

The Science of a Healthier Life® LifeExtension.com November 2024 FEATURE ARTICLES

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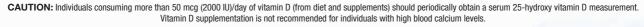
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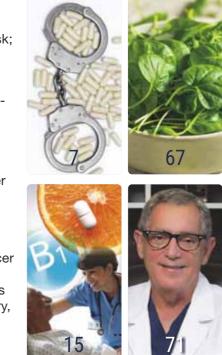
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Contributors

Ben Best • Michael Downey • Laurie Mathena • Randall Thompson

Advertising

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

Vice President, 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

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MEDICAL ADVISORY BOARD

Mark S. Bezzek, MD, FACP, FAARM, FAAEM,

is board-certified in internal medicine, emergency medicine, and anti-aging/ regenerative medicine. He holds U.S. patents for a multivitamin/mineral supplement, an Alzheimer's/dementia compilation, and a diabetic regimen.

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.*

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.

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

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

Sergey A. Dzugan, MD, PhD, was formerly chief of cardiovascular surgery at the Donetsk Regional Medical Center in Donetsk, Ukraine. Dr. Dzugan's current primary interests are 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. **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.

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

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

Professor Francesco Marotta, MD, PhD, of Montenapoleone Medical Center, Milan, Italy, is a gastroenterologist and nutrigenomics expert with extensive international university experience. He is also a consulting professor at the WHOaffiliated 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 boardcertified 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.

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.

SCIENTIFIC ADVISORY BOARD



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, D0, 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.



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.



Joel Kahn, MD, FACC of Detroit, Michigan, is a practicing cardiologist, and a Clinical Professor of Medicine at Wayne State University School of Medicine. He graduated Summa Cum Laude from the University of Michigan Medical School. Known as "America's Healthy Heart Doc", Dr. Kahn has triple board certification in Internal Medicine, Cardiovascular Medicine and Interventional Cardiology. He was the first physician in the world to certify in Metabolic Cardiology with A4M/MMI and the University of South Florida. He founded the Kahn Center for Cardiac Longevity in Bingham Farms, MI.



Peter H. Langsjoen, MD, FACC, is distinguished by a long career in cardiology with a specialization in congestive heart failure, primary and statin-induced diastolic dysfunction and other heart diseases. He is a leading authority on coenzyme Q10, having been involved with its clinical application since 1983. He is a founding and executive committee member 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 *Heart Attacks Are Not Worth Dying For, The Great American Heart Hoax,* and *The Complete Mediterranean Diet.* For more information visit www.DrOzner.com.

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

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













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When Vitamins Became Legal



WILLIAM FALOON



A law took effect **30 years** ago that prohibited the **FDA** from **criminalizing** the dissemination of truthful, non-misleading information about dietary supplements.¹

Before **October 1994**, the FDA raided vitamin companies at gunpoint, seizing the vitamins and sometimes arresting the owners.²⁻⁴

Nutrients like **coenzyme Q10** were considered **"unapproved drugs**." One company pled guilty to the crime of selling CoQ10 and providing information about it to the public.⁵

Consumers often stocked up on a year's supply of nutrients in the event the FDA forcibly removed them from the market.

When the **FDA** threatened to convert many supplements into **prescription drugs**, consumers rebelled. **Congress** was inundated with mail asking that legislation be enacted to curb the FDA's arbitrary powers.

Critics of the legislation predicted that without strict **FDA oversight**, a health catastrophe would erupt. They argued that mass injuries and deaths would occur if dietary supplements were not heavily regulated like **drugs** were.

Somehow, after **30** years, the health catastrophe never happened with responsible supplement use.*

What did occur was the removal of dozens of FDA-approved **drugs** because of mass **injuries/ deaths** that collectively cost pharmaceutical companies over \$25 billion in damages. Pharma still largely profited from selling **dangerous drugs** even when later paying enormous civil/criminal **penalties**.

As we mark three decades of greater **health freedom**, consumers often pay <u>less</u> per-milligram for **nutrients** today compared to what they cost prior to **October 1994**. Prescription drug prices, on the other hand, soared to exorbitant levels.

The majority of Americans now take supplements⁶ and are able to learn about how they work in the body.

For supporters who fought to achieve the legislative victory, **October 15, 2024**, represents a celebratory **30-year** anniversary of relative **health freedom**.^{7**}



Americans today enjoy access to low-cost, highpotency **vitamin D** supplements available from many reputable companies.

In countries that regulate supplements as "drugs," health authorities have historically limited vitamin D potencies to only **400-800 IU** per day.

This is far <u>less</u> than what's needed to achieve even modest *25-hydroxyvitamin D* blood levels.^{9,10}

A 2024 published review⁸ described:

- 1) Widespread vitamin D deficiencies,
- 2) The adverse impacts of these deficits,
- 3) Recommendations to <u>increase</u> the minimum daily **vitamin D** intake.⁸

This **2024** publication argues for a *higher* vitamin D supplementation dose than currently recommended by many health authorities.⁸

While modest by standards we pioneered decades ago, the authors of this review advocate for a vitamin D dose of **2000 IU** (**50 mcg**) per day as an efficient/safe approach to prevent and treat vitamin D deficiency in adult populations worldwide.

The authors recognize that the evidence underpinning recommendations for **2000 IU per day** is not (yet) well-recognized or established in the scientific literature or the currently published vitamin D guidelines.

They nevertheless drafted their review with the aim that it may serve as a basis for consideration regarding future health-authority guidelines for **vitamin D**.

> itaminD Deficienc

They emphasize worldwide prevalence of **25-hydroxyvitamin D** blood levels that are a frighteningly low **10-12 ng/mL** in **5% to 18%** of the population.

In 24% to 49% of people worldwide, 25-hydroxyvitamin D blood (serum) levels are below 20 ng/mL.

Minimum adequate **25-hydroxyvitamin D** levels by conventional standards are at least **30 ng/mL**.¹² Many in the alternative fields advocate for ranges of **40-60 ng/mL** and higher.

The authors of the 2024 published review suggest that while <u>individualized</u> dosing to protect against vitamin D <u>deficiency</u> is the **optimal** approach, it is not practical or feasible in many at-risk populations.





Individualized approaches require baseline and follow-up **25-hydroxyvitamin D** blood tests, which most readers of **Life Extension Magazine**[®] do at modest cost. These tests are not feasible or affordable for most at-risk populations globally.

The authors of this **2024** review, therefore, argue that a universal daily **2000 IU** dose of **vitamin D** is reasonable.

They suggest adjusting doses according to <u>individual</u> needs, with characteristics such as low baseline *25-hydroxyvitamin D*, obesity, or malabsorption syndromes justifying the **2000 IU/day** dose.

Widespread Individual Variability

We at **Life Extension** have collectively reviewed tens of thousands of **25-hydroxyvitamin D** blood test results.

Some people are high *absorbers* and only need **2000-3000 IU** a day of supplemental **vitamin D** to achieve **25-hydroxyvitamin D** levels above **40-50 ng/mL**.

Many aging individuals, on the other hand, require **vitamin D** doses of around **7000 IU** a day to optimize their **25-hydroxyvitamin D** status.

I've observed when I temporarily discontinue taking a **5000 IU** daily vitamin D capsule and rely on a **2000-3000 IU** dose in multi-nutrient supplements, my **25-hydroxyvitamin D** levels decline faster than anticipated.

Easy Way to Boost Vitamin D Blood Levels

For those challenged to achieve the desired **25-hydroxyvitamin D** blood levels, in many cases all one needs to do is take their vitamin D supplement with a meal that contains some **fat**.

One study found >**50%** greater *absorption* of **vitamin D** when taken with a **fat-containing** meal compared to taking it on an empty stomach.¹⁴

Taking vitamin D with some fat enhances absorption and can reduce the potency/ frequency of vitamin D capsules needed. Vitamin D is **fat soluble** and can remain stored in a good range in the body for variable time periods after a high dose is lowered.¹³ I've reviewed hundreds of vitamin D blood test results and often find **25-hydroxy-vitamin D** levels do not always correlate to the dose of vitamin D ingested.

This is why **25-hydroxyvitamin D** blood tests are so important.

The next page describes a **CBC/Chem/Lipids Panel** with **25-hydroxyvitamin D** blood test that costs around **\$700** at commercial labs. This comprehensive panel is available with a **25-hydroxyvitamin D** blood test as a special offer for only **\$56**, through November 4, 2024.

Most of our readers perform **blood tests** frequently.

I want to make it easy for <u>all</u> of you to conveniently and affordably test your blood to optimize health parameters, including ensuring adequate **vitamin D** blood levels.

For longer life,

Bill Faloon, Co-Founder Life Extension

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* Examples of irresponsible use are taking high-dose stimulant supplements while engaging in excess physical exertion in hot climates. This can cause heat stroke. Even without excess physical activity/heat, high-dose stimulants can cause heartbeat irregularity, transient hypertension, and other health issues. 1st Amendment

VITAMINS BECOME LEGAL

Thirty years ago, Congress amended the **Food, Drug and Cosmetic Act** to enable qualified health information to be disseminated to the public.

In doing so, it prohibited the **FDA** from restricting the **First Amendment** protections of **free speech** and limited the FDA's authority to regulate dietary supplements. This resulted in the explosive growth of the industry.

Before **October 1994**, the FDA raided vitamin companies at gunpoint, seizing some dietary supplements and sometimes arresting the owners. Some companies were driven out of business.

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** The Dietary Supplement Health and Education Act (DSHEA), enacted in October 1994, had two primary goals: to ensure continued consumer access to a wide variety of dietary supplements, and to provide consumers with more information about the intended use of dietary supplements.¹¹

SPECIAL BLOOD TEST OFFER!

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For a limited time, we are offering this **CBC/Chem/Lipid Panel** <u>plus</u> the *25-hydoxy-vitamin D* blood test for only **\$56**—over **30%** off the normal price of these two tests. Sale price effective through **November 4, 2024**.

