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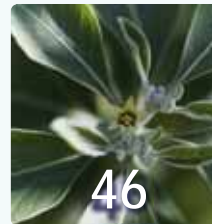
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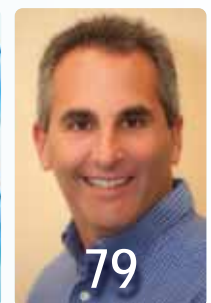
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Why Vitamin Studies Sometimes Fail



WILLIAM FALOON

A study published in **2020** evaluated **vitamin K** and **vitamin D** status in a large group of people, average **age 70**.¹

Over a 17-year period the researchers found:

- A death rate of **68.2%** in the **low vitamin K** and **low vitamin D** group.
- Fewer deaths (**38.6%**) in the normal **vitamin D** and normal **vitamin K** group.

This translates into a **60% increased mortality risk** in the **low vitamin D** and **low vitamin K** group after adjusting for variables such as age and glycemic control.¹

This 2020 published report describes mechanisms by which the body needs ample levels of **vitamin D** and **vitamin K** to derive their benefits.

What struck me about this study is how it pulls together conflicting findings about the disease-preventing potential of **vitamin D**.

Studies that **fail** to show robust benefits might involve population groups that are **deficient** in **other** nutrients required for **vitamin D** to function, such as **vitamin K** and **magnesium**.

Most **Life Extension**[®] readers supplement with these complementary nutrients, but much of the public remains deficient in **magnesium**, with less-than-optimal intake of **vitamin K**.



A meta-analysis of 84 articles published in **2019** reported **reductions** in **all-cause mortality** in people with **higher** blood levels of **25-hydroxyvitamin D**.²

Another meta-analysis of 21 randomized clinical trials published the same year did not show significant longevity benefits using vitamin D supplements.³

In **2007**, a randomized placebo-controlled study found a **60% reduced** risk for developing **any cancer** in those supplementing with **vitamin D** and **calcium**.⁴

When cancers diagnosed the first year were excluded from this **2007** study, the **overall cancer risk** was **reduced** by about **77%**.⁴

The **2007** study received widespread media coverage and led more Americans to supplement with **vitamin D**. Other studies, however, did not find the same cancer rate reductions.

These conflicting data sets about **vitamin D** caused some doctors to discredit its lifesaving potential. Others said more research is needed before **higher**-potency vitamin D supplementation is recommended.

Much of the public remains confused.

Putting the Pieces Together

Studies published in the 2003-2007 period suggest a synergistic effect of vitamins **D** and **K** on **cardiovascular** health.⁵⁻⁸

Calcifications of coronary **arteries** and **valves** are common causes of **heart disease**.^{9,10}

Vitamin D upregulates a protein (matrix GLA)¹¹ that is a powerful inhibitor of **vascular calcification**.

The upregulated **matrix GLA protein** then requires **vitamin K** to activate into **calcium-blocking** mode.

Deficiency of either **vitamin D** or **vitamin K** prevents proper activation of this calcium-blocking protein, which leads to **vascular calcification**.¹²

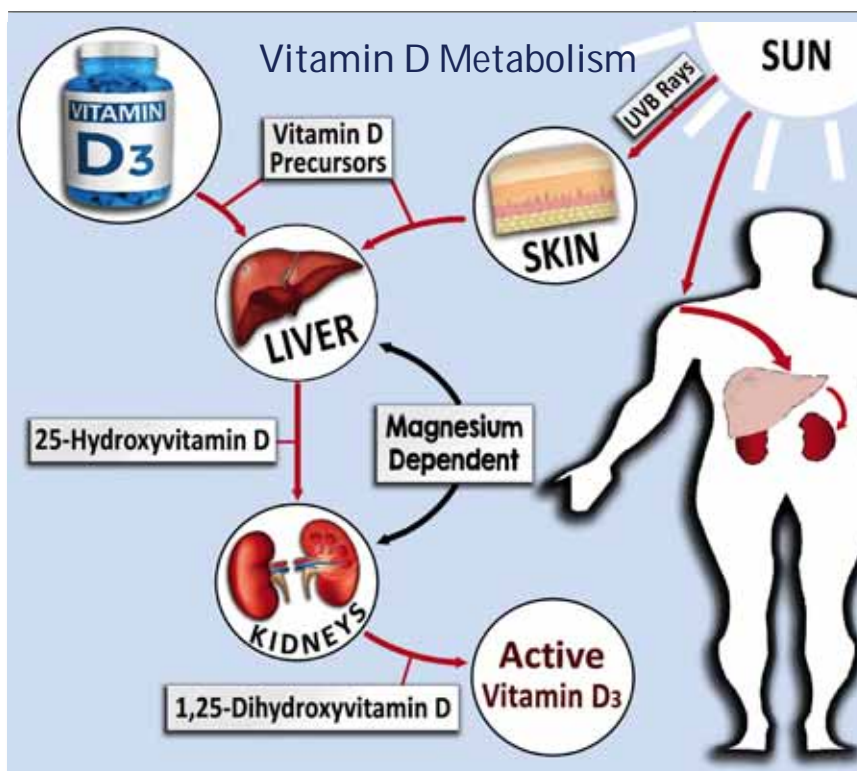
The introduction of this editorial described a **2020** published study showing a statistically significant **60% increased mortality risk**, after adjustment for age, gender, and glycemic control, in people with **low vitamin D+ low vitamin K** status.¹

