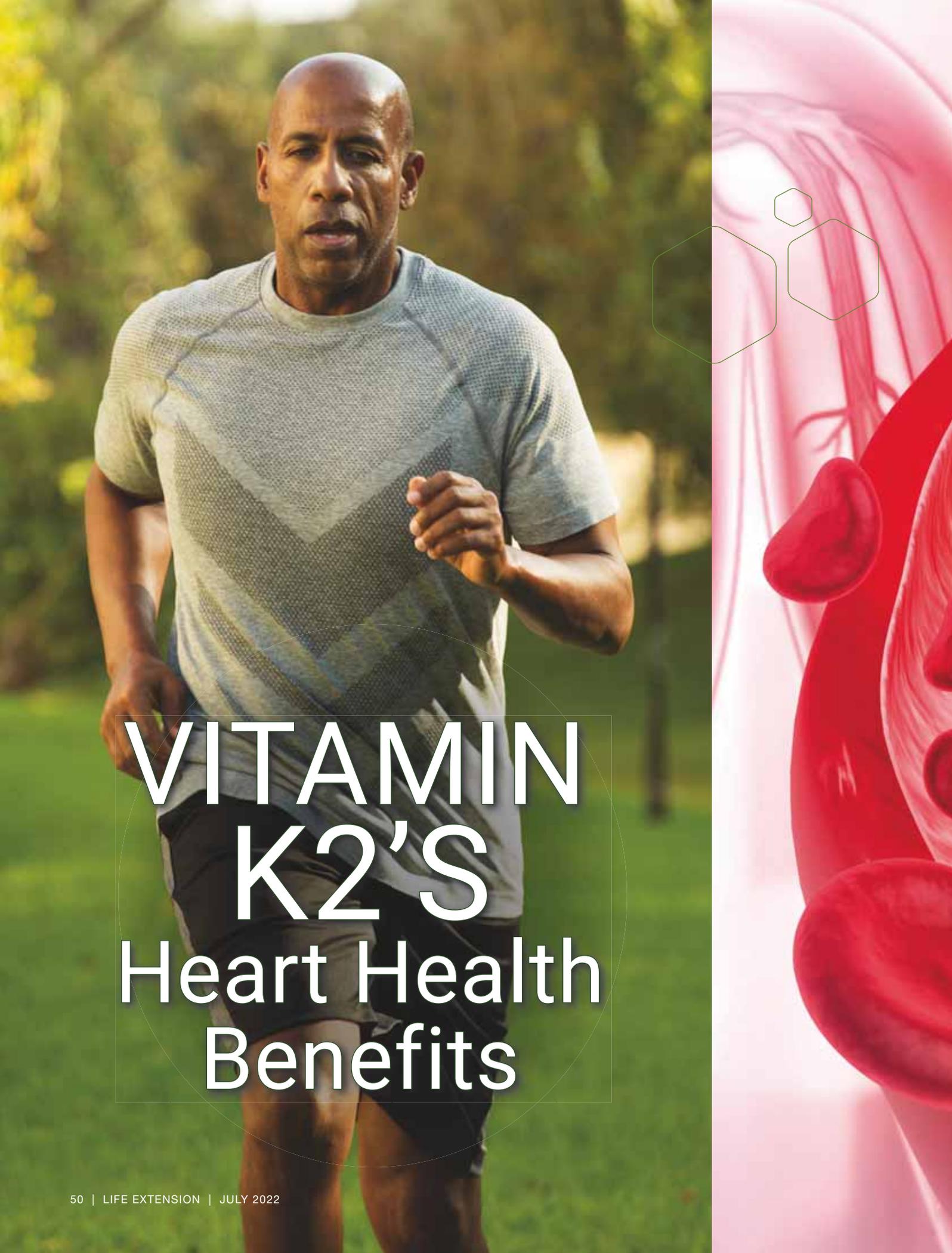
For full product description and to order **Melatonin Gummy**, call 1-800-544-4440 or visit www.LifeExtension.com



1. *Sleep Med Rev.* 2005 Feb;9(1):41-50. 2. *Lancet.* 1995 Aug 26;346(8974):541-4. 3. *Neurol Res.* 2017 Jun;39(6):559-65.

Caution: Do not consume alcohol, drive or operate machinery after taking this product.

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



VITAMIN
K2'S
Heart Health
Benefits



BY ANTHONY PAYNE, N.M.D., PH.D., M.D. (HONORARY)

Vitamin K2 is best known for helping to build strong, healthy bones.

Some of the same skeletal benefits make it a powerful protector of the **cardiovascular system**.¹

Cardiovascular disease is the leading killer in the U.S.² **Vitamin K2** may help to:^{1,3}

- Reduce arterial stiffness,
- Slow the progression of arterial and valve calcification,
- Lower the incidence of diabetes, and
- Decrease cardiovascular mortality.

In one study, adults 55 and older were followed for up to **10 years**. Those with the *highest* intake of **vitamin K2**, compared to the *lowest*, had a **57%** lower risk of death from coronary heart disease—and a **26%** lower risk of death **from any cause**.⁴

About Vitamin K

There are two main types of **vitamin K**.⁵

Vitamin K1 is primarily found in green leafy vegetables. It has long been used to promote healthy **blood clotting** and prevent abnormal bleeding.⁵

Vitamin K2 is also known as **menaquinone**. It is essential for the health of bones and the cardiovascular system. Emerging evidence indicates it may play a vital role in **immune** function and in the health of the nervous system.¹

Vitamin K2 exists in several forms. Among these, **menaquinone-4 (MK-4)** and **menaquinone-7 (MK-7)** have been studied most extensively.^{6,7}

MK-4 is found mainly in dairy foods. **MK-7** is primarily found in fermented foods, such as kefir (fermented milk) and sauerkraut.^{5,8}

Preventing Atherosclerosis

In the U.S., over **650,000** people die from **heart disease** each year. That's roughly **one in every four deaths**.²

More than half of these deaths are from **coronary artery disease**, caused by a buildup of **plaque** (made of fats, calcium, and other substances) in the walls of arteries that restricts blood flow.²

This buildup is known as **atherosclerosis**. It can result in chest pain, **heart attacks**, and **strokes**.^{9,10}

Daily oral intake of **vitamin K2** may *prevent* atherosclerosis from progressing.

Last year, the **American Heart Association** released research showing that *higher* vitamin K intake was associated with significantly lower risk of **hospitalizations** resulting from atherosclerotic cardiovascular disease.¹¹



Combating Arterial Stiffness

One of the most significant ways **vitamin K2** protects against cardiovascular disease is by preventing **arterial stiffness**.

This physical stiffening of arteries contributes to cardiovascular disease.¹²

Vitamin K2 activates **matrix Gla**, a protein that helps prevent **calcium** from being incorporated into **arterial tissue**.¹

It also activates another protein that binds calcium to **bone**. This strengthens bone while at the same time helping to prevent **calcification** of our **arteries**.

Protecting Endothelial Function

All blood vessels are lined with a very thin layer of cells called the **endothelium**. This tissue helps regulate the flow of **calcium** and other substances into and out of the bloodstream.^{13,14}

A healthy endothelium is needed for optimal cardiovascular health.¹⁵

Endothelial dysfunction is a major contributor to aging, atherosclerosis, hypertension, and the complications of diabetes.¹⁵

It is characterized by an imbalance in the constriction and relaxation (dilation) of arteries, a decrease in nitric oxide bioavailability, and an increase in reactive oxygen species and pro-inflammatory factors.¹⁵

A hallmark of many types of cardiovascular disease is **endothelial dysfunction**.

When endothelial cells cannot function properly, plaque builds up and calcifies, and narrows the artery.¹⁶

Vitamin K provides cardiovascular protection thanks to its role in calcium homeostasis.

In a preclinical study, giving **vitamin K2** to mice prone to developing atherosclerosis increased nitric oxide production. This improved the ability of arteries to dilate.¹⁷

A **2021** review published in *Open Heart Journal* stated that:

*"Increased vitamin K2 intake may reduce arterial stiffness, slow progression of vascular and valvular calcification, lower the incidence of diabetes and coronary artery disease, and decrease cardiovascular mortality."*³

WHAT
YOU
NEED
TO
KNOW

Real-World Results

The heart-protective effects of **vitamin K2** have been demonstrated in multiple studies.

In observational studies, *higher* intakes of vitamin K2 were associated with *lower* rates of **arterial calcification** and **death** from coronary artery disease.¹⁸

In one study, women with the *highest* K2 intake were found to be at a **20% lower** risk for coronary artery **calcification** than women who had the lowest intake.¹⁹

Researchers analyzing more than 16,000 Dutch women who were followed for an average of 8.1 years found that *each 10 mcg/day increase* in vitamin K2 intake was associated with a **9% reduction** in coronary heart disease risk.²⁰

In another study, researchers followed more than 4,800 adults over age 55 for up to **10 years**.⁴

Overall, those with the *highest* K2 intake had a **57% lower** rate of death due to **coronary heart disease** and a **26% lower** rate of **death from any cause**.⁴

Safety of High-Dose Vitamin K2

Research suggests that **higher doses** of vitamin K2 intake are most likely to prevent the development or progression of cardiovascular disease.

In clinical studies involving daily K2 doses ranging from **10 mcg to 135 mg**, there have been **no reports** of adverse side effects.²¹ (The vitamin K2 dose of **135 mg** is very high by historic standards, yet no toxicity was observed.)

Protecting the Heart with Vitamin K2

- Cardiovascular disease is the leading cause of death in the U.S. It is frequently driven by **atherosclerosis**, buildup of plaque in arteries.
- **Vitamin K2** can help prevent and reduce calcification in arteries. It also reduces endothelial dysfunction, further decreasing atherosclerosis risk.
- In observational studies, those with the *highest* intake of vitamin K2 have *lower* rates of heart disease and as much as a **57% lower** rate of death due to **coronary heart disease**.

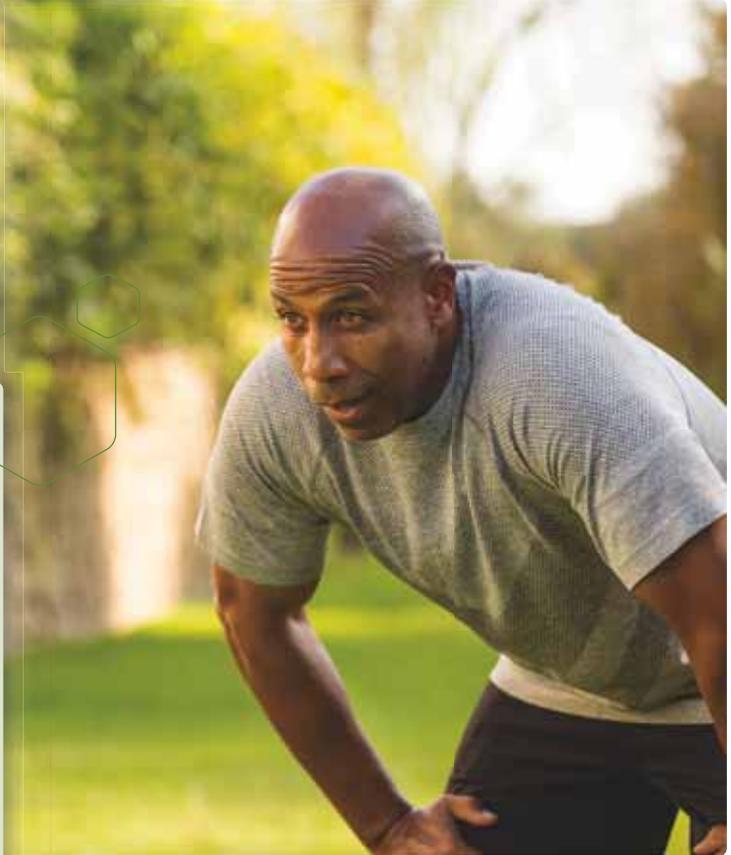
Japanese doctors routinely prescribe **45 mg** of vitamin K2 daily to women with **osteoporosis**.^{21,22}

These amounts may also help prevent the progression of atherosclerosis.