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1. Br J Nutr. 2018 Apr;119(8):928-36.

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References

 EBioMedicine. 2018 Oct;36:18-28.
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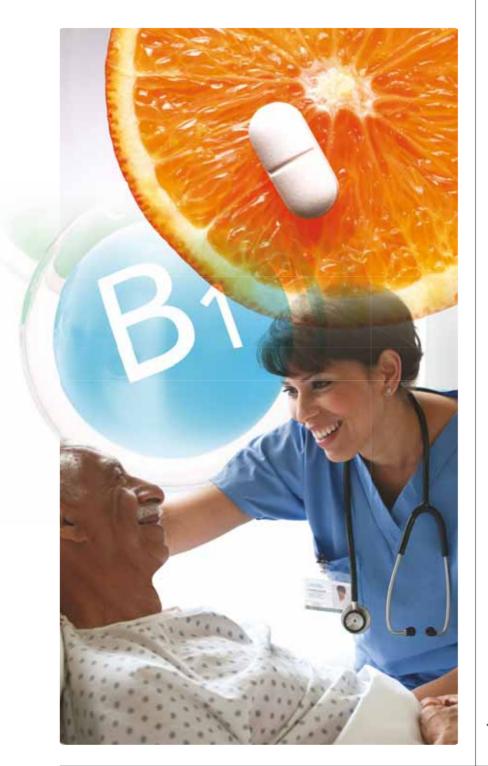
Inflammation and Discomfort: This virtually conducted study on inflammation and discomfort found that a PRM-enriched marine oil/ bioavailable curcumin combo significantly reduced pain severity, intensity, and total pain scores over the course of 60 days.

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In the News



Antioxidants Improve Short-Term Mortality Risk in Sepsis Patients

Findings from a systematic review and metaanalysis revealed that the administration of antioxidants was associated with improved short-term survival among men and women with sepsis, a complication of infection that results in body-wide inflammation.*

A total of 60 studies were analyzed, which included 130,986 sepsis patients. There were 35 randomized controlled trials and 25 non-randomized controlled studies.

An analysis of all studies that examined in-hospital mortality and 28-day mortality found a **19%** <u>reduction</u> among patients who received antioxidant therapy in comparison with the odds of in-hospital mortality of those receiving standard care.

When separate therapies were analyzed, **vitamin B1** and **vitamin C** were associated with respective **36%** and **34%** <u>lower</u> odds of in-hospital mortality compared to the odds of mortality in those receiving standard care.

When separate therapies were analyzed, **vitamin C** treatment was associated with **34%** <u>lower</u> odds of in-hospital mortality and **57%** <u>reduction</u> in 28-day mortality compared to the odds of mortality in those receiving standard care.

Editor's Note: An analysis of only the randomized controlled trials found that the odds of short-term mortality were 43% lower among the vitamin C group compared to the odds of mortality in the group receiving standard care.

* Heliyon. 2024 Apr 4;10(8):e29156.

Melatonin and Age-Related Macular Degeneration

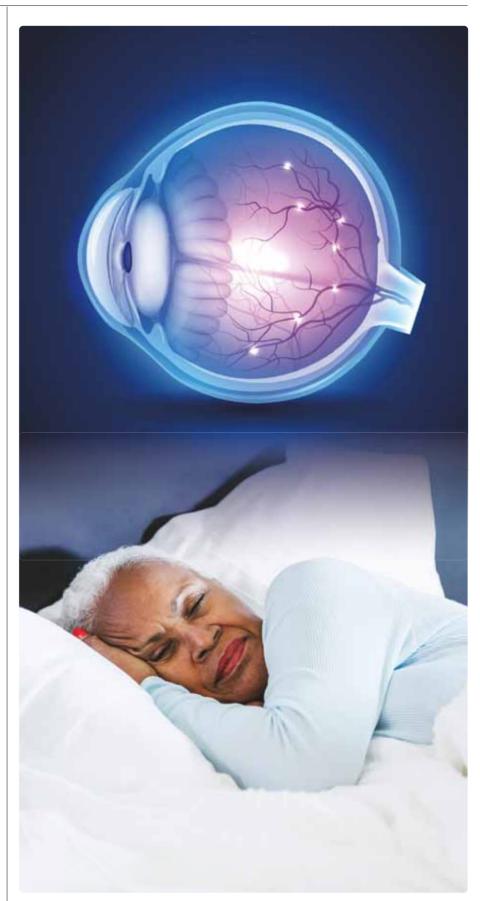
Adults who used the sleep hormone melatonin had a significantly lower risk of developing age-related macular degeneration (AMD) and had less disease progression according to a retrospective study.*

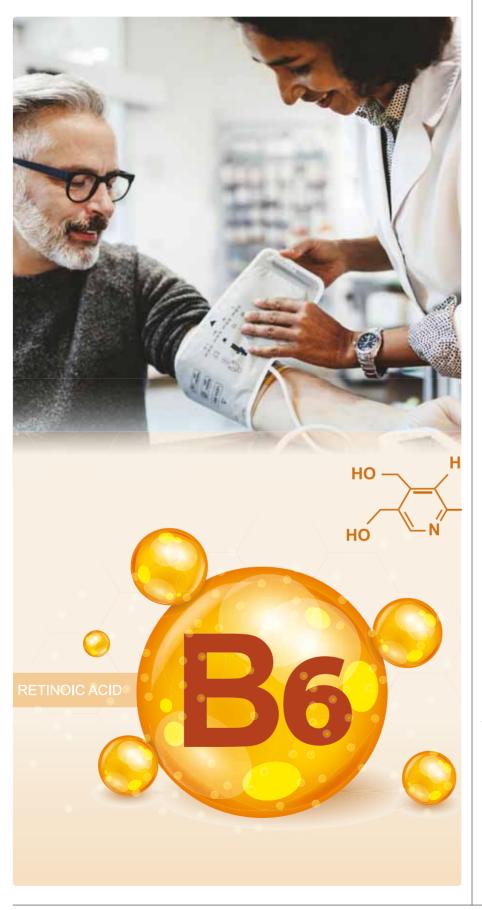
Researchers analyzed information from the health records of 121,523 men and women aged 50 or older who had at least one record of receiving an eye examination or being screened for eye disorders that did not reveal wet AMD beginning in November 2008 to November 2023. Individuals who reported melatonin use on four or more occasions at least three months apart were categorized as melatonin users.

Among subjects who did not initially have AMD, those who used melatonin had a **58%** <u>lower</u> risk of developing the disease through 2023 compared to the risk of those who did not use melatonin. For people who had dry AMD, the risk of progressing to wet AMD was **56%** <u>less</u> among melatonin users compared to the risk of nonusers.

Editor's Note: When people aged 60 and older were examined, melatonin use was associated with a **64%** lower risk of developing AMD and a **62%** lower risk of progression from dry to wet AMD.

* JAMA Ophthalmol. 2024 Jun 6.





Lower Odds of Stroke with Higher Vitamin B6 Intake

A study including 24,214 men and women found lower odds of stroke among those who consumed higher amounts of vitamin B6.*

Researchers analyzed data collected between 2005–2018 from participants in the National Health and Nutrition Examination Survey (NHANES). It included 921 people who had been diagnosed with stroke and 23,293 with no stroke history. Vitamin B6 intake was determined from responses to two dietary recall interviews.

People whose vitamin B6 intake was among the top **25%** of the study's subjects had **52%** <u>lower</u> odds of stroke in comparison with individuals whose intake was among the lowest **25%**. The authors observed that B vitamins lower levels of the amino acid homocysteine. Higher levels of homocysteine are associated with an increased risk of stroke.

Editor's Note: Vitamin B6 also helps support a healthy inflammatory response by inhibiting the activation of nuclear factor kappa-B, interleukin-6 and tumor necrosis factor-alpha.

* Heliyon. 2024 May 11;10(10):e31125.

Alpha-Lipoic Acid Shows Benefits for Polycystic Ovary Syndrome

A retrospective study revealed improvements in insulin sensitivity and liver enzymes among overweight or obese women with polycystic ovary syndrome (PCOS) who received alpha-lipoic acid (ALA) daily for 12 weeks.*

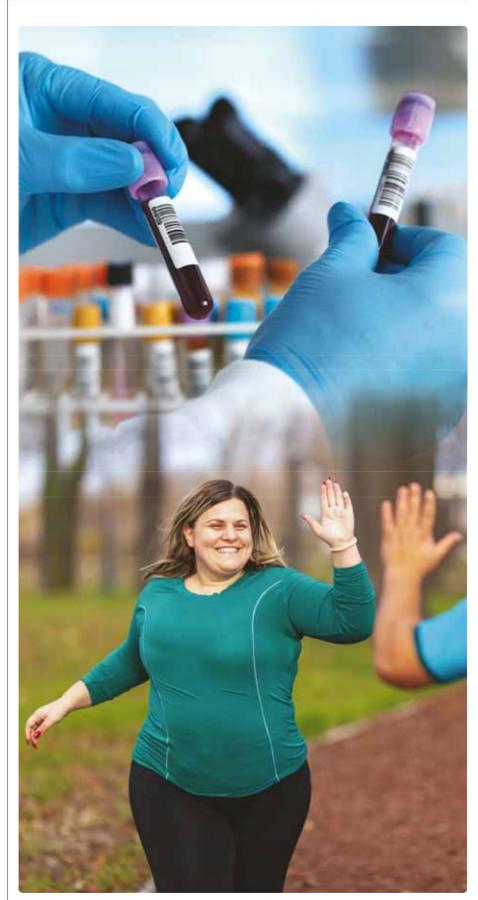
PCOS is a condition caused by elevated levels of hormones known as androgens. The condition is characterized by ovarian cysts, weight gain, difficulty becoming pregnant and other signs. Women with PCOS may have elevated levels of insulin and/or a family history of diabetes.