The authors of this study emphasized the synergistic effects of vitamin D and vitamin K and concluded their paper stating:

“Future studies should investigate whether vitamin D and K supplementation could help improve cardiovascular health and decrease cardiovascular disease risk.”¹

We at **Life Extension**® partially concur with this recommendation but opine that *greater* synergistic benefits might occur if supplemental **magnesium** is also included.





Conversion Steps Needed To Obtain Active Vitamin D

Magnesium is involved in the conversion of **vitamin D** from dietary supplements and/or sunlight to a biologically active form.

Vitamin D from sunlight or supplements is converted in a **magnesium-dependent enzymatic** reaction to *25-hydroxyvitamin D* in the liver.

It then converts to its biologically active *1,25-dihydroxy-vitamin D* form in the kidneys via a **magnesium-dependent enzymatic** reaction.

Activated vitamin D (1,25-hydroxyvitamin D) is transported throughout the body in the blood via **vitamin D-binding protein**, for which **magnesium** is a cofactor.

Magnesium Activates Vitamin D

Magnesium activates over 300 enzymes in the body, including **enzymes** needed for **vitamin D** to become **functional**.¹³⁻¹⁵

Optimal benefits of **vitamin D** might not be achieved without adequate **magnesium**.

That's because the biological **activity** of vitamin D is dependent on **magnesium**!

When you swallow a capsule of **vitamin D**, it is first converted in the liver into **25-hydroxyvitamin D**, and then further transformed in the kidneys into biologically active **1,25-dihydroxyvitamin D**.¹⁵ (See graphic above.)

The transformation into **activated vitamin D** that occurs in the **liver** and **kidneys** is required, whether you obtain your vitamin D from sunlight, food, or supplements.

Both **liver** and **kidney** enzymatic conversions of vitamin D are **magnesium-dependent**. This means that without adequate **magnesium**, people might not derive optimal benefits of vitamin D because it will not convert into its **active** form.

The major carrier of vitamin D in blood throughout the body is **vitamin D-binding protein**. The **activity** of vitamin D-binding protein is also a **magnesium-dependent** process.

The graphic above depicts how **magnesium** is essential for **vitamin D** to activate and be transported throughout the body.

Researchers continue to explore the degree of **magnesium deficiency** that has the greatest negative effect on **vitamin D activation** in the body.^{16,17}

Widespread Magnesium Deficits

It is estimated that the magnesium content in various food and vegetables is **25%** to **80%** lower compared with the levels before **1950**.¹⁸

Today's drinking water contains little or no magnesium.

Approximately **64%** of men and **67%** of women in the U.S. have inadequate dietary intake of magnesium.

Among those above age 71, roughly **81%** of men and **82%** of women have inadequate dietary intake of **magnesium**.^{19,20}

Inadequate magnesium levels have been linked with an increased risk for cardiovascular disease, including stroke, coronary heart disease, heart failure, arrhythmia, and death.^{21,22}

Higher blood levels of **magnesium** are associated with a lower cardiovascular disease risk.²²



Are Vitamin D Studies Influenced by Magnesium Intakes?

In the conventional medical setting where **vitamin D** is used to treat rickets, **magnesium supplementation** was shown to improve vitamin D status.²³⁻²⁵

In observational studies where **vitamin D deficiency** was associated with increased cardiovascular mortality risk, consumption of **magnesium** yielded favorable results.²⁶

The activities of **vitamin D-converting enzymes** in the liver and kidneys, along with **vitamin D-binding proteins** in blood rely on **magnesium**.