Summary

Vitamin K2 helps prevent arterial stiffening, buildup of plaque in artery walls, and endothelial dysfunction.

These and other actions reduce the development and progression of **atherosclerosis**, a major cause of heart disease. ●



A Warning About Warfarin

Anyone taking the anticoagulant drug **warfarin** should consult a physician before taking any form of vitamin K.

That's because *warfarin* *interferes* with the action of vitamin K in the body. Those taking newer anticoagulant drugs such as **Eliquis®**, **Pradaxa®**, and **Xarelto®** do not need to restrict vitamin K intake.

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

References

- Halder M, Petsophonsakul P, Akbulut AC, et al. Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *Int J Mol Sci*. 2019 Feb 19;20(4):896.
- Available at: <https://www.cdc.gov/heartdisease/facts.htm>. Accessed April 12, 2022.
- Hariri E, Kassiss N, Iskandar JP, et al. Vitamin K2—a neglected player in cardiovascular health: a narrative review. *Open Heart*. 2021 Nov;8(2):e001715.
- Geleijnse JM, Vermeer C, Grobbee DE, et al. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *J Nutr*. 2004 Nov;134(11):3100-5.
- Shioi A, Morioka T, Shoji T, et al. The Inhibitory Roles of Vitamin K in Progression of Vascular Calcification. *Nutrients*. 2020 Feb 23;12(2).
- Walther B, Karl JP, Booth SL, et al. Menaquinones, bacteria, and the food supply: the relevance of dairy and fermented food products to vitamin K requirements. *Adv Nutr*. 2013 Jul 1;4(4):463-73.
- Marles RJ, Roe AL, Oketch-Rabah HA. US Pharmacopeial Convention safety evaluation of menaquinone-7, a form of vitamin K. *Nutr Rev*. 2017 Jul 1;75(7):553-78.
- Schwalfenberg GK. Vitamins K1 and K2: The Emerging Group of Vitamins Required for Human Health. *J Nutr Metab*. 2017;2017:6254836.
- Available at: <https://www.ncbi.nlm.nih.gov/books/NBK507799/>. Accessed April 12, 2022.
- Available at: https://www.cdc.gov/heartdisease/coronary_ad.htm. Accessed April 14, 2022.
- Bellinge JW, Dalgaard F, Murray K, et al. Vitamin K Intake and Atherosclerotic Cardiovascular Disease in the Danish Diet Cancer and Health Study. *J Am Heart Assoc*. 2021 Aug 17;10(16):e020551.
- Hansen L, Taylor WR. Is increased arterial stiffness a cause or consequence of atherosclerosis? *Atherosclerosis*. 2016 Jun;249:226-7.
- Rajendran P, Rengarajan T, Thangavel J, et al. The vascular endothelium and human diseases. *Int J Biol Sci*. 2013;9(10):1057-69.
- Plank MJ, Wall DJ, David T. Atherosclerosis and calcium signalling in endothelial cells. *Prog Biophys Mol Biol*. 2006 Jul;91(3):287-313.
- Sun HJ, Wu ZY, Nie XW, et al. Role of Endothelial Dysfunction in Cardiovascular Diseases: The Link Between Inflammation and Hydrogen Sulfide. *Front Pharmacol*. 2019 2020-January-21;10:1568.
- Xu S, Ilyas I, Little PJ, et al. Endothelial Dysfunction in Atherosclerotic Cardiovascular Diseases and Beyond: From Mechanism to Pharmacotherapies. *Pharmacol Rev*. 2021 Jul;73(3):924-67.
- Bar A, Kus K, Manterys A, et al. Vitamin K2-MK-7 improves nitric oxide-dependent endothelial function in ApoE/LDLR(-/-) mice. *Vascul Pharmacol*. 2019 Nov - Dec;122-123:106581.
- Knapen MH, Braam LA, Drummen NE, et al. Menaquinone-7 supplementation improves arterial stiffness in healthy postmenopausal women. A double-blind randomised clinical trial. *Thromb Haemost*. 2015 May;113(5):1135-44.
- Beulens JW, Bots ML, Atsma F, et al. High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis*. 2009 Apr;203(2):489-93.
- Gast GC, de Roos NM, Sluijs I, et al. A high menaquinone intake reduces the incidence of coronary heart disease. *Nutr Metab Cardiovasc Dis*. 2009 Sep;19(7):504-10.
- Akbulut AC, Pavlic A, Petsophonsakul P, et al. Vitamin K2 Needs an RDI Separate from Vitamin K1. *Nutrients*. 2020 Jun 21;12(6).
- Iwamoto J. Vitamin K(2) therapy for postmenopausal osteoporosis. *Nutrients*. 2014 May 16;6(5):1971-80.



Maintain Better Memory Function

VINPOCETINE

A compound originally found in the leaf of the periwinkle plant, vinpocetine has been shown to support brain health and memory function as people age.

Among its many benefits, vinpocetine has been shown to:

- Provide support for age-related cognitive decline
- Support healthy blood flow inside the brain



Item #01327 • 100 vegetarian tablets

1 bottle **\$13.50**

4 bottles \$10.50 each



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



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

ZINC

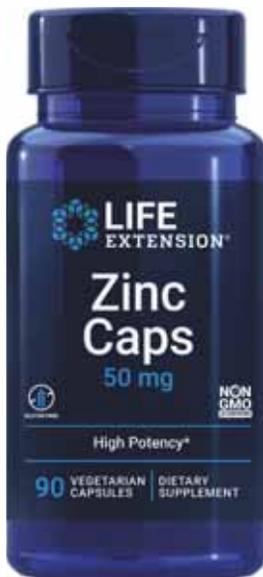
UP

YOUR IMMUNE HEALTH

"It gives my immune system an extra kick when needed."

Tina

VERIFIED CUSTOMER REVIEW



Item #01813

50 mg • 90 vegetarian capsules

1 bottle **\$6.75** • 4 bottles \$6 each



OptiZinc® is a registered trademark of InterHealth Nutritionals, Inc.

You know zinc is good for you—but are you getting enough?

Zinc promotes critical **immune** functions and healthy **bones**.

This formula provides **50 mg** of zinc in a convenient, vegetarian capsule.

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

Caution: Supplemental zinc can inhibit the absorption and availability of copper. If more than 50 mg of supplemental zinc is to be taken daily for more than four weeks, 2 mg of supplemental copper should also be taken to prevent copper deficiency.

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

THREE WAYS TO GET



FOR HEALTHY BONES
+ HEALTHY HEART

"I have been using this for bone building, and my bone density tests have improved."

– Dolores

VERIFIED CUSTOMER
REVIEW



MEGA VITAMIN K2

Japanese physicians use **high-dose vitamin K2** for maintaining healthy bone density.



Vitamin K2 (MK-4) 45,000 mcg
(for bone & vascular health)

SUPER K ELITE

Provides 2 additional forms of vitamin K and even **higher** potencies of K1, MK4, and MK7.



1
DAILY

Vitamin K1 2,000 mcg
(converts to K2 in some people)

Vitamin K2 (MK-4) 1,500 mcg (for bone & vascular health)
Vitamin K2 (MK-7) 181 mcg (long-acting protection)
Vitamin K2 (MK-9) 43 mcg (added cardiovascular support)
Vitamin K2 (MK-6) 11 mcg (added cardiovascular support)

SUPER K

The best-selling **vitamin K** formula for bone and heart health.



1
DAILY

Vitamin K1 1,500 mcg
(converts to K2 in some people)
Vitamin K2 (MK-4) 1,000 mcg
(for bone & vascular health)
Vitamin K2 (MK-7) 100 mcg
(long-acting protection)

Mega Vitamin K2 Item #02417 • 30 capsules
1 bottle \$28.50 • 4 bottles \$26 each

Super K Elite Item #02335 • 30 softgels
1 bottle \$18 • 4 bottles \$16 each

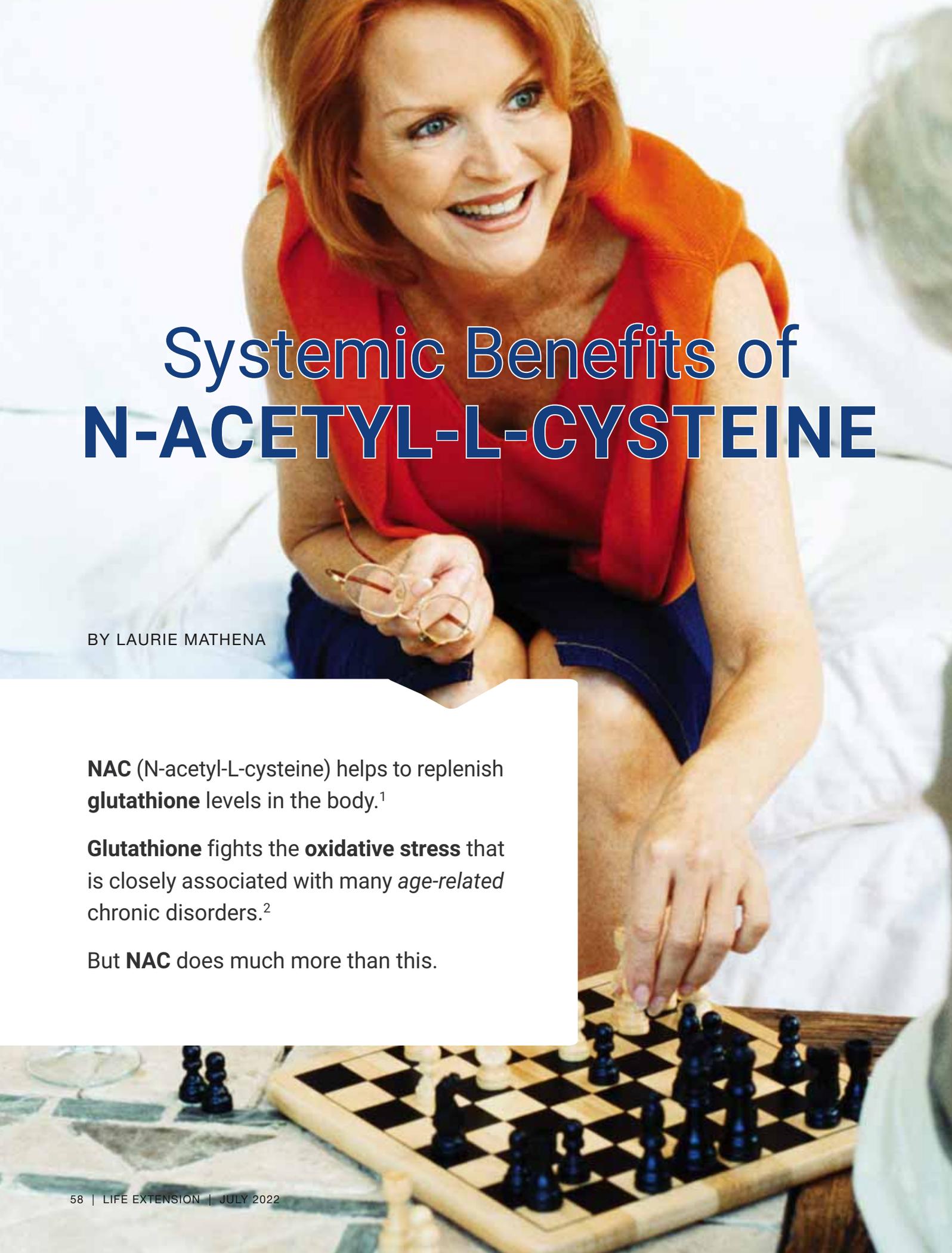
Super K Item #02334 • 90 softgels
1 bottle \$22.50 • 4 bottles \$20.25 each

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

CAUTION: If you are taking a vitamin K antagonist (e.g. warfarin), consult your healthcare practitioner before taking this product.



These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.