The study included 32 women with PCOS who received **400 mg** daily of ALA. Routine examinations and blood tests for hormones, insulin, glucose tolerance, liver enzymes and other factors were conducted at the beginning and end of the study.

At the end of the treatment period, participants had significant improvement in insulin sensitivity and reduced levels of the liver enzymes ALT and AST without changes in reproductive hormones. After three months plasma insulin levels decreased together with an index (HOMA) of **insulin resistance**.

Editor's Note: The authors noted that the combination of high insulin levels and elevated ALT and AST has been considered a trigger for nonalcoholic fatty liver disease, which occurs at a higher rate among women with PCOS than in those who do not have the condition.

* Gynecol Endocrinol. 2024 Dec;40(1): 2341701.



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

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References: 1. Neuropharmacology. 2016 2016/09/01/;108:426-39. 2. Journal of Cellular Physiology. 2016;231(9):1903-12. 3. J Alzheimers Dis. 2016;49(4):971-90. Magtein® is a trademark of Magceutics®, Inc. and is distributed exclusively by AIDP, Inc. Magtein® is protected under a family of US patents, pending patents, and is protected worldwide.

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Help Your HEART PUMP BETTER

BY MICHAEL DOWNEY

Over time, our heart muscles weaken.

Age-related degenerative changes are often major culprits.¹

These changes may result in *reduced* efficiency of the heart to pump blood, which *reduces* the amount of oxygen that is pumped to the rest of our body. This often becomes symptomatic during periods of exertion or stress.¹⁻³

Weaker pumping of the left ventricle over time may result in debilitating **cardio**vascular disease and even cardiac failure.⁴

For centuries, the **arjuna** plant has been used in Indian Ayurvedic medicine to treat heart disorders and other diseases.⁵ Modern research has found that **arjuna** supports **cardiac function** by strengthening the heart muscle's "squeeze," increasing the volume of blood it can pump with each heartbeat.^{6,7}

Clinical trials show that a specific **arjuna bark extract** *boosts* the left ventricle's pumping output, supporting cardiac endurance and decreasing **physical fatigue** by a clinically significant average of **23%**.^{6,7}

ARJUNA BARK



Measuring Cardiac Pumping Power

The **ejection fraction** test measures how effectively one's heart pumps blood during each heartbeat.

Testing **left ventricular ejection fraction** enables doctors to assess how effectively one's heart pumps blood out of the left ventricle. The **left ventricle** is the heart chamber that directly pushes oxygen-rich blood to the rest of the body.⁸

In a healthy heart, the **left ventricular ejection fraction** is usually **50%** to **70%**.⁸ A lower number indicates the heart is having trouble keeping up with your body's needs, especially under exertion. A left ventricular ejection fraction **below 50%** can indicate left-sided heart dysfunction.⁸

Left ventricular ejection fraction generally declines with **age**, though healthy eating, exercise, and reducing stress can help inhibit this decline.^{3,4,9}

In recent years, an extract of the **arjuna tree** has been clinically shown to <u>increase</u> left ventricular **ejection fraction** and improve cardiac output.

What Your Left Ventricular Ejection Fraction Means

Ejection fraction refers to the percentage of blood that is pumped out of the ventricles with each heartbeat.

It is a key measure used to assess how well the heart is functioning, particularly the left ventricle.

A physician can help interpret the implications of your **left ventricular ejection fraction**, or **LVEF**, number. But here is a general guideline:¹⁴

- LVEF above 70% Hyperdynamic (a possible sign of a heart condition)
- LVEF 50% to 70% Normal
- LVEF 40% to 49% Mild dysfunction
- LVEF 30% to 39% Moderate dysfunction
- LVEF below 30% Severe dysfunction
 - * LVEF below 30% may indicate heart failure.

Arjuna Bark

Parts of the **arjuna** tree, which grows widely on the Indian subcontinent, have long been studied for medicinal properties.

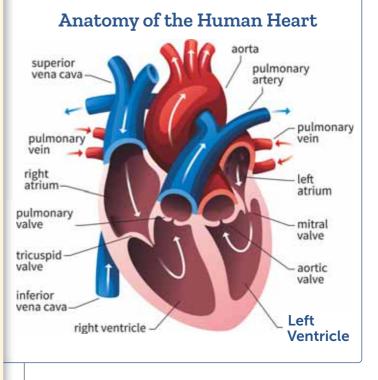
In pre-clinical studies, **bioactive** compounds found in **arjuna** were shown to be:¹⁰

- Anti-inflammatory,
- Antioxidative,
- Anti-atherosclerotic,
- Cardioprotective, and
- Anti-tumor.

Compared to the fruit, seed, leaf, and root of the tree, **arjuna bark** has a substantially *higher* concentration of **flavonols** (quercetin, myricetin, and kaempferol), **flavanole** (catechin), and **phenolic acids** (gallic acid, p-coumaric acid, and ferulic acid).¹⁰

These compounds appear to have the ability to *increase* the force of the heart's muscular contractions.^{6,7} This improves pumping, increases **cardiac output**, and reduces physical **fatigue**.^{6,7}

Two randomized, controlled clinical studies have confirmed these benefits in an **arjuna bark** extract standardized to provide **30% polyphenols** and **15% glycosides**.^{6,7}



WHAT YOU NEED TO KNOW

Better Pumping, Less Fatigue

In one study, researchers enlisted 72 male and female volunteers between the ages of 30–70 years, sedentary, and overweight. They had left ventricular **ejection fraction** ratios (assessed using a type of echocardiogram) ranging from **48%** to **60%**,⁶ which are mildly reduced to normal.

One group took **400 mg** of **arjuna extract** daily for eight weeks, while another took a **placebo**. Both groups maintained normal dietary and exercise regimens.⁶

Those who took the arjuna *increased* their left ventricular **ejection fraction** by a clinically significant **3.6 percentage points**, improving their cardiac endurance.⁶

Research shows that even modest changes in left ventricular ejection fraction may be clinically important in determining the risk of future **mortality**.^{11,12}

Physical fatigue levels were also evaluated, using a standard questionnaire that measures fatigue severity and how it affects activities and lifestyle.

Those who took the **arjuna extract** reported clinically significant improvement in fatigue scores¹³ with an average of **23%** <u>improvement</u>, compared to less than **10%** in the **placebo** group.⁶

Arjuna extract provided a decrease in fatigue's interference in:⁶

- Physical functioning,
- Sustained physical functioning, and
- Performance of duties and responsibilities.

Support Healthy Heart Function

- With age, the heart's left ventricle loses its ability to effectively pump oxygen-rich blood to the body. Over time this may lead to cardiovascular disease/cardiac failure.
- A standardized extract of arjuna tree bark has been shown to increase the left ventricular ejection fraction, a measure of how much blood the heart can pump out of the left ventricle with each heartbeat.
- In a clinical study, arjuna extract increased left ventricular ejection fraction by a clinically meaningful 3.6% in participants in the mildly reduced to normal ranges. Their fatigue scores decreased by a clinically significant 23%.
- A similar improvement in left ventricular ejection fraction was demonstrated in a clinical trial of active young men with LVEF numbers well into the healthy range, showing that arjuna improved cardiac output in a wide range of subjects.

Effects in Healthy Adults

Scientists also tested **arjuna** extract's effect on the heart's pumping capability in **active** adults with a **healthy** left ventricular ejection fraction.

Researchers enlisted 31 healthy, enduranceexercising men, aged **18-40** years. Their left ventricular ejection fraction scores ranged from **55%** to **70%**.⁷

All volunteers' left ventricular ejection fraction and fatigue levels were assessed after physical exertion on a treadmill.

After eight weeks, participants who took the **arjuna extract** had improved their *already* healthy left ventricular **ejection fraction** by a clinically significant **3.7** percentage points.⁷

This shows that this extract may benefit individuals whether their left ventricular ejection fraction is mildly **reduced** *or* **healthy**.

Researchers also used a scale measuring subjects' perceived exertion to assess physical fatigue. Those taking arjuna had statistically significant *increase* in **time-to-exhaustion** score, and their perceived level of **exertion** was significantly *reduced*.⁷

No serious adverse events were reported in either study. $^{\scriptscriptstyle 6,7}$

Arjuna extract can help maintain a strong, healthy heart and decrease physical fatigue by increasing cardiac output.

Research suggests that **arjuna** extract may have potential to improve **ejection fraction** in patients with **heart failure**.^{6,7} While preliminary studies are promising, more extensive clinical trials are needed to confirm these effects in heart failure patients who must rely on cocktails of drugs and nutrients to maintain barely sufficient cardiac output.

Summary

Over time, the heart's **left ventricle** tends to pump less oxygen-rich blood to your body.

This can eventually lead to **cardiovascular disease/** cardiac failure.

Clinical studies show that **arjuna bark** extract increases the **left ventricular ejection fraction**, a measure of the amount of blood the heart can pump out of the left ventricle with each heartbeat.

This ability to support healthy heart function was seen in individuals with mildly **reduced** and **healthy** left ventricular ejection fractions. Both groups also had a significant decrease in **fatigue** 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.

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Aortic Stenosis and Transcatheter Aortic Valve Replacement (TAVR)

Aortic stenosis is a common disorder seen in adults 65 years and older. It involves scarring and calcification of the aortic valve¹⁵

When working normally, the aortic valve helps ensure that blood flows in only one direction, blocking backward flow into the heart's left ventricle.16

But with age, heart valves can become diseased. The pathology reflects cardiac valve dysfunction, where calcium and scar tissue build-up impedes valve functionality, such as in aortic valve stenosis, which can also be genetic in origin.15 This makes the valve stiff and difficult to open.