According to data from the **National Health and Nutrition Examination Survey**, higher consumption of **magnesium** was associated with a reduced risk of **vitamin D deficiency** or insufficiency.²⁶

Magnesium is an essential cofactor to transform vitamin D into its active form (1,25-dihydroxyvitamin D).

Vitamin D in turn can increase intestinal **absorption** of magnesium.

Clinical Trials Should Include all Three Nutrients

Despite this array of data, **clinical trials** often test **vitamin D** by itself.

If miraculous benefits are not found, **vitamin D** is proclaimed to have failed by the study authors and this is parroted by the media.

I wish there were a way to analyze the studies showing vitamin D's robust benefits and compare them to those that fail. It could be that the **magnesium content** of food and water in the area where studies were conducted varied widely.

Dietary intakes of **magnesium** and **vitamin K** can be unaccounted confounding factors in studies that test **vitamin D** alone.



I look forward to studies that combine **vitamin D + vitamin K + magnesium** to ascertain what degree of overall **mortality risk reduction** might occur.

These nutrients are inexpensive.

Widespread use might induce meaningful improvements in healthy longevity and lower medical expenditures faced by today's aging population.

In this month's issue...

Research into the regenerative properties of **NAD⁺** continues to yield intriguing findings. The article on page 26 describes why increasing numbers of people are using precursors like **nicotinamide riboside** to boost cellular **NAD⁺**.

Immune senescence is a widespread cause of **chronic inflammation** and inability to mount **immune responses** against pathogens and aberrant cells. Defective immune responses are a common cause of premature illness and mortality, especially in persons over age 65.

The article on page 36 describes a low-cost method of improving immune function.

Summary

The title of this editorial is:

“Why Vitamin Studies Sometimes Fail”

The succinct answer in many cases is the failure to include cofactors like **magnesium** to enable **vitamin D** to convert to its active form.

Even more intriguing is **2020** published data showing a **60% increased risk of death** in people with low vitamin D and low vitamin K status.

Life Extension[®] readers should feel vindicated that they long ago began supplementing with **vitamin D + magnesium + vitamin K**.

For longer life,



William Faloon, Co-Founder
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References