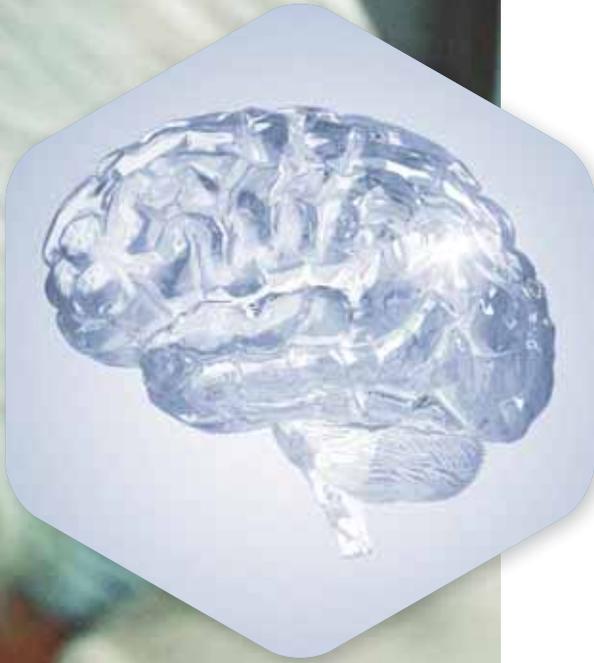
Systemic Benefits of N-ACETYL-L-CYSTEINE

BY LAURIE MATHENA

NAC (N-acetyl-L-cysteine) helps to replenish **glutathione** levels in the body.¹

Glutathione fights the **oxidative stress** that is closely associated with many *age-related* chronic disorders.²

But **NAC** does much more than this.



Applications for NAC

NAC is used in the medical setting as an antidote against **acetaminophen** poisoning.

Research interest has grown steadily over the years for its potential use in various pulmonary, cardiovascular, neurodegenerative, and liver disorders.¹

It protects against a broad array of **environmental toxins** and helps boost the body's **immune** system.¹

NAC supports healthy **respiratory tract** function and may be of value when combating bronchitis and chronic obstructive pulmonary disease.¹

The benefits of NAC extend to:¹

- Non-alcoholic steatohepatitis,
- Arterial hypertension of diabetic etiology,
- Chronic obstructive pulmonary disease (COPD),
- Chronic bronchitis,
- Male infertility,
- Cataract,
- Dry eye syndrome,
- Diabetic retinopathy, and
- Age-related macular degeneration.

NAC's Brain Benefits

Researchers summarized preclinical evidence showing NAC's ability to ameliorate symptoms and pathologies related to various psychiatric disorders.

They concluded that NAC is a strong candidate as an adjunctive approach for many psychiatric disorders.³

The progression of neuronal deterioration in certain areas of the brain may contribute to the development of **depressive** disorders.

In a rat model of depression, researchers found that NAC exerted antidepressant effects by helping protect neurons from injury. They concluded that NAC could be a potent therapeutic strategy for stress-related **depression**.⁴

Evidence continues to emerge for the benefits of this safe, inexpensive intervention.

Suggested Dosage

Most individuals gain benefits from using **600 mg to 1,800 mg/day** of N-acetyl-L-cysteine (NAC) in divided dosages. •

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

References

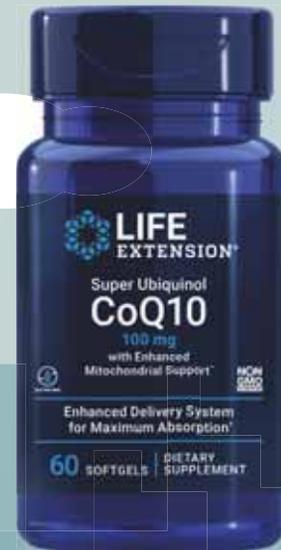
1. Salamon S, Kramar B, Marolt TP, et al. Medical and Dietary Uses of N-Acetylcysteine. *Antioxidants (Basel)*. 2019 Apr 28;8(5).
2. Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/Glutathione>. Accessed April 19, 2022.
3. Smaga I, Frankowska M, Filip M. N-acetylcysteine as a new prominent approach for treating psychiatric disorders. *Br J Pharmacol*. 2021 Jul;178(13):2569-94.
4. Fan C, Long Y, Wang L, et al. N-Acetylcysteine Rescues Hippocampal Oxidative Stress-Induced Neuronal Injury via Suppression of p38/JNK Signaling in Depressed Rats. *Front Cell Neurosci*. 2020;14:554613.



CoQ10

Fuel for Heart | Mind | Muscle

Educated consumers often choose the **ubiquinol** form of **CoQ10** because of studies showing it is *absorbed* up to **eight-times** better!



Item #01426 • 100 mg, 60 softgels
1 bottle \$46.50 • 4 bottles \$39 each



#1 Rated
CoQ10 Products
4 Time Winner!

For full product description and to order **Super Ubiquinol CoQ10 with Enhanced Mitochondrial Support™**, call **1-800-544-4440** or visit **www.LifeExtension.com**

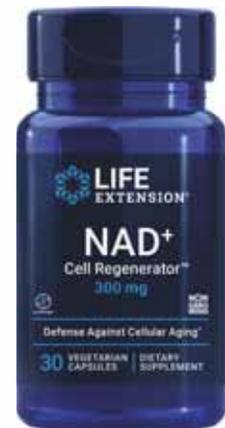
PrimaVie® is a registered trademark of Natreon, Inc. Q+®, Kaneka Ubiquinol™, and the quality seal™ are registered or pending trademarks of Kaneka Corp.

*Ratings based on results of the 2022 ConsumerLab.com Survey of Supplement Users. More information at www.consumerlab.com/survey

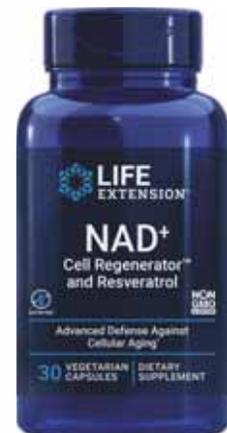
These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Multiple Benefits of **NAD⁺**

- Energy production
- DNA support
- Gene expression (Sirtuin 1-7)
- Immune cell signalling



Item #02344
300 mg • 30 veg. caps.
1 bottle*



Item #02348
30 veg. caps.
1 bottle*

"I love this product.
It's given me tons of energy."

Luis

VERIFIED CUSTOMER REVIEW

For those already taking resveratrol, **NAD⁺ Cell Regenerator™** provides **300 mg** of **nicotinamide riboside chloride**.

Optimized NAD⁺ Cell Regenerator™ combines **300 mg** of **nicotinamide riboside chloride** with **resveratrol** and other **plant extracts**.

For full product description, pricing and to order **NAD⁺ Cell Regenerator™**, call **1-800-544-4440** or visit **www.LifeExtension.com**

* For pricing available to readers of this magazine, call **1-800-544-4440** or visit **LifeExtension.com/NAD**

NIAGEN® is a registered trademark of ChromaDex, Inc., Patents see: www.ChromaDexPatents.com



These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.



"NAC is a powerful tool."

Maury

VERIFIED CUSTOMER REVIEW

TAP THE POWER OF N-ACETYL-L-CYSTEINE TO SUPPORT IMMUNE FUNCTION

N-Acetyl-L-Cysteine (NAC) has been shown to support healthy immune response and respiratory function.

NAC supports healthy levels of *glutathione* that helps promote a healthy **inflammatory response** and protect cells from **oxidative damage**.

For full product description and to order **N-ACETYL-L-CYSTEINE**, call **1-800-544-4440** or visit www.LifeExtension.com

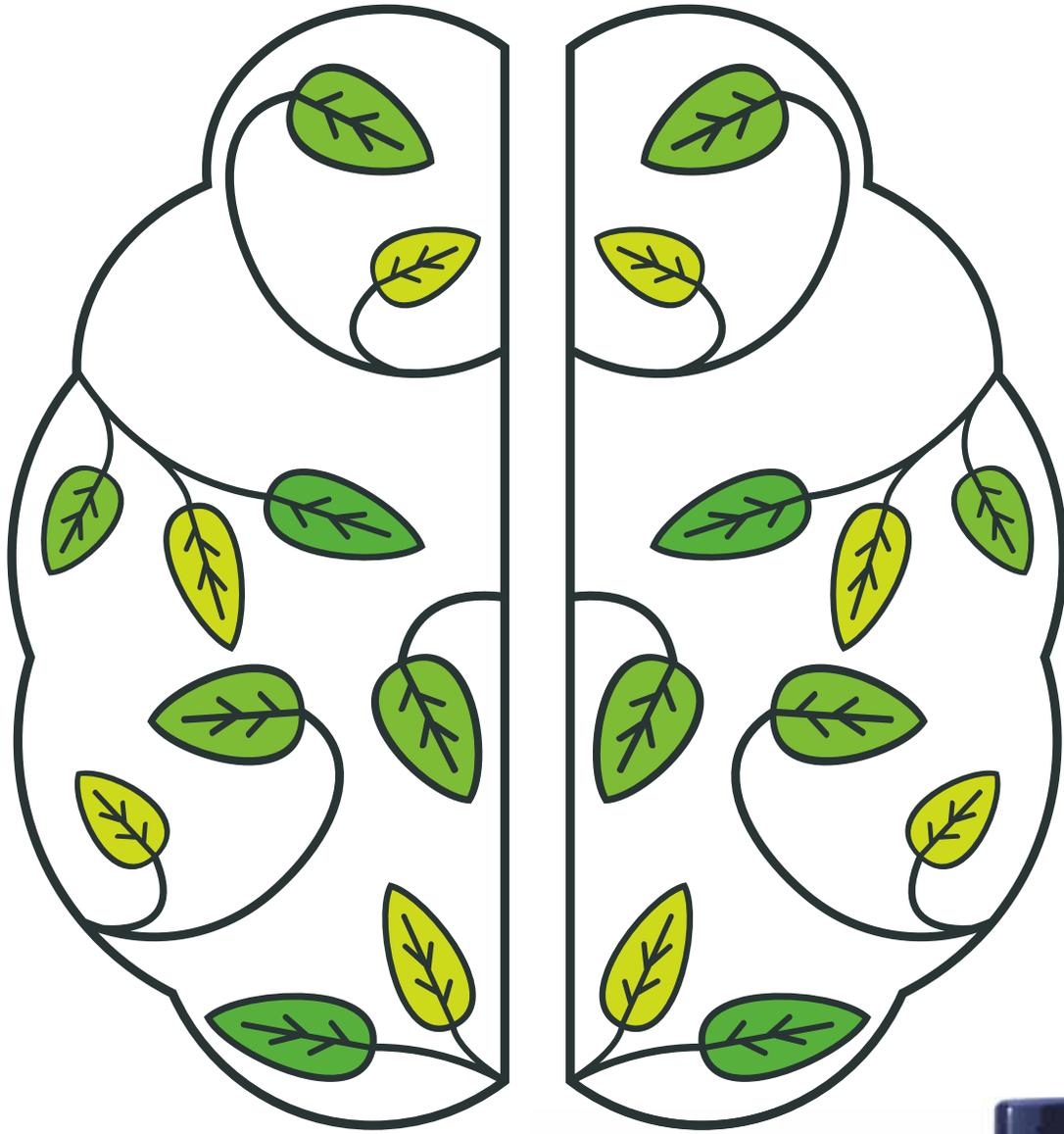


Item #01534 • 60 capsules

1 bottle \$11.25

4 bottles \$10 each

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



Optimized Ashwagandha EXTRACT

Ashwagandha has been shown to:

- Support a healthy response to everyday stress
- Promote emotional well-being
- Encourage already-healthy levels of cortisol, the stress hormone

Optimized Ashwagandha provides **standardized** leaf and root **extracts** at a low cost.