Stenosis of the aortic valve puts a large stress on the heart and impairs its ability to function. Because the main output pathway from the heart is partially blocked, the heart muscles must work harder to get adequate blood supply to the entire body.15

Over time, as aortic stenosis worsens, it can significantly impair the cardiac output, becoming symptomatic. Symptoms such as shortness of breath, chest pain, and fainting can occur with physical exertion. As the stenosis gets worse, the heart can eventually fail to generate enough blood flow and heart failure develops. Traditionally, the only option to correct aortic stenosis has been open heart surgery to replace the valve.¹⁵ Although this procedure can reverse aortic stenosis and take stress off the heart, it cannot be tolerated by all patients, especially the elderly.

Open heart surgery typically has long hospitalization and recovery times. Patients with severe disease or other agerelated conditions may be poor candidates for open heart surgery. The stress of these procedures and long anesthesia times increase the risk of complications and poor outcomes.

Fortunately for people suffering from aortic stenosis, there is now another option. **Transcatheter aortic valve** replacement (TAVR) is an alternative treatment in many cases. It is an effective and less invasive endovascular proceduremeaning that it does not require the chest to be opened and it is done almost entirely through catheters in the blood vessels with x-ray guidance.17

The advantages of this technology are that it is much less traumatic than open heart surgery and the resulting hospitalization and recovery times are significantly reduced compared to open heart surgery.

TAVR may not be indicated for all patients, depending on various details of their condition and general health. Furthermore, while generally less traumatic than open heart surgery, **TAVR** is not without its own risks. As with surgical valve replacement, complications such as bleeding, stroke, and others can occur in some cases, as well as death.

However, a recent trial that randomized patients with aortic stenosis to TAVR versus surgery found that outcomes were largely comparable. Most notably, the occurrence of poor outcomes (death, stroke, rehospitalization related to the procedure, and heart failure) was not significantly different between the two options.¹⁸ Therefore, this **TAVR** may be an option for a growing subset of patients suffering from symptomatic aortic stenosis who wish to avoid surgery or for whom open heart surgery is too risky.



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

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Long-Lasting Relief for Dry Eye Syndrome

Malulul





BY MICHAEL DOWNEY

Dry eye syndrome is an annoyance, causing redness, itching, and other frustrating symptoms.

This condition occurs when the eyes don't produce enough **quality tears**.²

When **dry eye syndrome** becomes severe, and is left untreated, it can lead to permanent **eye damage**.¹

Prevalence of dry eye syndrome is growing with greater use of smartphones, tablets, computers, and other **digital screens**.³

It has been estimated to affect about **16 million** Americans.⁴

Many turn to over-the-counter eye drops, which provide **short-term** relief but don't address underlying causes. Prescription treatments are available but can have side effects and may provide only symptomatic relief.⁵

Here's the good news: Scientists have identified a **berry extract** that combats dry eyes the natural way, by boosting the body's *own* production of **real tears**.⁶

A pilot study found that, taken *orally*, a **maqui berry** extract provided a **72%** improvement in **dry eye** symptoms after 60 days.⁶

A larger **clinical trial** showed that **maqui** extract, taken orally for four weeks increased **tear production** by **89%**, protecting the eyes and improving quality of life.⁷

Possible Eye Damage

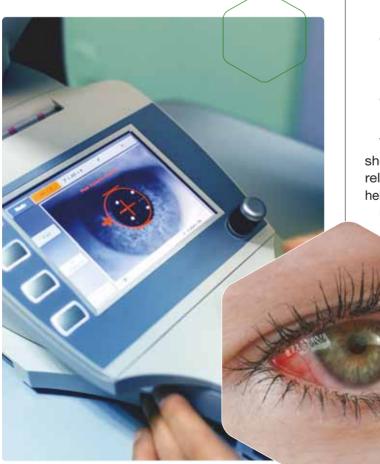
Dry eye syndrome can be caused by aging, wearing contact lenses, dry weather, air pollution, smoking, and allergies.⁵ It can also be associated with some medical conditions or can even occur after eye surgery.^{4,5} Use of computers, smartphones, tablets, e-readers, and other **digital screens** often worsens the condition.^{8,9}

The symptoms of dry eyes can include itching, burning, light sensitivity, and blurred vision.⁴ The discomfort and visual disturbances from dry eyes can impact **quality of life**.¹⁰ Studies have shown that the irritation of dry eyes is associated with lower scores on mental health scales,^{10,11} including depression and anxiety.¹²

Even worse, without treatment, chronic dry eyes can cause **eye damage**.^{1,4}

Tears are essential for lubricating and protecting the **cornea**, the front central surface of the eye. They protect the eye from infection, wash away foreign matter, and deliver critical nutrients to the surface.^{13,14}

As a result, dry eyes can eventually damage the **cornea**. If severe and left untreated, ulceration and scarring of the cornea can lead to permanent **impairment of vision**.⁵



Tear Quantity and Quality Matter

There are **three layers** of natural tears: oil, water, and mucus.¹⁵

The eye surface is lubricated, nourished, and protected by the normal, if tiny, amount of **tears** normally produced daily, about **0.7 mL** to over **3 mL** per eye.⁶ People affected by **dry eye syndrome** either:⁵

- Don't produce enough tears, or
- Have tears that evaporate too guickly.

Maqui Berry Restores Tears

Seeking a solution, scientists identified **maqui berries**, a fruit found in Chile, abundant in anthocyanidin pigments called **delphinidins**. Maqui berries and delphinidins exhibit protective effects to support eye and vision health.^{6,16}

Researchers have found in preclinical studies that a standardized **extract** of **delphinidin**-rich **maqui berries** may:^{16,17}

- Provide protection to the eye and tear producing lacrimal gland by reducing levels of free radicals,¹⁶
- Inhibit harm from light exposure, protecting critical **photoreceptor cells** that convert light into signals sent to the brain,¹⁷ and
- Help restore production of natural, highquality tears.¹⁶

Taken orally, an extract of maqui berries has been shown to *boost* **natural tear production**, delivering relief for dry and irritated eyes.^{6,7} This, in turn, may help prevent the damage that can occur with long term, unmanaged dry eyes.

> This eye benefit of **maqui berry** extract was seen in a rat model of dry eyes. The rats were randomized to receive pretreatment with **maqui** berry extract and with **placebo**.

> > Pretreatment with maqui berry extract significantly prevented loss of tears as compared to placebo. The animals pretreated with **maqui berry extract** retained clear eyes with no new corneal damage throughout the study.¹⁶

LONG-LASTING RELIEF FOR DRY EYE SYNDROME

WHAT YOU NEED TO KNOW



- Dry eye syndrome is increasingly common, causing burning, redness, itching, eye fatigue, and reduced quality of life.
 When severe, prolonged, and untreated, it can also lead to permanent eye damage.
- Eye drops only have a temporary effect, and prescription medications can have side effects.
- Taken orally, an extract of the maqui berry has been clinically shown to boost high-quality tear production by 89%, improving dry eye symptoms, quality of life, and eye health.

Clinically Validated

Moving on to the gold standard of medical research, scientists conducted a **randomized**, **placebo-con-trolled trial**.

This study enrolled 74 healthy adults with moderate eye dryness and eye fatigue and more than four hours of exposure to computer, cell phone or other screenbased devices. Each day, half took a placebo, and half took **60 mg** of **maqui berry extract** for four weeks.⁷

At the start, dryness levels were the same for each group. But after four weeks, the **maqui extract** group had:⁷

- Higher production of **tear fluid** in both eyes, with an average increase of **89%**,
- Reduced eye dryness, and
- Less eye fatigue.

Compelling Pilot Study

In a pilot **clinical trial**, researchers investigated the ability of **maqui berry extract** to relieve dry eyes by supporting healthy tear production. The study enrolled 13 adults with moderate eye dryness, which was tested by Schirmer's test to evaluate the amount of tear fluid produced by the tear glands.⁶

The 13 volunteers took either **30 mg** or **60 mg** of **maqui berry extract** daily for 60 days.

Both dosages led to about **50%** improved **tear production** after 30 days. After 60 days, however, the *lower*dose group lost half of their improvement, while the *higher*-dose group maintained **nearly all** their increased tear production.⁶

The participants were also evaluated to assess bothersome symptoms of dry eyes and their effect on daily life. This was done using a **Dry-Eye Related Quality-of-Life Score test** questionnaire. A *higher* score indicates *greater* impairment and *worse* quality of life.

The score for each group was about **40** at the start of the study. After taking daily **maqui berry extract**:⁶

- Scores for patients taking **30 mg** of maqui berry extract improved to almost **22** after 30 days. But their scores stayed much the same by day 60.
- Scores for patients taking 60 mg improved to almost 27 after 30 days. But their scores continued to drop to a beneficial low 11 points by day 60.

This constitutes a **72%** *improvement* in dry eyerelated quality-of-life symptoms after just two months.⁶ On a quality-of-life test, the maqui group had substantially *improved* total values for bothersome **ocular symptoms** (such as grittiness, dryness, or redness), compared to the placebo.

On another survey, the **Visual Analog Scale**, the maqui group reported significant improvements in **eye** fatigue.⁷

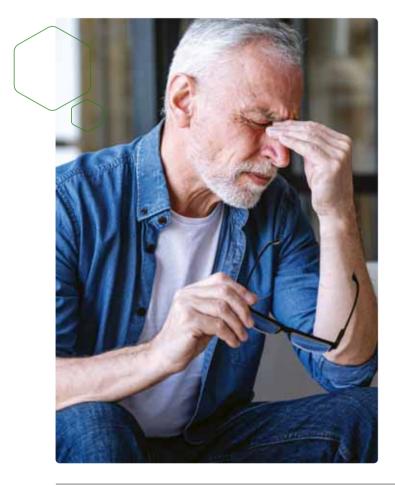
This clinical trial found that taking **60 mg** of **maqui berry extract** daily for four weeks reduces eye dryness and fatigue, which may help protect eyes from permanent damage.

Summary

Dry eye syndrome causes discomfort and reduced quality of life and can lead to long-term damage to eye tissue.