- Dal Canto E, Beulens JWJ, Elders P, et al. The Association of Vitamin D and Vitamin K Status with Subclinical Measures of Cardiovascular Health and All-Cause Mortality in Older Adults: The Hoorn Study. *J Nutr*. 2020 Dec 10;150(12):3171-9.
- Heath AK, Kim IY, Hodge AM, et al. Vitamin D Status and Mortality: A Systematic Review of Observational Studies. *Int J Environ Res Public Health*. 2019 Jan 29;16(3).
- Barbarawi M, Kheiri B, Zayed Y, et al. Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis. *JAMA Cardiol*. 2019 Aug 1;4(8):765-76.
- Lappe JM, Travers-Gustafson D, Davies KM, et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr*. 2007 Jun;85(6):1586-91.
- Bolton-Smith C, McMurdo ME, Paterson CR, et al. Two-year randomized controlled trial of vitamin K1 (phylloquinone) and vitamin D3 plus calcium on the bone health of older women. *J Bone Miner Res*. 2007 Apr;22(4):509-19.
- Braam LA, Hoeks AP, Brouns F, et al. Beneficial effects of vitamins D and K on the elastic properties of the vessel wall in postmenopausal women: a follow-up study. *Thromb Haemost*. 2004 Feb;91(2):373-80.
- Braam LA, Knapen MH, Geusens P, et al. Vitamin K1 supplementation retards bone loss in postmenopausal women between 50 and 60 years of age. *Calcif Tissue Int*. 2003 Jul;73(1):21-6.
- Kidd PM. Vitamins D and K as pleiotropic nutrients: clinical importance to the skeletal and cardiovascular systems and preliminary evidence for synergy. *Altern Med Rev*. 2010 Sep;15(3):199-222.
- Demer LL, Tintut Y. Vascular calcification: pathobiology of a multifaceted disease. *Circulation*. 2008 Jun 3;117(22):2938-48.
- Cheng HM, Wang JJ, Chen CH. The Role of Vascular Calcification in Heart Failure and Cognitive Decline. *Pulse (Basel)*. 2018 Mar;5(1-4):144-53.
- van Ballegooijen AJ, Beulens JWJ, Schurgers LJ, et al. Effect of 6-Month Vitamin D Supplementation on Plasma Matrix Gla Protein in Older Adults. *Nutrients*. 2019 Jan 22;11(2):231.
- Hou YC, Lu CL, Zheng CM, et al. Emerging Role of Vitamins D and K in Modulating Uremic Vascular Calcification: The Aspect of Passive Calcification. *Nutrients*. 2019 Jan 12;11(1):152.
- Workinger JL, Doyle RP, Bortz J. Challenges in the Diagnosis of Magnesium Status. *Nutrients*. 2018 Sep 1;10(9):1202.
- Available at: <https://lpi.oregonstate.edu/mic/minerals/magnesium>. Accessed April 19, 2021.
- Uwitonze AM, Razzaque MS. Role of Magnesium in Vitamin D Activation and Function. *J Am Osteopath Assoc*. 2018 Mar 1;118(3):181-9.
- Liu S, Liu Q. Personalized magnesium intervention to improve vitamin D metabolism: applying a systems approach for precision nutrition in large randomized trials of diverse populations. *Am J Clin Nutr*. 2018 Dec 1;108(6):1159-61.
- Dai Q, Zhu X, Manson JE, et al. Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial. *Am J Clin Nutr*. 2018 Dec 1;108(6):1249-58.
- Thomas D. The mineral depletion of foods available to us as a nation (1940-2002)--a review of the 6th Edition of McCance and Widdowson. *Nutr Health*. 2007;19(1-2):21-55.
- Qu X, Jin F, Hao Y, et al. Magnesium and the risk of cardiovascular events: a meta-analysis of prospective cohort studies. *PLoS One*. 2013;8(3):e57720.
- Kostov K, Halacheva L. Role of Magnesium Deficiency in Promoting Atherosclerosis, Endothelial Dysfunction, and Arterial Stiffening as Risk Factors for Hypertension. *Int J Mol Sci*. 2018 Jun 11;19(6).
- DiNicolantonio JJ, Liu J, O'Keefe JH. Magnesium for the prevention and treatment of cardiovascular disease. *Open Heart*. 2018;5(2):e000775.
- Rosique-Esteban N, Guasch-Ferre M, Hernandez-Alonso P, et al. Dietary Magnesium and Cardiovascular Disease: A Review with Emphasis in Epidemiological Studies. *Nutrients*. 2018 Feb 1;10(2).
- Reddy V, Sivakumar B. Magnesium-dependent vitamin-D-resistant rickets. *Lancet*. 1974 May 18;1(7864):963-5.
- Rude RK, Adams JS, Ryzan E, et al. Low serum concentrations of 1,25-dihydroxyvitamin D in human magnesium deficiency. *J Clin Endocrinol Metab*. 1985 Nov;61(5):933-40.
- Fuss M, Bergmann P, Bergans A, et al. Correction of low circulating levels of 1,25-dihydroxyvitamin D by 25-hydroxyvitamin D during reversal of hypomagnesaemia. *Clin Endocrinol (Oxf)*. 1989 Jul;31(1):31-8.
- Deng X, Song Y, Manson JE, et al. Magnesium, vitamin D status and mortality: results from US National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 and NHANES III. *BMC Med*. 2013 Aug 27;11:187.



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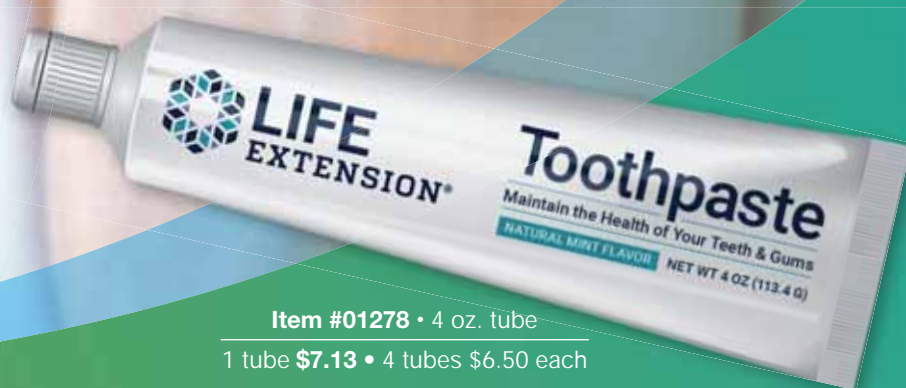
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References

1. *J Indian Soc Periodontol.* 2011 Jul;15(3):205-9.
2. *Br J Dermatol.* 2001 Oct;145(4):535-45.
3. *J Am Dent Assoc.* Jan 2013; 144(1): 21-30.
4. *J Clin Periodontol.* 1984 Oct;11(9):619-28.
5. *Ann Stomatol (Roma).* 2011 Mar-Jun; 2(3-4):10-8.