Item #00888 • 60 vegetarian capsules

1 bottle \$7.50 • 4 bottles \$6.75 eac

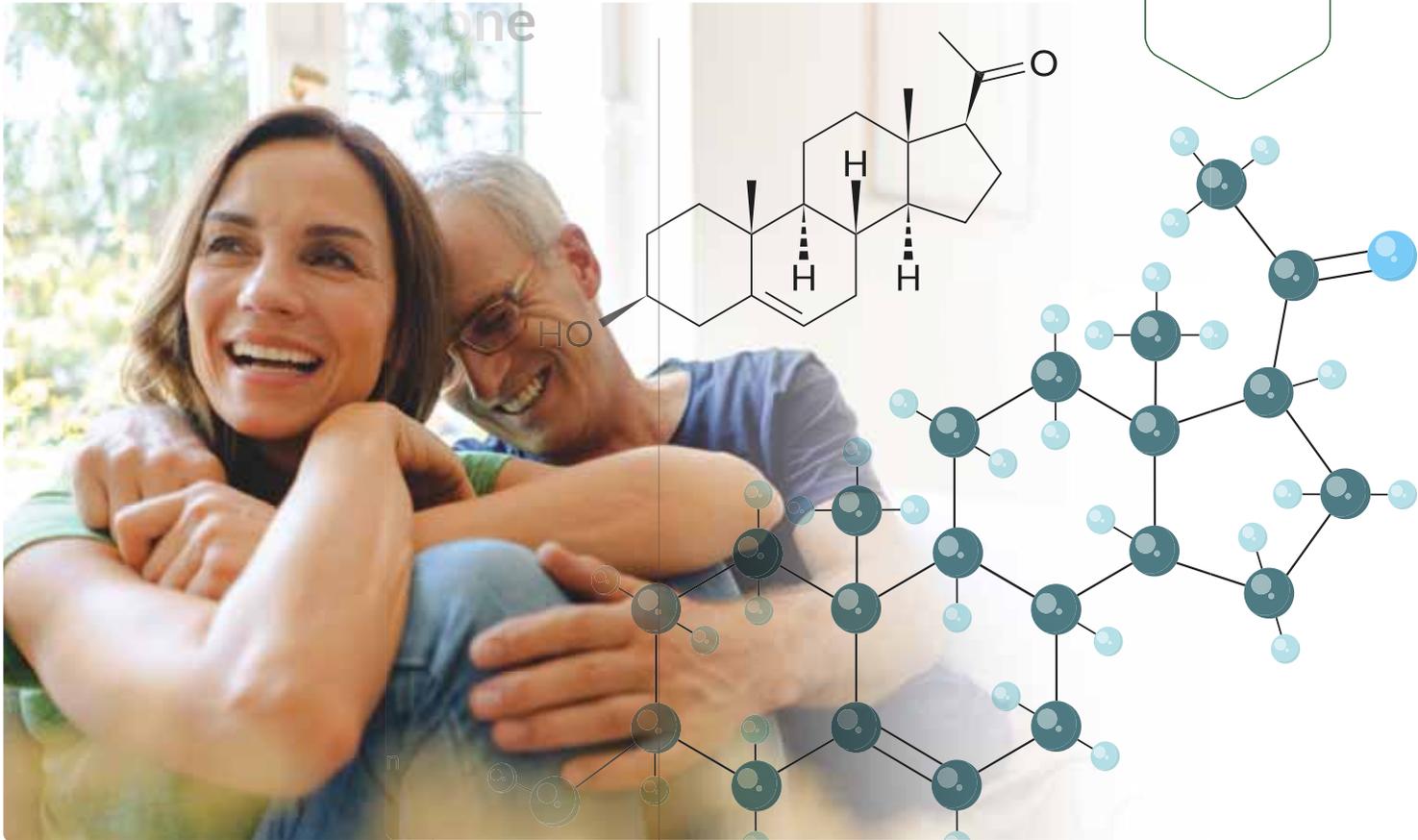
Sensori® is protected under US Patent No. 7,318,938 and is a registered trademark of Natreon, Inc.



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

What Is Pregnenolone?

BY LAURIE MATHENA



Pregnenolone is a hormone naturally produced in the body.

It has beneficial properties of its own and converts to other hormones such as **DHEA**, **progesterone**, **estrogen**, **testosterone**, and **cortisol**.

For this reason, it is sometimes called the mother of all hormones.

The body's production of pregnenolone declines with age as does that of DHEA, progesterone, estrogen, and testosterone.^{1,2}

Reduced Back Pain in Military Veterans

Previous studies have associated **pregnenolone** with improved memory, increased cognition, and elevated mood.³⁻⁵

A recent study highlighted another benefit: It significantly **reduced low-back pain** in Iraq- and Afghanistan-era U.S. military veterans.⁶

Compared to the **placebo** group, the **pregnenolone** group reported significant reductions in **low-back pain** at the end of the study.

They also reported **improvements** on scores for the degree to which their **pain** interfered with work and activity.

Based on the results of this study, the researchers suggest that **pregnenolone** could represent a novel, safe, and potentially effective treatment for **chronic low-back pain** in this population.

Improved Depression Symptoms

Low pregnenolone levels have been linked to **depression**.

In **clinically depressed** patients not receiving medication, researchers observed *lower* cerebrospinal pregnenolone levels, compared to healthy volunteers.⁷

In a clinical study, patients with **bipolar depression** were randomized to receive **pregnenolone** or a **placebo** as an add-on medication. After 12 weeks, researchers observed *higher* remission rates in the pregnenolone group than in the placebo group. The authors concluded that:

“The results suggest that pregnenolone may improve depressive symptoms in patients with bipolar disorder and can be safely administered.”⁸

Several **clinical trials** are now on the way.

At the **University of Texas Southwestern Medical Center** a clinical trial will evaluate the impact of **pregnenolone** on improvements in the severity of **depressive symptoms** in women.⁹

We look forward to reporting on human studies as their results are published.

Suggested Dosage

For those looking to support youthful hormone levels along with mental focus, memory, and more, optimal blood (serum) pregnenolone levels should be between **125-175 ng/dL**.

This can usually be achieved with daily pregnenolone doses ranging between **50 mg** and **100 mg**, preferably taken early in the day. •

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

References

- Hill M, Lukac D, Lapcik O, et al. Age relationships and sex differences in serum levels of pregnenolone and 17-hydroxy-pregnenolone in healthy subjects. *Clin Chem Lab Med*. 1999 Apr;37(4):439-47.
- Havlikova H, Hill M, Hampl R, et al. Sex- and age-related changes in epitestosterone in relation to pregnenolone sulfate and testosterone in normal subjects. *J Clin Endocrinol Metab*. 2002 May;87(5):2225-31.
- Charalampopoulos I, Remboutsika E, Margioris AN, et al. Neurosteroids as modulators of neurogenesis and neuronal survival. *Trends Endocrinol Metab*. 2008 Oct;19(8):300-7.
- Smith CC, Gibbs TT, Farb DH. Pregnenolone sulfate as a modulator of synaptic plasticity. *Psychopharmacology (Berl)*. 2014 Sep;231(17):3537-56.
- Vallee M. Neurosteroids and potential therapeutics: Focus on pregnenolone. *J Steroid Biochem Mol Biol*. 2016 Jun;160:78-87.
- Naylor JC, Kilts JD, Shampine LJ, et al. Effect of Pregnenolone vs Placebo on Self-reported Chronic Low Back Pain Among US Military Veterans: A Randomized Clinical Trial. *JAMA Netw Open*. 2020 Mar 2;3(3):e200287.
- George MS, Guidotti A, Rubinow D, et al. CSF neuroactive steroids in affective disorders: pregnenolone, progesterone, and DBI. *Biol Psychiatry*. 1994 May 15;35(10):775-80.
- Brown ES, Park J, Marx CE, et al. A randomized, double-blind, placebo-controlled trial of pregnenolone for bipolar depression. *Neuropsychopharmacology*. 2014 Nov;39(12):2867-73.
- Available at: <https://clinicaltrials.gov/ct2/show/NCT03645096>. Accessed April 1, 2022.



D EFEND YOUR HEALTH

"Keeps my body in tip-top condition!"

Pamela

VERIFIED CUSTOMER REVIEW

VITAMIN D3

Systemic support for immune function, bone health, and normal blood-sugar levels.

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.



Item #01713 • 5,000 IU • 60 softgels
1 bottle \$7.50 • 4 bottles \$6.50 each

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

THREE WAYS TO BUILD
STRONGER BONES

CUSTOMIZE YOUR **BONE-HEALTH** PROGRAM

Bone Restore helps maintain healthy bone density with three different forms of **calcium** plus vitamin D3 and magnesium, boron, zinc, manganese, and silicon.

Bone Restore with Vitamin K2, same formula as Bone Restore plus **200 mcg** of **vitamin K2**.

Bone Restore Elite, same formula as Bone Restore plus **45,000 mcg** of **vitamin K2**.



Bone Restore

Item #01726 • 120 capsules

1 bottle **\$16.50** • 4 bottles \$14.25 each



Bone Restore with Vitamin K2*

Item #01727 • 120 capsules

1 bottle **\$18** • 4 bottles \$16.50 each



Bone Restore Elite with Super Potent K2*

Item #02416 • 120 capsules

1 bottle **\$34.50** • 4 bottles \$31.50 each

For full product description and to order all **BONE RESTORE** products,
call **1-800-544-4440** or visit www.LifeExtension.com



* **CAUTION:** If you are taking a vitamin K antagonist (e.g. warfarin), consult your healthcare practitioner before taking this product.

Fruitex B® and OsteoBoron® are registered trademarks of VDF Futureceuticals, Inc. U.S. Patent No. 5,962,049.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

For Cognitive and Hormone Support

Pregnenolone provides systemic benefits, especially in the **brain**.

Beneficial mechanisms include modulating **brain plasticity** and promoting **neuronal health**.

Caution: Consult your healthcare provider before taking this product if you are at risk for or have been diagnosed with prostate or breast cancer. Do not take this product if you have a history of seizures.

1. *Trends Endocrinol Metab.* 2008 Oct;19(8):300-7.
2. *Psychopharmacology (Berl).* 2014 Sep;231(17):3537-56.
3. *J Steroid Biochem Mol Biol.* 2016 Jun;160:78-87.
4. *Steroids.* 2016;111:54-9.
5. *Psychiatry Res.* 2010;178(2):309-12.

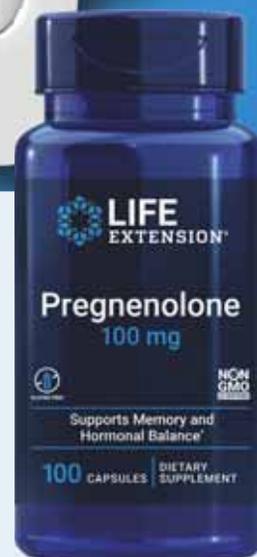
Studies show that pregnenolone helps maintain:¹⁻⁵

- Memory
- Cognitive function
- Positive mood
- Mental focus
- Youthful sex-hormone levels

One daily capsule contains **100 mg** of pregnenolone.

Item #00700 • 100 capsules

1 bottle **\$16.50** • 4 bottles \$15 each



"I feel like things are much clearer and memory seems to be better."