An oral extract of the **maqui berry** helps the body produce more of its *own* high-quality tears.

It has been shown in clinical research to boost natural tear production by **89%**, improving dry eye symptoms, protecting eye health, and boosting quality of life. •



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

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Cry me a river Tears are a good thing-until you don't have enough.



30 VEGETARIAN DIETARY

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MELATONIN: Potential Anti-Cancer Effects

BY RANDALL THOMPSON

The hormone **melatonin** has long been used to help improve sleep.¹

But its effects go much further.

Scientists have found that taking **oral melatonin** may influence many physiological processes that could potentially provide **anti-cancer** benefits.²⁻⁵

Oral melatonin has been shown in clinical studies to reduce side effect severity when taken along with conventional cancer treatments.^{2,5-7}

Even more impressively, in multiple studies of **cancer** patients, adding melatonin to standard treatment improved **tumor regression** and **survival** rates.

Too Much Light!

When we are exposed to regular light and dark cycles, our bodies produce and release the hormone **melatonin** mostly at night in the dark.^{2,4}

Melatonin helps induce and control **sleep**. But it determines much more than just sleep/wake cycles: It affects hormone levels, immune function, inflammation, reproduction, and cell protection^{4,8} One of its important roles is DNA protection and repair.^{3,9}

These days, many people get too much **artificial light** exposure in the evenings, whether from overnight work shifts, late night television watching, or staying up looking at phones, tablets, or computer screens.

This *disrupts* the natural light and dark cycle and can cause **melatonin** levels to plunge.¹⁰ To make matters worse, melatonin secretion also tends to diminish with **older age**.¹¹

Disruption of this natural cycle and of melatonin secretion has negative effects throughout the body. Research has shown that taking **oral melatonin** at night may help mitigate these problems, aiding sleep and activating the hormone's other vital functions.

Anti-Cancer Actions

Preclinical data have shown that melatonin can regulate different physiological pathways in the body that can help protect against **cancer**. These include inhibition of **tumor cell growth**, promotion of **immune cell response**, and enhanced **apoptosis** (normal cell death).¹²

Three pathways involved in these effects include:

- Signaling Pathways. In preclinical studies melatonin has been shown to inhibit malignant transformation of healthy cells by downregulating growth factors, suppressing tumor progression, and initiating apoptosis.² Studies on breast cancer cells and animals have reported melatonin combined with chemotherapy treatment showed improved **apoptotic** effects compared to melatonin alone.⁸
- 2. Supporting healthy immune function. Preclinical studies have shown that melatonin plays an instrumental role in modulating immunity, which suggests

potential as an adjuvant against certain viral and bacterial infections.¹³⁻¹⁵ Modulation of immune response has potential to enhance the effectiveness of anti-tumor therapy and ease normal tissue toxicity.¹⁶ This immune-modulating property of melatonin may also help the immune system identify and target cancerous and precancerous

cells, meaning it might be able to impede the growth of cancerous cells and reduce tumor size.^{8,16}

 Oxidative stress. Oxidative stress can cause DNA damage, increasing the risk of cancer. The antioxidant activity of melatonin is a protective mechanism that might reduce cancer risk and progression.^{2,9}

MELATONIN: POTENTIAL ANTI-CANCER EFFECTS

WHAT YOU NEED TO KNOW

Help Fighting Cancer

- Best known for helping to promote quality sleep, the hormone melatonin has wide-ranging effects on cells throughout the body. In preclinical settings it has also shown **anti-cancer** activity.
- In observational studies, lower levels of urinary melatonin metabolites are linked with higher risks of some cancers.
- Human trials have shown that taking oral melatonin, alone or with other treatments, has improved outcomes for cancer patients, increasing survival rates and tumor regression.
- Melatonin may also ease and protect against many harmful side effects of chemotherapy and radiation.

Through these and other actions, melatonin has been shown to have **anti-cancer** effects on cancer cell lines, including:

- Prostate,^{8,17}
- Breast,^{8,17}
- Stomach,^{2,17}
- Lung,^{5,18}
- Ovarian,^{5,8}
- Colorectal, 5,17
- Oral,^{2,5}
- Liver,^{8,12} and
- Kidney.⁵



Improving Response to Human Standard Treatment

Observational studies have shown that exposure to light at night is associated with increased risk of breast cancer. And suppression of melatonin is believed to play an important role in this association.¹⁹⁻²¹

Human studies have reported that lower levels of urinary melatonin metabolites are associated with increased risk of advanced prostate²² and breast cancer.²³

One study evaluated women with estrogen receptor negative ER (-) **metastatic breast cancer**. These women had late-stage advanced disease and could not tolerate further chemotherapy (due to age, low performance status) and/or had previously received chemotherapy.²⁴

They were randomized to receive **20 mg** of **mela-tonin** or a **placebo** nightly, in addition to the cancer medication tamoxifen. For such aggressive cancer, the outcomes were remarkable:²⁴

- The **tumor response rate**, the percentage of patients who had improvement in their cancer, was significantly better in those receiving melatonin and tamoxifen.
- The one-year survival rate more than *doubled* in those taking melatonin.

A Note About Melatonin Dosing

To improve sleep, it's generally suggested to take **1** to **3 mg** of melatonin before bedtime.¹ However, human studies evaluating melatonin's effects on **cancer** often use higher doses, typically around **20 mg** per night.^{6,18,31}

Several other studies in cancer patients have shown benefits of melatonin added to treatments such as immunotherapy or chemotherapy.^{2,6,7,18,25-28}

In one of these studies, patients with **metastatic solid tumors** of various types were randomized to receive chemotherapy alone, or **20 mg** of **melatonin** daily in addition to their chemotherapy. The one-year **survival rate** and rate of **tumor regression** was *higher* with melatonin, with positive outcomes approximately **doubled**.²⁸

Another study of patients with cancer that had metastasized to the **brain** showed that taking melatonin improved one-year survival rates and mean survival times.²⁶

Meta-analyses of human trials have shown that cancer patients taking melatonin along with conventional treatment had <u>better</u> **survival rates** and **tumor response rates** than patients who don't receive melatonin.^{6,7,25}

These studies show that melatonin, when taken with standard cancer treatment, may enhance the efficacy of chemotherapy and mitigate side effects.

Easing Side Effects

Melatonin may also help minimize the negative effects of cancer treatments.²⁹

A review of human studies showed that melatonin may improve sleep quality and insomnia in patients with cancer.³⁰

In one trial of women with breast cancer, the treatment group received **18 mg** of melatonin daily, beginning one week prior to the treatment until two years after completion. After two years researchers concluded that long-term use of melatonin decreased the level of fatigue, which is common in cancer patients undergoing cancer treatment.³¹ Impaired cognitive function is a common side effect of chemotherapy. In a randomized controlled trial in women undergoing **chemotherapy** for breast cancer, **20 mg** of daily melatonin was taken before and during their first cycle of chemotherapy. Those who received melatonin experienced improvement in several markers of **cognitive function** as compared to placebo. In addition, there was improvement in sleep quality and reduction in symptoms of depression, compared to placebo.³²

Many chemotherapy and radiation treatments also cause potentially **lethal side effects**. Studies have found that melatonin protects against many of these, including low platelet counts, neurotoxicity and cardiotoxicity, weakness, and more.^{6,7,31,32}

Melatonin has been shown to augment some cancer therapies and protect against harmful side effects of treatment.



Summary

The hormone **melatonin** exhibits **anti-cancer** properties.

Human observational studies have shown lower levels of urinary melatonin are associated with increased risk of advanced prostate and breast cancer.

Studies of patients with existing cancer show that taking **oral melatonin** may increase **survival rate**, improve **tumor response**, and protect against **side effects** of other cancer treatments.

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

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EXERCISE and HEALTH Recent Conference Presentations

BY BEN BEST

Exercise is a frequent topic at health and longevity summits.

This report focuses on highlights from recent conference presentations that suggest optimal ways of benefiting from exercise.

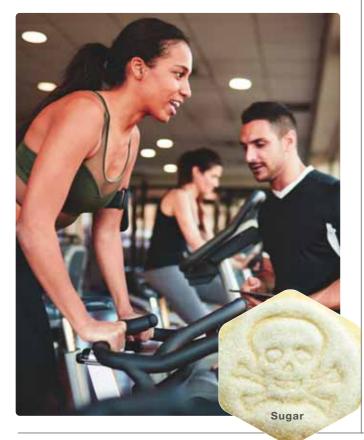
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Cardiorespiratory Fitness for Longevity

Rhonda Patrick, PhD (host of the FoundMyFitness podcast) is passionate about cardiorespiratory fitness for health and longevity. She has cited the fact that aerobic exercise, whether walking, running, or cycling, reduces both **systolic** (heart pumping) and **diastolic** (heart relaxing) blood pressure.¹

A meta-analysis of studies found that **longer** intervals of exercise will invariably increase cardiovascular fitness (measured by **VO**₂ **max**, the maximum volume of oxygen used by the body during intense exercise).² A recent study in men found that high-intensity interval training (short bursts of high-intensity full-body movements followed by short rest periods) increases VO₂ max more than sprint interval training (short bursts at maximal intensity followed by longer periods of rest). However, a review of 19 studies showed that both forms of exercise produce similar gains for cardiovascular fitness.^{3,4}

One study found that six minutes of high-intensity cycling intervals increased circulating **brainderived neurotropic factor**, important for learning and memory, four to five times more than prolonged, low-intensity cycling.⁵



A study of middle-aged men, followed for 46 years, showed that VO_2 max was a significant predictor of cardiovascular mortality and all-cause mortality. Those in the *highest* 5% lived about five years *longer* than those in the *lowest* 5%.⁶ This and other evidence suggest that VO₂ max is a greater predictor of cardiovascular mortality and all-cause mortality than conventional risk factors such as obesity, high blood pressure, and insulin resistance. The most accurate prediction of mortality can be made when VO₂ max is tested in conjunction with these other risk factors.⁷

Dr. Patrick recommends "**exercise snacks**" as a convenient alternative to structured exercise at a gym. Avoiding prolonged sitting by quickly ascending 60 steps of stairs as quickly as possible every few hours can result in significant improvements in cardiovascular fitness. Dynamic warm-up, including 10 jumping jacks, 10 air squats, and five lunges on each side, and a one-minute walk for cool-down will facilitate these "snacks."⁸

Aerobic exercise may even have benefits for **cancer** prevention and treatment. Scientists used a bio-mimicking circulatory system to recreate the environment of intense and low-intensity exercise to test its effects on cancer cells. The results showed that when cancer cells were in a high-intensity exercise environment they were able to be killed significantly better than in a low-stress environment. The cancer cells were killed by exercise-induced stress, while normal cells were unaffected.⁹ In colon cancer patients, a small clinical trial found that any intensity of exercise significantly reduced circulating cancer cells after six months.¹⁰

Metabolic Flexibilty and Aging

John P. Thyfault, PhD (Professor of Cell Biology and Physiology at the University of Kansas Medical Center) studies the effects of fasting and exercise on metabolic health.