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

* If you have a thyroid condition or are taking antithyroid medications, do not use without consulting your healthcare practitioner.



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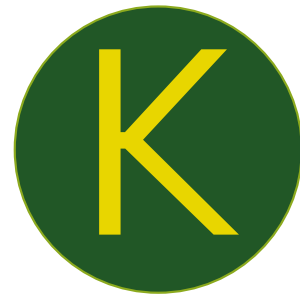


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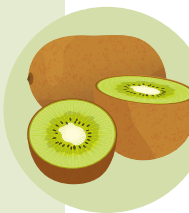


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Super K Elite provides 2 additional forms of vitamin K and even **higher** potencies of K1, MK4, and MK7. **Super K Elite** costs **60 cents** a day and provides in one capsule:

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Vitamin K2 (MK-4) (for bone & vascular health)	1,500 mcg
Vitamin K2 (MK-7) (long-acting protection)	181 mcg
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--	-------------------



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In the News



Visceral Fat Decrease Linked with *Higher* Carotenoid Levels

A study reported in *Nutrients* revealed an association between *higher* levels of **carotenoids** and a reduction in visceral **fat** area.*

The investigation included 310 men and 495 women who received an annual health examination as part of the Iwaki Health Promotion Project in Japan. Blood samples were analyzed for the carotenoids alpha carotene, beta carotene, beta cryptoxanthin, lycopene, lutein and zeaxanthin. Diet-history questionnaire responses provided information concerning food intake.

Total carotenoid levels were associated with the intake of leafy green vegetables, carrots and pumpkins, root vegetables and juice. Women's carotenoid levels were significantly higher than those of men.

Higher total carotenoid levels were associated with *decreased* visceral fat area and BMI in women, independent of fiber intake. Increased beta carotene, beta cryptoxanthin and lutein levels in women were also associated with a lower **visceral fat** area.

Editor's Note: "This suggests that consumption of a diet rich in carotenoids (especially lutein and beta-carotene) is associated with lower visceral fat area, which is a good predictor of cardiovascular disease, especially in women," the authors stated.

* *Nutrients*. 2021 Mar 11;13(3):912.

Women's Sexual Well-Being Improves with Testosterone Replacement

Women who receive testosterone hormone replacement have improved sexual function and well-being, according to a review and meta-analysis published in *The Lancet Diabetes & Endocrinology*.*