Sharon

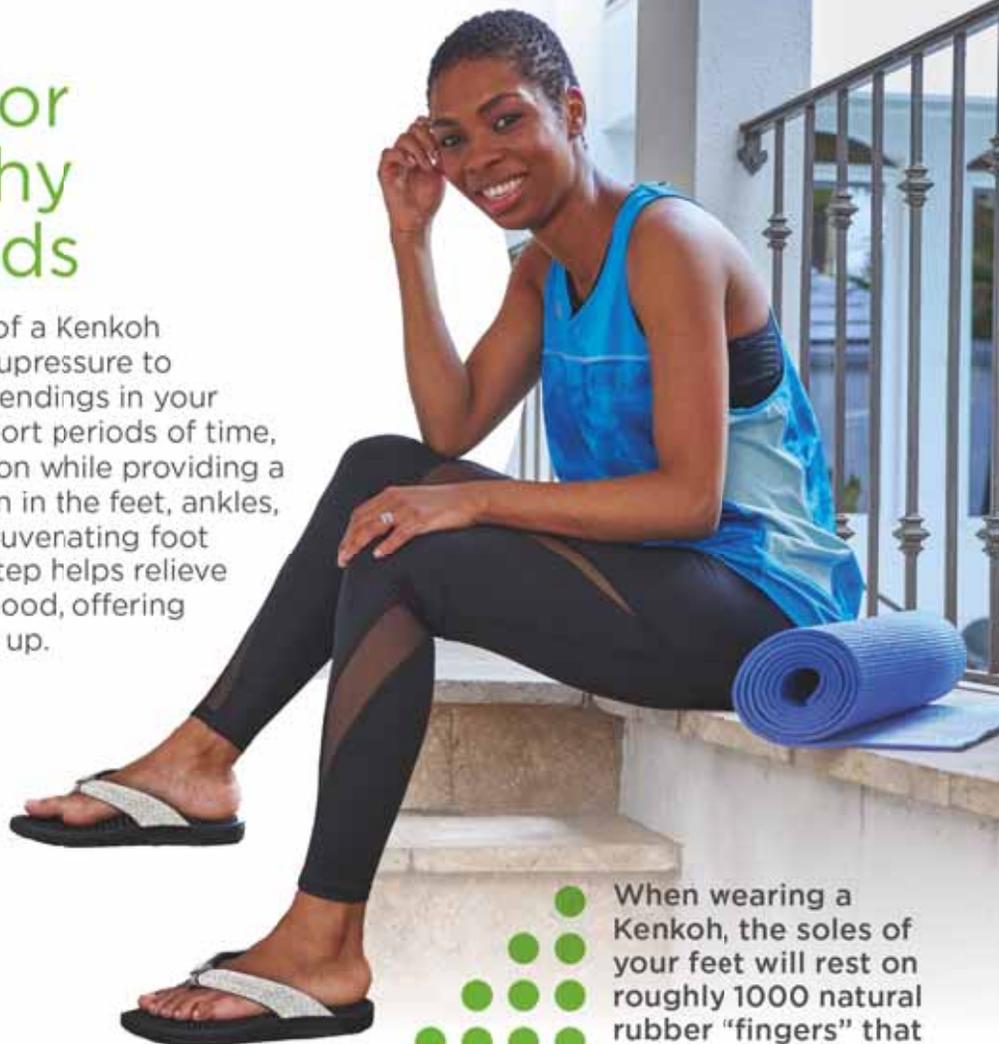
VERIFIED CUSTOMER REVIEW

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

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

Your source for *all* your healthy footwear needs

The precisely designed footbeds of a Kenkoh Massage Sandal work by using acupressure to revitalize and stimulate the nerve endings in your feet. When worn daily, even for short periods of time, Kenkoh helps to increase circulation while providing a non-intrusive way of reducing pain in the feet, ankles, knees, legs, hips and back. The rejuvenating foot massage you receive with every step helps relieve stress and enhance your overall mood, offering optimal wellness from the ground up.



When wearing a Kenkoh, the soles of your feet will rest on roughly 1000 natural rubber "fingers" that will massage and stimulate key reflex points. This targeted therapy, known as reflexology, has long been practiced in Eastern cultures as a way of reducing pain, stress and anxiety.



Spirit Black and White



Spirit Royal Blue



Spirit Brown



Serenity Black



Chai Champagne



Grace Pewter

Relieve pain & improve your health now!

Take the 14 day Kenkoh challenge

"Massage Improves Circulation..."
UNIVERSITY OF MIAMI SCHOOL OF MEDICINE

"Massage aids muscle recovery and speeds recovery times..."
McMASTER UNIVERSITY, ONTARIO

LEM.DiscoverKenkoh.com

1-866-442-1384

Kenkoh®

The Original Massage Sandal

“America’s Favorite Veterinarian”

Dr. Gary Richter Discusses Whole-Food Nutrition for Our Pets

GARY RICHTER, DVM



Eating a whole-food diet is critical for a human’s optimal health and longevity, but what you feed your **pets** is important for their health and well-being as well.

Dogs get cancer at approximately the same rate as humans. They also suffer from heart disease, arthritis, allergies, gastrointestinal problems, and many other health issues that are similar to those faced by humans.

Their diet could be the reason.

As veterinarian Gary Richter explains here, standard dry and canned foods are highly processed foods that produce inflammation and harmful advanced-glycation end products in pets the same way that processed food does in humans.

Pet owners who switch to more natural diets for their animals report that the pets experience benefits like more energy, a healthier hair coat, better digestion, and dramatic improvements in gastrointestinal issues and allergies.

In this eye-opening interview with *Life Extension*®, Dr. Richter explains why standard kibble and canned food are so harmful for your pet. He also details the best foods to feed your pets to support their overall health.

—LAURIE MATHENA

LE: We know that eating a healthy diet is critical for humans, but how critical is it for our pets to eat an optimal diet as well?

Dr. Richter: Readers of *Life Extension*® are no strangers to the concept of optimal nutrition being a cornerstone of good health and longevity.

Even to the uninitiated, it is common knowledge that fresh, whole foods are better for your health than highly processed foods.

Despite it being self-evident when it comes to our own health and longevity, it is likely many have not considered the concept of fresh, whole food for our pets.

Every animal on earth evolved eating a fresh, whole-food diet, and that is how all biological systems evolved to function optimally.

After all, there were no bags or cans of food millions of years ago when evolution was hard at work developing what has become today's animal kingdom.

All species function at their best when they consume the nutrients on which their bodies are designed to thrive.

While an optimal diet clearly varies from one species to the next (herbivores, carnivores, omnivores, etc.), the common through line is that fresh, whole foods are best for all animals.

LE: Does this mean that standard canned and dry kibble isn't good for our pets?

Dr. Richter: With the understanding that an optimal diet for any animal is going to be made from fresh, whole foods, let's consider most pet food today.

Walk into any large pet store and you are faced with shelves full of kibble and canned food.

The companies that make these foods would have you believe these are "optimal" nutrition for your dog or cat.

They put pictures of fresh food on the labels and aggressively advertise on TV, in print, and on the Internet to let you know the food in that bag or can will keep your pet healthy and happy for a lifetime.

On closer examination however, the veneers of these foods peel back surprisingly easily.

LE: How can you distinguish a beneficial product from a harmful one?

Dr. Richter: Start by reading the ingredient list. Many middle-to-lower tier foods use meat by-products and meat meal as protein sources.

While some ingredients that go into by-products or meal could be healthy for your pet, we have no way of knowing what is actually in there. Some of the possibilities include hooves, horn, beaks, feathers, and wool.

Similarly, many pet food companies use carbohydrates like grains, legumes, etc., as a cheaper source of calories than meat and as a filler and binder for dry foods.

Dogs, and especially cats, are not evolutionarily adapted to high-carbohydrate diets.

LE: Is this a problem with premium brands as well?

Dr. Richter: Even the "premium" brands of pet foods are highly problematic for dogs and cats.

Read the ingredients of top-tier dry and canned foods and you will find ingredients that look good. In fact, they *are* good ingredients—or at least they *were*.

When you open that bag or can of food for your pet, how much does what you see resemble the high-quality fresh ingredients you read listed on the label?

LE: How have such inferior products become the standard diet for our pets?

Dr. Richter: A good thing to remember is dry and canned pet food exists for only one reason—our convenience.

The ability to have food for our pets that requires no refrigeration and is shelf stable for years is undeniably attractive.

The trouble is, preventing fresh food from spoiling without refrigeration often requires things to be done to the food that aren't necessarily in the best interest of our pets.

The shelf stability we see in most processed pet foods is achieved through the use of very high heat and pressure during processing. This kills pathogens that could lead to spoilage but creates a host of concerns that could prove harmful to our pets.

LE: Why is something like high heat problematic?

Dr. Richter: High heat and pressure frequently lead to loss of vital nutrients.

Anyone who has experienced overcooked meat or vegetables will instantly understand what this does to food.

You don't need to be a clinical nutritionist to recognize that overcooked food is not as nutritious as fresh or lightly cooked food.

As problematic as what is *missing* from highly processed pet foods is what is *created* during the high-heat and high-pressure cooking process.

Advanced glycation end products (AGEs) and Maillard reaction products (MRPs) are both produced as a result of proteins and carbohydrates being exposed to heat and pressure.

These chemical compounds are well known to promote inflammation and have been linked to cancer.

AGEs and MRPs are one of the main reasons why it is so important for people to eat fresh whole foods. It is also why fried foods and charred meats are frowned upon by nutritionists and longevity experts.

These foods cause inflammation in our bodies, and inflammation is the root cause of many chronic diseases experienced by humans and animals alike.

Perhaps one of the most disturbing aspects of processed pet foods is the amount of these toxins our pets are consuming.

When researchers evaluated the presence of MRPs in dogs and cats that consumed kibble or canned diets, it was found that dogs and cats consume 122 and 38 times more MRPs per day, respectively, than the average adult human!

LE: Are there any guidelines or regulations for what can and cannot be included in commercial pet food?

Dr. Richter: While there are nutrition standards set forth by the American Association of Feed Control Officials (AAFCO), these are minimum standards that ensure animals will not suffer from illness due to nutrient deficiencies.

These standards are largely concerned with macronutrients like protein and fat, and vitamins like vitamin A, B, C, D, etc.

There is no accounting for where the nutrients come from, as well as many micronutrients.

AAFCO standards provide an excellent minimum standard for pet food, but there is a lot of daylight between “minimum” and “optimal” nutrition.

If you want your car to function perfectly, you need to put in the type of gas and oil with which it was designed to function optimally.

The same is true for any biological specimen. It can function with minimum standards, but if you want it to work as well as it can for as long as it can, we need to do much better.

LE: If kibble and canned diets for our pets are so problematic, are there alternatives?

Dr. Richter: Fortunately, yes. And they don't all require you to home cook food for your dog or cat.

There are many fresh, whole-food diets for dogs and cats available in pet stores and on the Internet.

They come in several formats, including fresh-frozen cooked, fresh-frozen raw, freeze-dried raw, and dehydrated foods.

LE: What does an ideal diet look like for our pets?

Dr. Richter: In a perfect world our pets would all be eating either raw or lightly cooked diets. These diets are about as close to our pet's evolutionary diet as we can get.

These diets come in a variety of proteins and can be either purchased or made at home.

Clearly, buying food that merely needs to be thawed and fed is more convenient, but it also is more costly.

Making fresh food at home is an excellent, and more cost-effective option for people who don't mind spending a little time in the kitchen.

The goal with making food at home is to make as much food as you have space for in the freezer. Some people with multiple pets or large dogs purchase a chest freezer for the garage and store the pre-portioned food in there and thaw it as necessary.

The one critical thing to remember when making pet food at home is you must use a recipe balanced by a nutritionist. You cannot create a balanced diet by putting meat and vegetables in a bowl.

Books are available with balanced recipes and nutritionists are also available for consultations.

LE: You mentioned freeze-dried foods. Are these a good option for someone who doesn't want to make homemade food?

Dr. Richter: Freeze-dried and dehydrated foods are an excellent option for many pet owners.

Freeze-drying is a process by which moisture is removed from cold, fresh food under a vacuum, while dehydrating uses heat to remove the moisture.

Either way, the result is food that is shelf stable, weighs very little, and is much better for pets than more highly processed foods.

The amount of processing with freeze-drying and dehydrating does not lead to the degree of nutrient loss or the creation of AGEs and MREs we see in kibble and canned diets.

Feeding these foods is about as easy as it gets. Just add water.

LE: What about cost?

Dr. Richter: Freeze-dried and dehydrated foods are often a little less costly than frozen foods, and they have the added benefit of being shelf stable.

This is a great option for people lacking extra freezer space.

It's also great if you tend to travel with your pet. You won't need to worry about traveling with frozen food if you are using a freeze-dried or dehydrated option.

LE: What are the benefits of feeding our pets this type of food?

Dr. Richter: In my experience as a veterinarian, most people who convert their pet to a fresh, whole-food diet report having an overall healthier pet, with more energy, a healthier haircoat, and better digestion.