For people who are not exercising, after a meal the liver stores glucose as **glycogen**, which can provide glucose as an energy source for 10-14 hours. After that time, the body begins to use stored fat as energy. However, an hour of medium-intensity aerobic exercise, such as running, even four hours after a meal may be enough to start burning **fat**.¹¹ The ability to switch from glucose to fat as an energy source ("**metabolic flex-ibility**") is enhanced by exercise but can be adversely affected by a poor diet. Animals fed high amounts of fat and sugar show impaired learning and memory,¹² which may be counteracted by exercise.

Dr. Thyfault noted that insulin resistance plays an important role in reducing metabolic flexibility.¹³ Getting **150 minutes per week** of moderate to vigorous exercise will reduce the risk of **type II diabetes** by **30%**.¹³ Insulin sensitivity declines rapidly within 24 to 48 hours after physical movements regardless of intensity.¹⁴ Even low-intensity exercise is sufficient to mobilize fat from fat cells, as well as increasing release of glucose from the liver.^{13,15}

Although aging is associated with increased insulin resistance and reduced metabolic flexibility, Dr. Thyfault contends that it is the chronic **inactivity** equally associated with getting older, compared to aging itself, that results in these effects.¹⁴

Benefits of Creatine

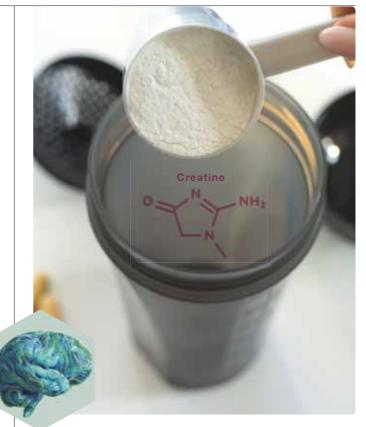
Eric Rawson, PhD (Professor of Health, Nutrition, and Exercise Science at Messiah University in Mechanicsburg, Pennsylvania) has devoted his career to studying the effects of **creatine** on the human body. Approximately **95%** of the creatine in the human body is found in skeletal muscle, where it makes energy rapidly available.¹⁶

The major source of creatine in the diet is meat. Creatine content in muscle is lower in **vegetarians** and the **elderly**. For this reason, creatine supplementation increases muscle creatine much more in the **elderly** and in **vegetarians** than in young people or meateaters.^{17,18}

Creatine supplementation combined with **resistance exercise** increases muscle strength and reduces fatigue more than exercise or supplementation alone.¹⁹ Some studies presented in a review paper show that **creatine supplementation** combined with resistance training produced beneficial impacts on bone health.²⁰

Creatine is important for **brain function**, although the brain can synthesize creatine and is therefore less dependent on other organs; however, it responds to supplementation. Research shows that creatine supplementation may increase brain creatine content by **5%-15%**.²¹ Creatine supplementation has been shown to be more beneficial for memory in vegetarians than in meat-eaters.²²

Creatine is safe and well tolerated in dosages up to **30 grams daily** for five years. However lower dosages may be all that are required. ²³ One study found that **8 grams daily** for five days reduced mental fatigue on a math test and increased oxygen utilization to the brain.²⁴



Concluding Remarks

Most people understand that exercise contributes to health and longevity. Learning the mechanisms and conditions by which this occurs may increase people's motivation to exercise.

The effects on cognitive health are less often recognized, so it is worthwhile to learn about these benefits from experts. •

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



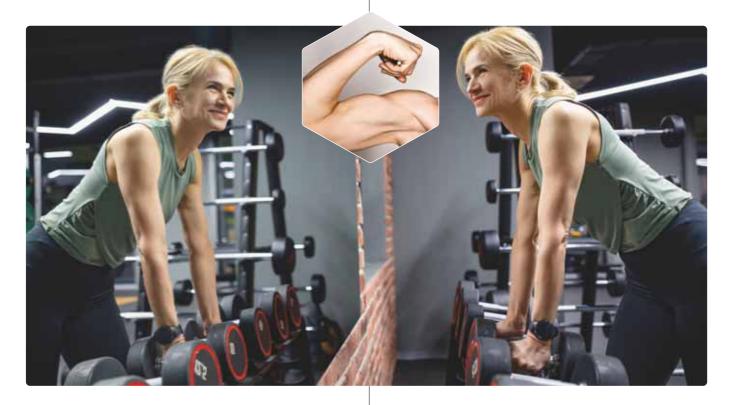


RHONDA PATRICK, PhD TH

JOHN P. THYFAULT, PhD



ERIC RAWSON, PhD



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What are Tocotrienols?

BY LAURIE MATHENA



Tocotrienols are one of two primary forms of **vitamin E**.¹

They play key roles in fighting oxidation,^{2,3} modulating immune function,⁴ combatting skin aging,⁴ and more.

While **tocopherols** are the wellknown form of vitamin E, research has shown that **tocotrienols** carry greater antioxidant potential.⁵

Research further indicates that **tocotrienols** can help combat aging by blocking DNA damage,^{4,6} and they promote healthy aging by supporting immune functions,^{7,8} and improving cholesterol values^{9,10} and bone biomarkers.³

Five Effects of Tocotrienols

Tocotrienols come in four varieties: alpha-tocotrienol, beta-tocotrienol, gamma-tocotrienol, and delta-tocotrienol.¹¹

These tocotrienol forms of vitamin E provide a variety of anti-aging and health-supporting effects.

Below are five benefits, as demonstrated primarily in **human** studies:

1. Tocotrienols may protect against DNA damage.

A clinical trial in elderly people has suggested a beneficial effect of tocotrienols against DNA damage,⁶ which is an underlying factor in many aging processes.

In this human study, 64 elderly participants were randomized to receive either a **160 mg** tocotrienol supplement or a **placebo**, daily for six months. At the end of six months researchers found total DNA damage decreased significantly among the **tocotrienols** group compared to the **placebo**.

The ability to reduce DNA damage was likely due to antioxidant and signaling properties of tocotrienols either <u>lowering</u> **DNA damage** or improving repair.⁶

2. Tocotrienols could reduce the risk of cardiovascular disease in those with poor kidney function.

Elevated triglycerides and low levels of HDL (good) cholesterol are risk factors for cardiovascular disease.¹² In one study, tocotrienols were shown to help improve levels of both factors in patients with advanced kidney disease.

In patients undergoing dialysis for **kidney failure**, supplementation with a combination vitamin E supplement

containing tocotrienols (**180 mg**) and tocopherols (**40 mg**) resulted in a drop in triglyceride levels of **33 mg/dL** after 12 weeks and **36 mg/dL** after 16 weeks. Levels of HDL ("good") cholesterol also increased.⁷

3. Tocotrienols could improve bone health.

A systematic review of preclinical studies suggested that tocotrienols could be useful in conditions characterized by excessive bone loss.¹⁰

In a separate study, a placebocontrolled clinical trial, the impact of supplementing with tocotrienols was evaluated in 89 postmenopausal women with **osteopenia** (a decrease in bone density that is less severe than osteoporosis). Results were measured in terms of biomarkers of bone metabolism in blood and urine.

Participants were randomized into three groups to receive daily:

- Placebo
- Low dose tocotrienols 430 mg
- High dose tocotrienols 860 mg

Blood and urine samples were collected at the beginning of the study and after 6 and 12 weeks. After 12 weeks, supplementation decreased markers of bone resorption (the breakdown of bone) and improved markers of bone turnover rate (the replacement of <u>new **bone**</u>) compared to placebo. The high and low doses appeared to be equally effective at improving the status of the bone biomarkers.⁹

4. Tocotrienols may help manage metabolic health.

In individuals with pre-diabetes, supplementation with **delta-tocotrienol (300 mg)** for 12 weeks led to significantly greater reductions in fasting plasma glucose, glycosylated hemoglobin A1C, insulin, and HOMA-IR (an indicator of insulin resistance and pancreatic beta cell function), compared to placebo.¹³

The researchers concluded that supplementation with delta-tocotrienol significantly improves glycemic control in pre-diabetics.



WHAT ARE TOCOTRIENOLS?

And in type II diabetics who were using anti-diabetic drugs, taking **250 mg** of delta-tocotrienol once daily for six months led to improvements in markers of glycemic control, inflammation, oxidative stress, and miRNA expression.¹⁴

5. Tocotrienols can help modulate immune response.

Rheumatoid arthritis (RA) is an autoimmune disease that attacks joints. In RA, the immune system attacks healthy tissue, causing inflammation and damage, leading to pain and tissue destruction in joints.

Cell studies have shown that tocotrienols help mitigate the bonedestructive processes that contribute to rheumatoid arthritis by decreasing the production of proteins involved in excess osteoclast activation.

Tocotrienols also decreased the differentiation of pro-inflammatory cells, called **Th17 cells**.² Th17 cells have been implicated in the development of many autoimmune diseases and inflammation.¹⁵

A different type of immune dysfunction can happen when an aging immune system has a weak response to a vaccine, resulting in diminished stimulation of immunity, and thus less protection from the immunization.

In one placebo-controlled clinical trial, participants were randomly assigned to receive supplementation with **400 mg** of mixed tocotrienols and tocopherols daily for two months or placebo, to evaluate the effects of the supplement on immune response. Participants' blood samples were evaluated at the beginning of the study and on days 28 and 56. They received the tetanus vaccine on day 28. The supplemented group showed a significantly **enhanced** production of **immune cells** and proteins compared with the **placebo** group.¹⁶ By bolstering the immune system, these forms of vitamin E may potentially enhance immune response to vaccines, improving their efficacy.

Summary

As potent antioxidants, tocotrienols have benefits throughout the entire body.

Studies show that *tocotrienols* support **DNA repair**.

In human studies, tocotrienols have demonstrated benefits in the areas of heart disease risk factors, immune regulation, metabolic health, and biomarkers of bone health. •

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

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Tart Cherry with **CherryPURE®** matches the anthocyanin dose used in clinical trials.2,5

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Watercress

BY LAURIE MATHENA



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The Centers for Disease Control and Prevention has a list called "Powerhouse Fruits and Vegetables" that rates the foods most strongly associated with reducing the risk of chronic disease.

Watercress tops the list with the *highest nutrient density* score of 100.

It earned this number-one spot because it has the greatest bioavailability of 17 different key nutrients, including protein, calcium, iron, vitamins A, B6, B12, C, D, E, K, and others.¹ When compared to 12 other cruciferous vegetables, watercress was found to be one of the highest in phenols and the ability to neutralize free radicals.² Another study identified 132 flavonoid metabolites among four varieties of watercress.³

Traditionally, watercress was used as a remedy for high blood pressure, high cholesterol, high blood sugar, and conditions ranging from arthritis to bronchitis to scurvy.⁴

It also has well-documented antibacterial, anticancer, and anti-inflammatory properties, as well as protective effects for the heart, liver, kidneys, and more.⁴

One study showed that consuming watercress every day for eight weeks was associated with reduced DNA damage and increased concentrations of carotenoids. The researchers concluded that by decreasing damage to DNA and modulation of antioxidant status, consuming watercress could potentially contribute to a reduced risk of cancer.⁵

Like other cruciferous vegetables, watercress contains **glucosinolates**, which are plant compounds that are activated to a range of bioactive compounds including isothiocyanates and sulforaphane.

In animal and cell studies, these active glucosinolates have demonstrated actions against breast, colorectal cancer,^{4,6} prostate cancer,^{4,7} and skin cancer.⁸

In a study of human colon cancer cells, watercress extract was found to exert protective effects against three different stages of the cancer process.⁹

Watercress extract has also been shown to reduce liver injury that occurs as a result of arsenic, gamma radiation, and cholestatic hepatic injury.⁴

Watercress is as versatile as it is nutritious. It can be consumed in salads, tossed into smoothies, placed atop a sandwich, added to stir fries and omelets, and much more.

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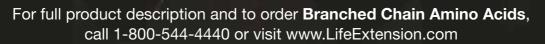
BCAAs are not produced by the body and are considered *essential*.

In one clinical study, **BCAA** supplementation was shown to reduce muscle-related soreness and accelerate muscle recovery after exercise, compared to placebo.³

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

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Cancer Treatment Update



Over the past 40 years, Dr. Gary Onik has created and implemented multiple methods to detect and treat challenging malignancies.

And when Dr. Onik *himself* was faced with metastatic prostate cancer, he successfully used his own technique.

Five years later, Dr. Onik has personally celebrated something he has given to hundreds of patients before him—another anniversary of being *cancer-free*.

A Novel Cancer Vaccine

Dr. Onik was diagnosed with metastatic prostate cancer in 2018.

"I had prostate cancer with a very high PSA, and eventually I was going to die from it," said Dr. Onik. "I refused to go on hormone treatment that would chemically castrate me. Instead, I knew of something else that could help: my own treatment."

Three years earlier, Dr. Onik had pioneered a new therapy called intra-tumor immunotherapy. Or, as Dr. Onik calls it, the *first* cancer vaccine of its kind.

Intra-tumor immunotherapy involves freezing a small portion of the tumor in a special way, which releases tumor proteins that the immune system can recognize. This is different from traditional cryosurgery, where freezing kills the tumor completely. The tumor is then directly injected with a checkpoint inhibitor* drug.¹

"We treat one small area of one tumor. After that, the patient's immune system can recognize that tumor, go to other sites where metastatic tumors reside, and often kill those tumors as well," said Dr. Onik. "We only have to do a procedure on one tumor, and all of them often go away."

This patented process arms the immune system to create its own cancer vaccine out of the patient's tumor <u>without</u> the side effects of *systemic* **checkpoint inhibitor** drugs or **CAR T****.

While Dr. Onik himself had successfully treated many cancer patients using his intra-tumor immunotherapy, no one else knew how to perform the procedure when he received his own cancer diagnosis.

But Dr. Onik wasn't fazed by this roadblock.

Dr. Onik decided to have spinal anesthesia so that he could be awake to guide a colleague through the procedure.

"He thought I was out of my mind," laughed Dr. Onik.

But eight weeks and two procedures later, Dr. Onik was *cancer-free*.

"On December 4, I reached my five-year anniversary with no meta-static disease," said Dr. Onik.

40% Success Rate

Dr. Onik's success story has been repeated in patients whose lives have been saved by his innovative cancer discoveries.

One of the first patients to undergo intra-tumor immunotherapy was Joe Lee, who was dying from metastatic prostate cancer. After undergoing a radical prostatectomy, the cancer had recurred, and he had tumors throughout his body.

"Lee was going to hospice. He only had weeks to live because he was essentially bleeding to death from a tumor invading his bladder," said Dr. Onik.

He had a dramatic response to intra-tumor immunotherapy.

After the first month, Lee's PSA went down by almost two-thirds. After the second month, his tumors vanished.

Nine years later, Lee remains cancer-free.

Dr. Onik has since treated nearly 200 patients with every kind of tumor using intra-tumor immunotherapy.

A preliminary retrospective analysis of 27 patients showed that this treatment has a complete response of **40%** in metastatic cancers including prostate, bladder, colon, and breast.² A complete response means that all signs of cancer have disappeared in response to treatment.

"These results are unheard of in patients previously deemed untreatable—and this is just the beginning," said Dr. Onik.

Dr. Onik is currently working with Nova Southeastern University on sophisticated immune tests to identify which patients respond to the immune therapy and which do not.

Many types of cancers respond to intra-tumor immunotherapy.

A Track Record of Success

Dr. Onik has been revolutionizing the cancer industry since his days in radiology residency training in 1982, when he pioneered a new approach to cancer treatment called **image**guided tumor ablation.

This radical new approach utilized ultrasound guidance in real-time to allow the doctor to guide a probe directly into the tumor, and then to destroy it with either freezing or heating. The tumor is left in place to be removed naturally by the body.

This procedure is especially useful for treating liver cancers that can't be surgically removed (called unresectable tumors) due to their location.

"Image-guided tumor ablation changed that scenario. Finally, we had a method that could reliably destroy a tumor that couldn't be surgically removed or destroyed by radiation or chemotherapy," said Dr. Onik. "Patients with these unresectable tumors had no hope. Since then, data has shown that by using liver cryosurgery, we could benefit many patients."

Marsha Sawyer was one of those patients.

- * Some of the checkpoint inhibitor drugs that Dr. Onik injects directly into the tumor include pembrolizumab (Keytruda®) and ipilimumab (Yervoy®). These drugs can cause serious side effects when systemically administered, but not when injected directly into a tumor.
- ** CAR T-cell therapy, or chimeric antigen receptor therapy, is a type of immunotherapy that helps the immune system identify and destroy cancer cells. It's a complex treatment that can only be performed at registered hospitals with specialized healthcare professionals.

At only 33 years old, this mother of two young children was diagnosed with a rare form of liver cancer called hepatic leiomyosarcoma. She was told that her cancer was inoperable and **100%** fatal.

Dr. Onik performed liver cryosurgery using image-guided tumor ablation on Marsha in 1987. Now, 37 years later, she is alive and cancerfree.

Many more followed, with overwhelmingly positive results.

"At five years after the procedure, the majority of patients who have undergone cryosurgery for liver cancer have no evidence of disease," said Dr. Onik. "This procedure is done tens of thousands of times every year. It's a part of the cancer treatment landscape now."

Prostate Cancer

Another innovation of Dr. Onik's that is widely used today, called image-guided focal ablation, has been shown to improve disease-free survival in prostate cancer while dramatically reducing side effects.

Until recently prostate cancer was treated as if the whole gland was involved, either by irradiation, freezing, or complete removal. All of these treatments come with complications like incontinence and impotence.

Adding insult to injury, in approximately **30%** of cases, *the cancer returns anyway*.³

Dr. Onik improved prostate cancer treatment in two ways: first by creating 3D prostate mapping, a new biopsy technique that is more accurate than the traditional biopsy, and second, by utilizing image-guided focal ablation to selectively destroy the cancer while leaving the rest of the prostate unharmed. A study published in the *Journal* of *Men's Health* followed 70 men who underwent optimized focal therapy to treat their prostate cancer.⁴

Maintaining potency and preventing incontinence were the main concerns. After 10 years, overall disease-free survival was **89%**. There was <u>no</u> urinary incontinence after the first treatment and **94%** of the study participants remained potent.

Focal therapy is also effective in men who have *recurrent* prostate cancer whose options would otherwise be limited to radical prostatectomy, chemical castration chemotherapy and/or radiation.