I have seen countless pets with chronic gastrointestinal issues and allergies dramatically improve on nothing more than converting to a fresh, whole-food diet.

LE: How difficult is it to switch your pet to a whole-food diet?

Dr. Richter: Switching to a fresh diet is easy.

The goal is to make a gradual transition. This allows your pet's digestive tract to make the adjustment from processed foods to fresh foods.

In addition, for picky eaters (I'm looking at you, cat owners), a very slow transition is often the key to getting pets to accept a new food.

Begin by adding a very small amount of new food to their old food. Each day, add a little more new food and take away a little more old food.

Depending on whether your pet has a sensitive GI tract or if it's a picky eater, take anywhere from one to three weeks in the transition.

There is no hurry. Take longer if you need to.

LE: Once you find a food that works for your pet, should you stick with that one food exclusively?

Dr. Richter: When it comes to fresh-food diets, there is no absolute right or wrong, although there are some good guidelines to follow.

Variety is a good thing to provide a spectrum of nutrients and to prevent dietary sensitivities caused by prolonged exposure to one protein over a very long period of time.

Some pets can easily switch from one protein to another with no problem, while others are a little more sensitive.

For our pet friends with sensitive tummies, consider a gradual transition to a new protein every three to four months.

Feeding more than one format of food is fine, as long as your pet does OK with it.

In other words, if you want to feed some fresh and some freeze-dried, that is fine. Some people do this so

their pet is accustomed to freeze-dried for when they go out of town with it.

Additionally, if it is financially challenging to feed your pet exclusively a fresh, whole-food diet, feed them as much as you can, and for the rest use high-quality canned food or kibble.

Just as with us humans, eating some fresh food and some processed food is better than eating exclusively processed foods.

LE: What about table scraps? Should you feed your pet food from your plate?

Dr. Richter: That depends on what you are eating.

Pets don't do well with spicy or highly seasoned foods so those should be avoided. Also, avoid foods high in fat as they can cause GI upset, and never give them foods containing onions, grapes, raisins, or macadamia nuts, as these can be toxic.

With that said, if you want to put a little something from your plate in your dog or cat's bowl, go ahead—sharing is caring.

Just make sure it's only a little because we want them to be mostly eating a fully balanced, fresh whole-food diet to meet all their nutritional needs.

LE: How difficult is it for a pet owner to make the switch?

Dr. Richter: Feeding your pet a fresh, whole-food diet is easier than it has ever been.

Whether you choose fresh frozen, homemade, freeze-dried, or dehydrated foods, you are taking the single biggest step anyone can take to ensure a long and healthy life for an animal.

The greatest thing about pet nutrition is that we are completely in control of what they eat.

It is much easier to feed a pet an optimal fresh, whole-food diet than it is for us humans. Their willpower doesn't come into play.

It's no secret how critical optimal nutrition is for human health and longevity. It is all the same for our pets. •

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

Dr. Gary Richter specializes in holistic veterinary care. From 2002-2021, he was the owner and medical director of Montclair Veterinary Hospital in Oakland, California. He launched Holistic Veterinary Care in 2009, also in Oakland.

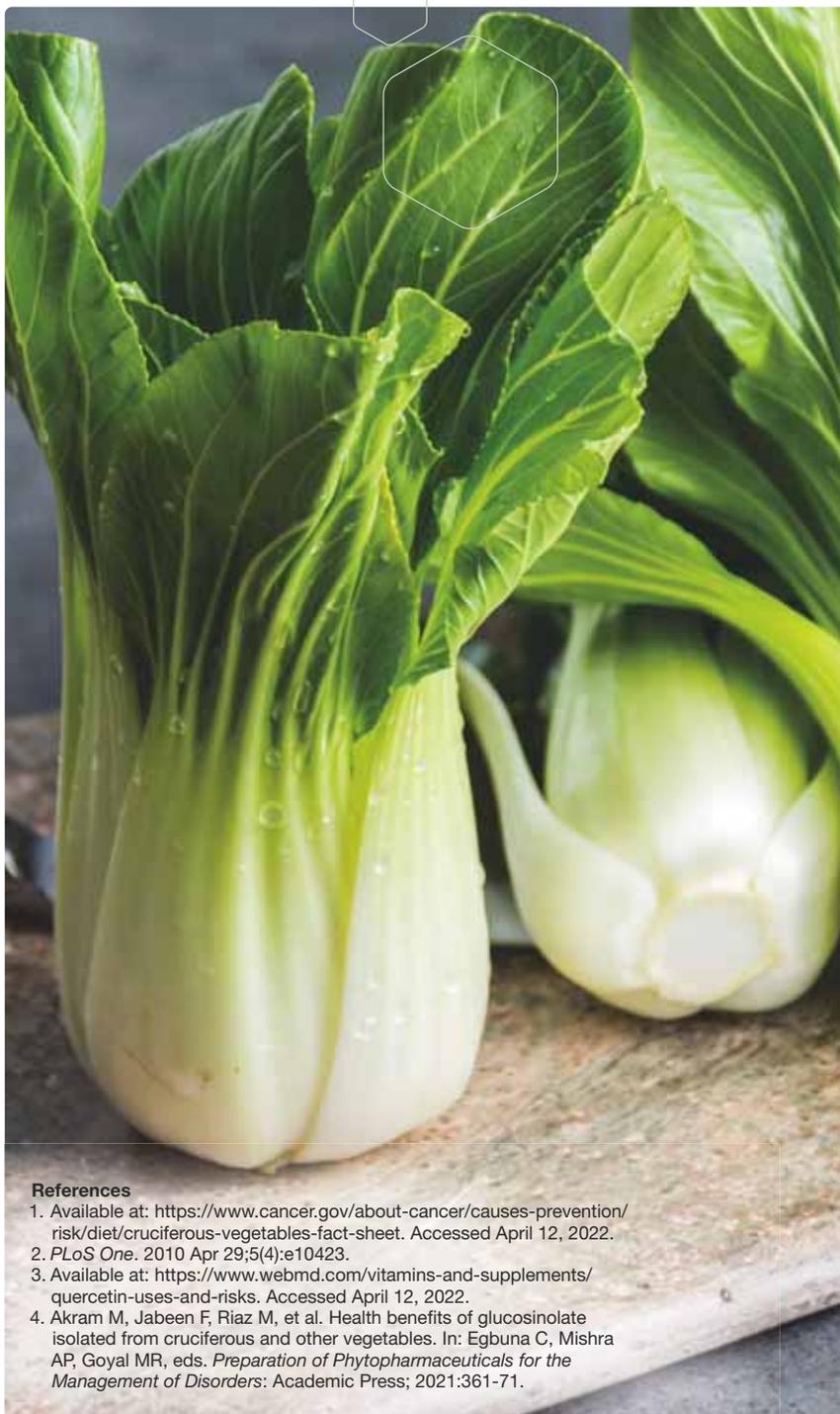
His animal hospitals have received more than 30 local and national awards, including Best Veterinary Hospital, Best Veterinarian, and Best Alternative Medicine Provider. He was named one of the top 10 veterinarians in the US in 2012, America's Favorite Veterinarian in 2015, and he received the Holistic Practitioner of the Year Award in 2019.

Dr. Richter also wrote an Amazon Best-Selling book, *The Ultimate Pet Health Guide*. For more information, visit www.mypetthrives.com.



Bok Choy

BY LAURIE MATHENA



References

1. Available at: <https://www.cancer.gov/about-cancer/causes-prevention/risk/diet/cruciferous-vegetables-fact-sheet>. Accessed April 12, 2022.
2. *PLoS One*. 2010 Apr 29;5(4):e10423.
3. Available at: <https://www.webmd.com/vitamins-and-supplements/quercerin-uses-and-risks>. Accessed April 12, 2022.
4. Akram M, Jabeen F, Riaz M, et al. Health benefits of glucosinolate isolated from cruciferous and other vegetables. In: Egbuna C, Mishra AP, Goyal MR, eds. *Preparation of Phytopharmaceuticals for the Management of Disorders*: Academic Press; 2021:361-71.

Chinese cabbage—more commonly known as bok choy—is a cruciferous vegetable that’s been eaten in China for more than 1,500 years.

It continues to be a common ingredient in many Asian soups and stir-fries, but it deserves a spot at the table here in the US as well.

Bok choy has been ranked the **sixth** most nutrient-dense food (based on the Aggregate Nutrient Density Index).

Like other cruciferous vegetables, bok choy comes loaded with nutrients that can help reduce cancer risk, fight inflammation, reduce heart disease risk, and more.

People who eat more cruciferous vegetables like bok choy have a lower risk of numerous types of cancer, including lung, prostate, and colon cancer.¹

Bok choy contains selenium, an important mineral that helps detoxify cancer-causing compounds from the body. It’s also been shown to decrease the growth rate of tumors in rats.²

Bok choy’s “superfood status” comes from the variety of disease-fighting nutrients packed into its green leaves and crunchy white stalk.

For example, it contains the flavonoid quercetin, which helps reduce inflammation in the body.³

Like all other cruciferous vegetables, bok choy is rich in compounds called glucosinolates, which provide protection from serious diseases like cancer and myocardial infarction.⁴

Bok choy can be prepared in a variety of ways. Enjoy it shredded and tossed in a salad, chopped and added to soups, or sauteed with other vegetables. •

ACTIVE LIFESTYLE & FITNESS

- 01529 Creatine Capsules
- 02020 Super Carnosine
- 02023 Tart Cherry with CherryPURE®
- 02146 Wellness Bar—Chocolate Brownie
- 02147 Wellness Bar—Cookie Dough
- 02246 Wellness Code® Advanced Whey Protein Isolate Vanilla
- 02221 Wellness Code® Muscle Strength & Restore Formula
- 02127 Wellness Code® Plant Protein Complete & Amino Acid Complex
- 02261 Wellness Code® Whey Protein Concentrate Chocolate
- 02260 Wellness Code® Whey Protein Concentrate Vanilla
- 02243 Wellness Code® Whey Protein Isolate Chocolate
- 02242 Wellness Code® Whey Protein Isolate Vanilla

AMINO ACIDS

- 00038 Arginine Ornithine Powder
- 01253 Branched Chain Amino Acids
- 01829 Carnosine
- 01671 D,L-Phenylalanine Capsules
- 01624 L-Arginine Caps
- 01532 L-Carnitine
- 00345 L-Glutamine
- 00141 L-Glutamine Powder
- 01678 L-Lysine
- 01827 Taurine
- 00133 Taurine Powder
- 00326 Tyrosine Tablets

BLOOD PRESSURE & VASCULAR SUPPORT

- 01824 Advanced Olive Leaf Vascular Support
- 02004 Arterial Protect
- 02497 Endothelial Defense™ Pomegranate Plus
- 02320 NitroVasc™ Boost
- 00984 Optimal BP Management
- 01953 Pomegranate Complete
- 00956 Pomegranate Fruit Extract
- 02024 Triple Action Blood Pressure AM/PM
- 02102 Venoflow™

BONE HEALTH

- 01726 Bone Restore
- 02123 Bone Restore Chewable Tablet
- 02416 Bone Restore Elite with Super Potent K2
- 01727 Bone Restore with Vitamin K2
- 01725 Bone Strength Collagen Formula
- 00313 Bone-Up™
- 01963 Calcium Citrate with Vitamin D
- 01506 Dr. Strum's Intensive Bone Formula
- 02417 Mega Vitamin K2
- 01476 Strontium Caps

BRAIN HEALTH

- 01524 Acetyl-L-Carnitine
- 01974 Acetyl-L-Carnitine Arginate
- 02419 B12 Elite
- 02510 Brain Fog Relief
- 01659 CDP Choline
- 02321 Cognitex® Basics
- 02396 Cognitex® Elite
- 02397 Cognitex® Elite Pregnenolone
- 01540 DMAE Bitartrate
- 02006 Dopa-Mind™
- 02413 Dopamine Advantage
- 02212 Focus Tea™
- 01658 Ginkgo Biloba Certified Extract™
- 01527 Huperzine A
- 00020 Lecithin
- 02101 Memory Protect

- 00709 Migra-Eeze™
- 01603 Neuro-Mag® Magnesium L-Threonate Caps
- 02032 Neuro-Mag® Magnesium L-Threonate Powder
- 00888 Optimized Ashwagandha
- 01676 PS (Phosphatidylserine) Caps
- 02406 Quick Brain Nootropic
- 01327 Vinpocetine

CHOLESTEROL MANAGEMENT

- 01828 Advanced Lipid Control
- 01359 Cho-Less™
- 01910 CHOL-Support™
- 01030 Red Yeast Rice
- 01304 Theaflavins Standardized Extract
- 00372 Vitamin B3 Niacin Capsules

DIGESTION SUPPORT

- 53348 Betaine HCl
- 02412 Bloat Relief
- 30747 Digest RC®
- 07136 Effervescent Vitamin C - Magnesium Crystals
- 02021 Enhanced Super Digestive Enzymes
- 02022 Enhanced Super Digestive Enzymes and Probiotics
- 02033 EsophaCool™
- 01737 Esophageal Guardian
- 01706 Extraordinary Enzymes
- 02100 Gastro-Ease™
- 01122 Ginger Force™
- 00605 Regimint
- 01386 TruFiber®

ENERGY MANAGEMENT

- 01628 Adrenal Energy Formula • 60 veg capsules
- 01630 Adrenal Energy Formula • 120 veg capsules
- 00972 D-Ribose Powder
- 01473 D-Ribose Tablets
- 01900 Energy Renew
- 01544 Forskolin
- 01805 Ginseng Energy Boost
- 00668 Metabolic Advantage Thyroid Formula™
- 01869 Mitochondrial Basics with PQQ
- 01868 Mitochondrial Energy Optimizer with PQQ
- 01904 NAD+ Cell Regenerator™ • 100 mg, 30 veg capsules
- 02344 NAD+ Cell Regenerator™ 300 mg, 30 veg capsules
- 02348 NAD+ Cell Regenerator™ and Resveratrol
- 01500 PQQ Caps • 10 mg, 30 vegetarian capsules
- 01647 PQQ Caps • 20 mg, 30 vegetarian capsules
- 00889 Rhodiola Extract
- 02003 Triple Action Thyroid

EYE HEALTH

- 01923 Astaxanthin with Phospholipids
- 00893 Brite Eyes III
- 02323 Digital Eye Support
- 01514 Eye Pressure Support with Mirtogenol®
- 01992 MacuGuard® Ocular Support with Saffron
- 01993 MacuGuard® Ocular Support with Saffron & Astaxanthin
- 01873 Standardized European Bilberry Extract
- 01918 Tear Support with MaquiBright®

FISH OIL & OMEGAS

- 01937 Mega EPA/DHA
- 02218 Mega GLA Sesame Lignans
- 01983 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 softgels
- 01988 Super Omega-3 Plus EPA/DHA Fish Oil, Sesame Lignans, Olive Extract, Krill & Astaxanthin
- 01982 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 softgels

- 01985 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 enteric coated softgels
- 01984 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 enteric coated softgels
- 01986 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 240 softgels
- 01812 Provinal® Purified Omega-7
- 01640 Vegetarian DHA

FOOD

- 02008 California Estate Extra Virgin Olive Oil
- 02170 Rainforest Blend Decaf Ground Coffee
- 02169 Rainforest Blend Ground Coffee
- 02171 Rainforest Blend Whole Bean Coffee
- 00438 Stevia™ Organic Liquid Sweetener
- 00432 Stevia™ Sweetener

GLUCOSE MANAGEMENT

- 01503 CinSulin® with InSea²® and Crominex® 3+
- 01620 CoffeeGenic® Green Coffee Extract
- 02122 Glycemic Guard™
- 00925 Mega Benfotiamine
- 01803 Tri Sugar Shield®

HEART HEALTH

- 01066 Aspirin (Enteric Coated)
- 01842 BioActive Folate & Vitamin B12 Caps
- 01700 Cardio Peak™
- 02121 Homocysteine Resist
- 02018 Optimized Carnitine
- 01949 Super-Absorbable CoQ10 Ubiquinone with *d*-Limonene • 50 mg, 60 softgels
- 01951 Super-Absorbable CoQ10 Ubiquinone with *d*-Limonene • 100 mg, 60 softgels
- 01929 Super Ubiquinol CoQ10
- 01427 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 30 softgels
- 01425 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 100 softgels
- 01437 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 30 softgels
- 01426 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 60 softgels
- 01431 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 200 mg, 30 softgels
- 01733 Super Ubiquinol CoQ10 with PQQ
- 01859 TMG Liquid Capsules
- 00349 TMG Powder

HORMONE BALANCE

- 00454 DHEA • 15 mg, 100 capsules
- 00335 DHEA • 25 mg, 100 capsules
- 00882 DHEA • 50 mg, 60 capsules
- 00607 DHEA • 25 mg, 100 vegetarian dissolve in mouth tablets
- 01689 DHEA • 100 mg, 60 veg capsules
- 02368 Optimized Broccoli and Cruciferous Blend
- 00302 Pregnenolone • 50 mg, 100 capsules
- 00700 Pregnenolone • 100 mg, 100 capsules
- 01468 Triple Action Cruciferous Vegetable Extract
- 01469 Triple Action Cruciferous Vegetable Extract and Resveratrol

IMMUNE SUPPORT

- 02411 5 Day Elderberry Immune
- 00681 AHCC®
- 02302 Bio-Quercetin®
- 02410 Black Elderberry + Vitamin C
- 01961 Enhanced Zinc Lozenges
- 01704 Immune Modulator with Tinofend®
- 02425 Immune Packs with Vitamin C & D, Zinc and Probiotic

- 02005 Immune Senescence Protection Formula™
- 00316 Kyolic® Garlic Formula 102
- 00789 Kyolic® Reserve
- 01681 Lactoferrin (Apolactoferrin) Caps
- 02426 Mushroom Immune with Beta Glucans
- 01903 NK Cell Activator™
- 01394 Optimized Garlic
- 01309 Optimized Quercetin
- 01811 Peony Immune
- 00525 ProBoost Thymic Protein A
- 01708 Reishi Extract Mushroom Complex
- 01906 Standardized Cistanche
- 13685 Ten Mushroom Formula®
- 01097 Ultra Soy Extract
- 01561 Zinc Lozenges

INFLAMMATION MANAGEMENT

- 01639 5-LOX Inhibitor with AprèsFlex®
- 02324 Advanced Curcumin Elite™
Turmeric Extract, Ginger & Turmerones
- 01709 Black Cumin Seed Oil
- 02310 Black Cumin Seed Oil and Curcumin Elite™
- 00202 Boswellia
- 02467 Curcumin Elite™ Turmeric Extract • 30 veg capsules
- 02407 Curcumin Elite™ Turmeric Extract • 60 veg capsules
- 01804 Cytokine Suppress® with EGCG
- 02223 Pro-Resolving Mediators
- 00318 Serrafazyme
- 01203 Specially-Coated Bromelain
- 00407 Super Bio-Curcumin® Turmeric Extract
- 01254 Zyflamend™ Whole Body

JOINT SUPPORT

- 02404 Arthro-Immune Joint Support
- 02238 ArthroMax® Advanced NT2 Collagen™ & AprèsFlex®
- 01617 ArthroMax® with Theaflavins & AprèsFlex®
- 02138 ArthroMax® Elite
- 00965 Fast-Acting Joint Formula
- 02430 Fast Acting Relief
- 00522 Glucosamine/Chondroitin Capsules
- 02420 Glucosamine Sulfate
- 02424 Joint Mobility
- 01600 Krill Healthy Joint Formula
- 01050 Krill Oil
- 00451 MSM (Methylsulfonylmethane)
- 02231 NT2 Collagen™

KIDNEY & BLADDER SUPPORT

- 00862 Cran-Max® Cranberry Whole Fruit Concentrate
- 01424 Optimized Cran-Max® with Ellirose™
- 01921 Uric Acid Control
- 01209 Water-Soluble Pumpkin Seed Extract

LIVER HEALTH & DETOXIFICATION

- 01922 Advanced Milk Thistle • 60 softgels
- 01925 Advanced Milk Thistle • 120 softgels
- 02240 Anti-Alcohol Complex
- 01651 Calcium D-Glucarate
- 01571 Chlorophyllin
- 01522 Milk Thistle • 60 veg capsules
- 02402 FLORASSIST® Liver Restore™
- 01541 Glutathione, Cysteine & C
- 01393 HepatoPro
- 01608 Liver Efficiency Formula
- 01534 N-Acetyl-L-Cysteine
- 00342 PectaSol-C® Modified Citrus Pectin Powder
- 01080 PectaSol-C® Modified Citrus Pectin Capsules
- 01884 Silymarin
- 02361 SOD Booster

LONGEVITY & WELLNESS

- 00457 Alpha-Lipoic Acid
- 01625 AppleWise
- 02414 Bio-Fisetin
- 01214 Blueberry Extract
- 01438 Blueberry Extract and Pomegranate
- 02270 DNA Protection Formula
- 02431 Essential Youth - L-Ergothioneine
- 02119 GEROPROTECT® Ageless Cell™
- 02415 GEROPROTECT® Autophagy Renew
- 02133 GEROPROTECT® Longevity A.I.™
- 02401 GEROPROTECT® Stem Cell
- 02211 Grapeseed Extract
- 00954 Mega Green Tea Extract (decaffeinated)
- 00953 Mega Green Tea Extract (lightly caffeinated)
- 01513 Optimized Fucoidan with Maritech® 926
- 02230 Optimized Resveratrol
- 01637 Pycnogenol® French Maritime Pine Bark Extract
- 02210 Resveratrol
- 00070 RNA (Ribonucleic Acid)
- 02301 Senolytic Activator®
- 01208 Super R-Lipoic Acid
- 01919 X-R Shield

MEN'S HEALTH

- 02209 Male Vascular Sexual Support
- 00455 Mega Lycopene Extract
- 02306 Men's Bladder Control
- 01789 PalmettoGuard® Saw Palmetto and Beta-Sitosterol
- 01790 PalmettoGuard® Saw Palmetto/Nettle Root Formula and Beta-Sitosterol
- 01837 Pomi-T®
- 01373 Prelox® Enhanced Sex for Men
- 01940 Super MiraForte with Standardized Lignans
- 02500 Testosterone Elite
- 01909 Triple Strength ProstaPollen™
- 02029 Ultra Prostate Formula

MINERALS

- 01661 Boron
- 02107 Extend-Release Magnesium
- 01677 Iron Protein Plus
- 02403 Lithium
- 01459 Magnesium Caps
- 01682 Magnesium (Citrate)
- 01328 Only Trace Minerals
- 01504 Optimized Chromium with Crominex® 3+
- 02309 Potassium with Extend-Release Magnesium
- 01740 Sea-Iodine™
- 01879 Se-Methyl L-Selenocysteine
- 01778 Super Selenium Complex
- 00213 Vanadyl Sulfate
- 01813 Zinc Caps

MISCELLANEOUS

- 00577 Potassium Iodide
- 00657 Solarshield® Sunglasses

MOOD & STRESS MANAGEMENT

- 02312 Cortisol-Stress Balance
- 00987 Enhanced Stress Relief
- 01074 5 HTP
- 01683 L-Theanine
- 02175 SAmE (S-Adenosyl-Methionine)
200 mg, 30 enteric coated vegetarian tablets
- 02176 SAmE (S-Adenosyl-Methionine)
400 mg, 30 enteric coated vegetarian tablets
- 02174 SAmE (S-Adenosyl-Methionine)
400 mg, 60 enteric coated vegetarian tablets
- 02429 Theanine XR™ Stress Relief