The treatment has also been found to be effective in liver, skin, lung, breast, and head and neck cancers.

Working Toward FDA Approval

Dr. Onik's goal is to achieve the same level of widespread integration with intra-tumor immunotherapy as he has had with image-guided tumor ablation and focal therapy.

He is working to obtain funding for clinical trials. After that, he hopes to obtain a breakthrough designation from the FDA. This is a process that fast-tracks the development and review of treatments that can save lives.

While each individual component of the therapy is approved by the FDA, the novel combination of methods utilized in intra-tumor immunotherapy is not.

Because of that, insurance companies don't cover the procedure, and as of now, only Dr. Onik and a handful of doctors he has trained are capable of performing it. Without insurance coverage, anyone electing to undergo intra-tumor immunotherapy will pay somewhere in the range of \$100,000.

Dr. Onik is optimistic that intratumor immunotherapy could receive approval in as little as three years.

"Right from the very beginning, we were treating patients that nobody else could treat," said Onik. "We were offering hope, and that's what we're continuing to offer now." •

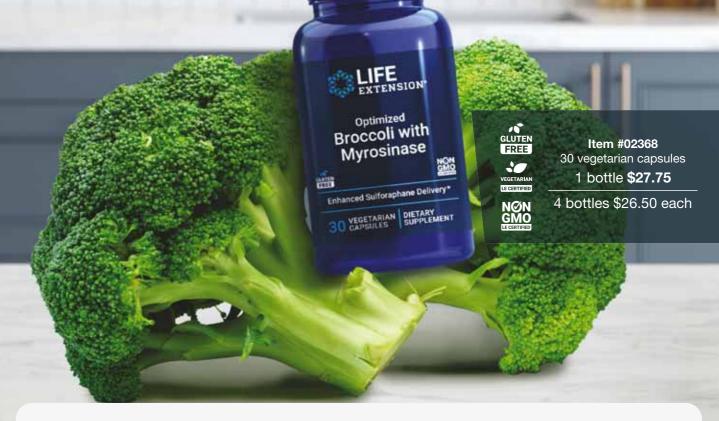
If you have any questions on the scientific content of this article, please call a **Life Extension** Wellness Specialist at 1-866-864-3027.

Anyone interested in utilizing any of the treatments mentioned in this article should contact Dr. Onik's office by visiting https://garyonikmd.com/contact/ or calling 561-527-2380.

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Many of broccoli's benefits come from **sulforaphane**—a compound that is *activated* when the plant is cut or chewed.¹⁻³

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- 00882 DHEA 50 mg, 60 capsules
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- 02368 Optimized Broccoli with Myrosinase
- 00302 Pregnenolone 50 mg, 100 capsules
- 00700 Pregnenolone 100 mg, 100 capsules
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- 01708 Reishi Extract Mushroom Complex
- 01906 Standardized Cistanche
- 01561 Zinc Lozenges

INFLAMMATION HEALTH SUPPORT

- 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™
- 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
- 56886 Restore Activ Joint Muscle & Tissue
- 01203 Specially-Coated Bromelain
- 00407 Super Bio-Curcumin® Turmeric Extract

JOINT SUPPORT

- 02238 ArthroMax[®] Advanced NT2 Collagen[™] & AprèsFlex[®]
- 00965 Fast-Acting Joint Formula
- 02430 Fast Acting Relief
- 00522 Glucosamine/Chondroitin Capsules
- 02420 Glucosamine Sulfate
- 02424 Joint Mobility
- 01600 Krill Healthy Joint Formula
- 02529 Lower Back Relief
- 00451 MSM (Methylsulfonylmethane)
- 02231 NT2 Collagen™

KIDNEY & BLADDER SUPPORT

00862 Cran-Max[®] Cranberry Whole Fruit Concentrate
01424 Optimized Cran-Max[®]
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
02240C	Anti-Alcohol Complex
01651	Calcium D-Glucarate
01571	Chlorophyllin
02402	FLORASSIST [®] Liver Restore [™]
02521	Glutathione
01541	Glutathione, Cysteine & C
01393	HepatoPro
01608	Liver Efficiency Formula
01522	Milk Thistle • 60 veg capsules
01534	N-Acetyl-L-Cysteine
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
- 02401 GEROPROTECT[®] Stem Cell
- 02211 Grapeseed Extract
- 02527 Healthy Aging Powder
- 00954 Mega Green Tea Extract (decaffeinated)
- 00953 Mega Green Tea Extract (lightly caffeinated)
- 01513 Optimized Fucoidan with Maritech® 926
- 02230 Optimized Reservatrol Elite™
- 01637 Pycnogenol® French Maritime Pine Bark Extract
- 02210 Resveratrol Elite[™]
- 02301 Senolytic Activator®
- 01208 Super R-Lipoic Acid
- 01919 X-R Shield

LUNG HEALTH

02512 Healthy Lungs

MEN'S HEALTH

- 02209 Male Vascular Sexual Support
- 00455 Mega Lycopene Extract
- 02306 Men's Bladder Control
- 02515 Men's Vitality Packs
- 01789 PalmettoGuard® Saw Palmetto and Beta-Sitosterol
- 01790 PalmettoGuard® Saw Palmetto/Nettle Root Formula and Beta-Sitosterol
- 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

MOOD & STRESS MANAGEMENT

- 02519 Ashwagandha Plus
- 02434 Calm-Mag
- 02312 Cortisol-Stress Balance
- 00987 Enhanced Stress Relief
- 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
- 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
- 02428 Whole Food Multivitamin

NERVE & COMFORT SUPPORT

- 02202 ComfortMAX[™]
- 02303 Discomfort Relief

PERSONAL CARE

Hair, Skin & Nails Collagen Plus Formula
Life Extension Toothpaste
Venotone

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
02505	FLORASSIST [®] Probiotic Women's Health
SKIN	CARE

SKIN CARE

02423	Daily Skin Defense
01938	Shade Factor™
02129	Skin Care Collection Anti-Aging Serum
02130	Skin Care Collection Day Cream
02131	Skin Care Collection Night Cream
02096	Skin Restoring Ceramides
02528	Vegan Pro Collagen

SLEEP

- 01512 Bioactive Milk Peptides
- 02300 Circadian Sleep
- 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
- 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 tabs
- 01721 Optimized Tryptophan Plus
- 01445 Quiet Sleep Melatonin 5 mg, 60 veg capsules
- 02502 Rest & Renew
- 02526 Serene Sleep

VITAMINS

- 01533 Ascorbyl Palmitate
- 00920 Benfotiamine with Thiamine
- 01945 BioActive Complete B-Complex
- 00102 Biotin
- 00084 Buffered Vitamin C Powder
- 02229 Fast-C® and Bio-Quercetin®
- 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
- 00373 No Flush Niacin
- 01939 Optimized Folate (L-Methylfolate)
- 01217 Pyridoxal 5'-Phosphate Caps
- 01400 Super Absorbable Tocotrienols
- 02334 Super K
- 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[®] 60 veg tablets
- 02227 Vitamin C and Bio-Quercetin® 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
- 02207 AMPK Metabolic Activator
- 02504 Body Trim and Appetite Control
- 02478 DHEA Complete
- 01432 Optimized Saffron
- 02511 Thermo Weight Control
- 02509 Waistline Control™

WOMEN'S HEALTH

- 01942 Breast Health Formula
- 02534 Estrogen Balance Elite
- 01894 Estrogen for Women
- 02204 Menopause Relief
- 02319 Prenatal Advantage
 - 01649 Soy Isoflavones
 - 02513 Women's Bladder Support

THINK ZINC FOR IMMUNE HEALTH

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.



Item #01813 50 mg • 90 vegetarian capsules

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



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.

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

OptiZinc[®] is a Lonza trademark, registered in the USA.

SMART

BIOACTIVE FORMS OF VITAMIN B12

B12 Elite provides both:

ADENOSYLCOBALAMIN

- Active in brain cell mitochondria.
- Supports nerve cell function.
- Supports cellular energy production.

METHYLCOBALAMIN

- Supports brain cell function.
- Promotes red blood cell production.
- Helps maintain healthy homocysteine levels.

Dissolve in the mouth or chew one vegetarian **lozenge** daily.

BODY & BRAIN



B12 Elite

0

Two Bloactive Forms for Brain & Body* 60 LOZENGES SUPPLEMENT



Item #02419 60 vegetarian lozenges 1 bottle **\$8.25** 4 bottles \$7.50 each

For full product description and to order **B12 Elite**, 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.



The Science of a Healthier Life®

PO BOX 407198 FORT LAUDERDALE, FLORIDA 33340-7198







7 WHEN VITAMINS BECAME LEGAL

Thirty years ago, Congress **prohibited** the **FDA** from censoring truthful, non-misleading information about dietary supplements, saving countless lives.

22 HELP YOUR HEART PUMP BETTER

In a **clinical trial**, a plant extract *improved* the heart's **pumping ability**, *increased* **ejection fraction** and *reduced* physical **fatigue** by **23%**.

34 DRY EYE SYNDROME: SUSTAINED RELIEF

Dry eyes are annoying and can lead to permanent eye damage. A berry extract boosts the body's production of real tears by a clinically documented **89%**.

44 MELATONIN'S POTENTIAL ANTI-CANCER EFFECTS

Studies show that **melatonin**, when used with standard cancer treatment, *improves* **survival** rates while *reducing* chemo **side effects**.

56 EXERCISE AND HEALTH: CONFERENCE PRESENTATIONS

Recent exercise conference presentations cover **cardio-respiratory fitness** for longevity, **metabolic flexibility** for aging, and the benefits of **creatine**.

63 WHAT ARE TOCOTRIENOLS?

This form of **vitamin E** helps protect against **DNA damage**, and improves heart and bone health markers, while enhancing immune response and blood sugar control.