MULTIVITAMINS

- 02199 Children's Formula Life Extension Mix™
- 02354 Life Extension Mix™ Capsules
- 02364 Life Extension Mix™ Capsules without Copper
- 02356 Life Extension Mix™ Powder
- 02355 Life Extension Mix™ Tablets
- 02357 Life Extension Mix™ Tablets with Extra Niacin
- 02365 Life Extension Mix™ Tablets without Copper
- 02292 Once-Daily Health Booster • 30 softgels
- 02291 Once-Daily Health Booster • 60 softgels
- 02313 One-Per-Day Tablets
- 02428 Plant-Based Multivitamin
- 02317 Two-Per-Day Capsules • 60 capsules
- 02314 Two-Per-Day Capsules • 120 capsules
- 02316 Two-Per-Day Tablets • 60 tablets
- 02315 Two-Per-Day Tablets • 120 tablets

NERVE & COMFORT SUPPORT

- 02202 ComfortMAX™
- 02303 Discomfort Relief

PERSONAL CARE

- 01006 Biosil™ • 5 mg, 30 veg capsules
- 01007 Biosil™ • 1 fl oz
- 00321 Dr. Proctor's Advanced Hair Formula
- 00320 Dr. Proctor's Shampoo
- 02322 Hair, Skin & Nails Collagen Plus Formula
- 01278 Life Extension Toothpaste
- 00408 Venotone
- 00409 Xyliwhite Mouthwash
- 02304 Youthful Collagen
- 02252 Youthful Legs

PET CARE

- 01932 Cat Mix
- 01931 Dog Mix

PROBIOTICS

- 01622 Bifido GI Balance
- 01825 FLORASSIST® Balance
- 02421 FLORASSIST® Daily Bowel Regularity
- 02125 FLORASSIST® GI with Phage Technology
- 01821 FLORASSIST® Heart Health
- 02250 FLORASSIST® Mood Improve
- 02208 FLORASSIST® Immune & Nasal Defense
- 02120 FLORASSIST® Oral Hygiene
- 02203 FLORASSIST® Prebiotic
- 01920 FLORASSIST® Throat Health
- 02400 FLORASSIST® Winter Immune Support
- 52142 Jarro-Dophilus® for Women
- 00056 Jarro-Dophilus EPS® • 60 veg capsules
- 21201 Jarro-Dophilus EPS® • 120 veg capsules
- 01038 Theralac® Probiotics
- 01389 TruFlora® Probiotics

SKIN CARE

- 80157 Advanced Anti-Glycation Peptide Serum
- 80165 Advanced Growth Factor Serum
- 80170 Advanced Hyaluronic Acid Serum
- 80154 Advanced Lightening Cream
- 80155 Advanced Peptide Hand Therapy
- 80175 Advanced Probiotic-Fermented Eye Serum
- 80177 Advanced Retinol Serum
- 80152 Advanced Triple Peptide Serum
- 80140 Advanced Under Eye Serum with Stem Cells
- 80137 All-Purpose Soothing Relief Cream
- 80139 Amber Self MicroDermAbrasion
- 80118 Anti-Aging Mask
- 80151 Anti-Aging Rejuvenating Face Cream
- 80153 Anti-Aging Rejuvenating Scalp Serum
- 80179 Brightening Peptide Serum

- 80176 Collagen Boosting Peptide Cream
- 80156 Collagen Boosting Peptide Serum
- 02408 Collagen Peptides for Skin & Joints
- 80180 CoQ10 and Stem Cell Rejuvenation Cream
- 80169 Cucumber Hydra Peptide Eye Cream
- 02423 Daily Skin Defense
- 80141 DNA Support Cream
- 80163 Eye Lift Cream
- 80123 Face Rejuvenating Anti-Oxidant Cream
- 80109 Hyaluronic Facial Moisturizer
- 80110 Hyaluronic Oil-Free Facial Moisturizer
- 80138 Hydrating Anti-Oxidant Facial Mist
- 00661 Hydroderm
- 55495 Intensive Moisturizing Cream
- 80103 Lifting & Tightening Complex
- 80168 Melatonin Advanced Peptide Cream
- 80114 Mild Facial Cleanser
- 80172 Multi Stem Cell Hydration Cream
- 80159 Multi Stem Cell Skin Tightening Complex
- 80122 Neck Rejuvenating Anti-Oxidant Cream
- 80174 Purifying Facial Mask
- 80150 Renewing Eye Cream
- 80142 Resveratrol Anti-Oxidant Serum
- 01938 Shade Factor™
- 02129 Skin Care Collection Anti-Aging Serum
- 02130 Skin Care Collection Day Cream
- 02131 Skin Care Collection Night Cream
- 80166 Skin Firming Complex
- 02096 Skin Restoring Ceramides
- 80130 Skin Stem Cell Serum
- 80164 Skin Tone Equalizer
- 80143 Stem Cell Cream with Alpine Rose
- 80148 Tightening & Firming Neck Cream
- 80161 Triple-Action Vitamin C Cream
- 80162 Ultimate MicroDermabrasion
- 80173 Ultimate Peptide Serum
- 80178 Ultimate Telomere Cream
- 80160 Ultra Eyelash Booster
- 80101 Ultra Wrinkle Relaxer
- 80113 Under Eye Refining Serum
- 80104 Under Eye Rescue Cream
- 80171 Vitamin C Lip Rejuvenator
- 80129 Vitamin C Serum
- 80136 Vitamin D Lotion
- 80102 Vitamin K Cream

SLEEP

- 01512 Bioactive Milk Peptides
- 02300 Circadian Sleep
- 01551 Enhanced Sleep with Melatonin
- 01511 Enhanced Sleep without Melatonin
- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 02308 Herbal Sleep PM
- 01722 L-Tryptophan
- 01668 Melatonin • 300 mcg, 100 veg capsules
- 01083 Melatonin • 500 mcg, 200 veg capsules
- 00329 Melatonin • 1 mg, 60 capsules
- 02503 Melatonin • 3 mg, 60 gummies
- 00330 Melatonin • 3 mg, 60 veg capsules
- 00331 Melatonin • 10 mg, 60 veg capsules
- 00332 Melatonin • 3 mg, 60 veg lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release
300 mcg, 100 veg tablets
- 01788 Melatonin 6 Hour Timed Release
750 mcg, 60 veg tablets
- 01786 Melatonin 6 Hour Timed Release 3 mg, 60 veg tablets

- 01721 Optimized Tryptophan Plus
- 01444 Quiet Sleep
- 01445 Quiet Sleep Melatonin
- 02502 Rest & Renew

VITAMINS

- 01533 Ascorbyl Palmitate
- 00920 Benfotiamine with Thiamine
- 00664 Beta-Carotene
- 01945 BioActive Complete B-Complex
- 00102 Biotin
- 00084 Buffered Vitamin C Powder
- 02229 Fast-C® and Bio-Quercetin Phytosome
- 02075 Gamma E Mixed Tocopherol Enhanced with
Sesame Lignans
- 02070 Gamma E Mixed Tocopherol & Tocotrienols
- 01913 High Potency Optimized Folate
- 01674 Inositol Caps
- 02244 Liquid Vitamin D3 • 50 mcg (2000 IU)
- 02232 Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)
- 01936 Low-Dose Vitamin K2
- 00065 MK-7
- 00373 No Flush Niacin
- 01939 Optimized Folate (L-Methylfolate)
- 01217 Pyridoxal 5'-Phosphate Caps
- 01400 Super Absorbable Tocotrienols
- 02334 Super K
- 02335 Super K Elite
- 01863 Super Vitamin E
- 02422 Vegan Vitamin D3
- 02028 Vitamin B5 (Pantothenic Acid)
- 01535 Vitamin B6
- 00361 Vitamin B12 Methylcobalamin
- 01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges
- 01537 Vitamin B12 Methylcobalamin • 5 mg, 60 veg lozenges
- 02228 Vitamin C and Bio-Quercetin Phytosome • 60 veg tablets
- 02227 Vitamin C and Bio-Quercetin Phytosome • 250 veg tablets
- 01753 Vitamin D3 • 25 mcg (1000 IU), 90 softgels
- 01751 Vitamin D3 • 25 mcg (1000 IU), 250 softgels
- 01713 Vitamin D3 • 125 mcg (5000 IU), 60 softgels
- 01718 Vitamin D3 • 175 mcg (7000 IU), 60 softgels
- 01758 Vitamin D3 with Sea-Iodine™
- 02040 Vitamins D and K with Sea-Iodine™

WEIGHT MANAGEMENT & BODY COMPOSITION

- 02479 7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules
- 01807 Advanced Appetite Suppress
- 02207 AMPK Metabolic Activator
- 02504 Body Trim and Appetite Control
- 02478 DHEA Complete
- 01738 Garcinia HCA
- 01908 Mediterranean Trim with Sinetrol™ -XPur
- 01432 Optimized Saffron
- 00818 Super CLA Blend with Sesame Lignans
- 02509 Waistline Control™

WOMEN'S HEALTH

- 01942 Breast Health Formula
- 01626 Enhanced Sex for Women 50+
- 01894 Estrogen for Women
- 01064 Femmenessence MacaPause®
- 02204 Menopause 731™
- 02319 Prenatal Advantage
- 01441 Progesta-Care®
- 01649 Super-Absorbable Soy Isoflavones
- 02507 Youthful Woman 40+ with B-Complex



"I feel much more mentally clear."

Judith

VERIFIED CUSTOMER REVIEW

NEURO-MAG[®] THE SMART MAGNESIUM

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.



Item #01603 • 90 vegetarian capsules
1 bottle \$30.75 • 4 bottles \$27.50 each



Item #02032 • 93.35 grams of powder
1 jar \$28.50 • 4 jars \$26 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

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

Magtein[®] is a registered trademark of Magceutics, Inc. and is distributed exclusively by AIDP, Inc. Magtein[®] is protected under U.S. patents 8,178,118; 8,142,803; 8,163,301 and other patents pending.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

FORESIGHT FOR YOUR EYESIGHT

MacuGuard® Ocular Support provides:

- > **Lutein, trans-zeaxanthin, and meso-zeaxanthin** help maintain structural integrity of the **macula** and **retina**.¹⁻⁵
- > **Cyanidin-3-glucoside** assists with night vision.⁶⁻⁸
- > **Saffron** has been shown to help support **vision** as demonstrated by doctors' eye exams.¹
- > **Alpha-carotene** further helps support **macular density**.¹



For full product description and to order either of these **MacuGuard®** formulas, call 1-800-544-4440 or visit www.LifeExtension.com

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.

MacuGuard® Ocular Support with Saffron + Astaxanthin
Item #01993 • 60 softgels

1 bottle **\$33** • 4 bottles \$30 each

MacuGuard® Ocular Support with Saffron

Item #01992 • 60 softgels

1 bottle **\$18.75** • 4 bottles \$17.50 each

(Each bottle lasts for **two months**.)

MacuGuard® Ocular Support is available with or without astaxanthin.

LuteinPlus® and Mz® are registered trademarks of NutriProducts Ltd., UK, licensed under U.S. Patent 8,623,428.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.





IN THIS EDITION OF *LIFE EXTENSION* MAGAZINE®



7 A CASE FOR HIGHER-DOSE MELATONIN

Emerging data show that **higher-dose melatonin** may yield unexpected protection against common age-related disorders.



32 MUSHROOMS AND IMMUNE FUNCTION

Mushrooms contain compounds known to **activate** critical **immune functions**.



42 NEW WAY TO ENJOY MELATONIN

A **sugar-free** flavored **melatonin gummy** provides a tasty treat to chew on before bedtime.



50 VITAMIN K AND HEART HEALTH

Adults with the **highest vitamin K2** intake had a **lower risk** of death from coronary heart disease.



58 SYSTEMIC EFFECTS OF N-ACETYL-L-CYSTEINE

NAC (N-acetyl-L-cysteine) boosts **glutathione** levels in cells throughout the body.



71 AMERICA'S FAVORITE VETERINARIAN

Dr. Gary Richter explains why standard dry and canned food is harmful for your pet. He details the best foods to support your pets' overall health.