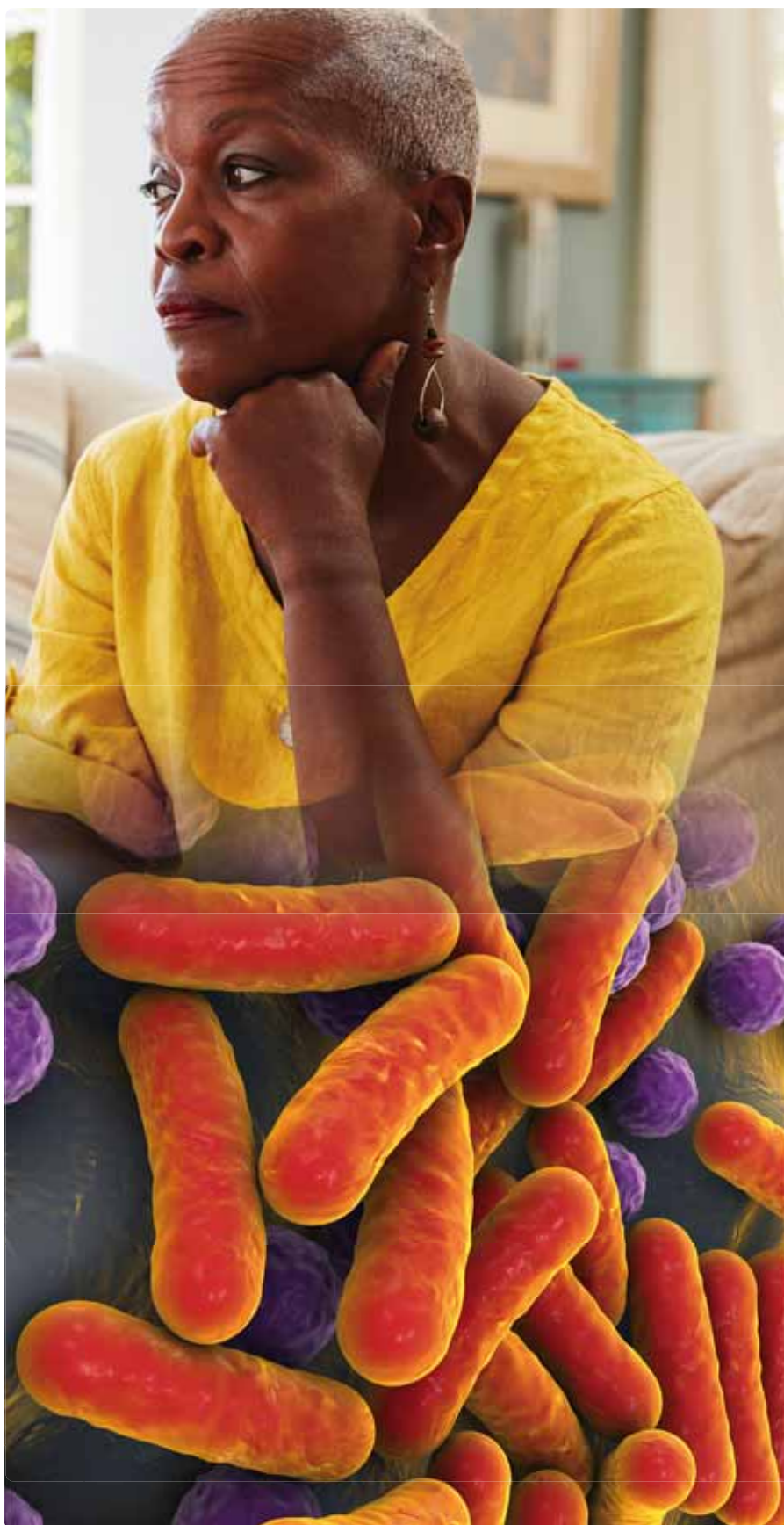
Researchers studied 46 reports regarding 36 randomized trials with a total of 8,480 female subjects (the majority of whom were postmenopausal). The trials looked at the effects of testosterone on female sexual function, compared to a placebo, or other hormone replacement.

Compared to the control subjects, women who received testosterone experienced improvements in sexual desire, arousal, responsiveness to stimuli, self-image, orgasm, and pleasure, and felt less concern and distress about sex.

Editor's Note: Women can increase their testosterone levels by using prescription **150 mcg** testosterone patches or try **15 mg** a day of DHEA that often boosts testosterone levels in women (but not much in men). DHEA is a low-cost supplement whereas testosterone patches are prescription drugs.

* *Lancet Diabetes Endocrinol.* 2019 Oct;7(10): 754-766.





Gut Microbiome Connected to Alzheimer's Disease

In an animal study, scientists identified a connection between the composition of the gut microbiome and Alzheimer's disease, according to an article published in *Scientific Reports*.*

Researchers compared wild mice with those genetically engineered to carry genes associated with Alzheimer's. They found a connection between gut composition (based on fecal pellets) and behavioral and cognitive performance in these mice.

They also observed a correlation between changes in the gut microbiome and epigenetic regulation of two genes associated with Alzheimer's disease (the apolipoprotein E and Tamm40 genes).

This means the composition of the gut microbiome could play a role in turning on genes that contribute to Alzheimer's disease. Importantly, these changes occurred in the hippocampus, the area of the brain impacted by Alzheimer's.

These findings are consistent with an observational study of people with Alzheimer's disease.

Editor's Note: "The exciting part of this is that you can manipulate the gut microbiome," said senior author Jacob Raber, MD. "We can use probiotics and see what the effect is."

* *Sci Rep* 2021 Feb 25;11(1):4678.

Ashwagandha Root Extract Boosts Cognitive Function

Ashwagandha root extract was shown to improve memory and cognitive function in people with mild cognitive impairment, according to a study published in the *Journal of Dietary Supplements*.*

This double-blind, randomized, placebo-controlled study included 50 adults over age 35 who reported having symptoms of mild cognitive impairment (such as forgetfulness, feeling overwhelmed with decision-making, and drifting thoughts).

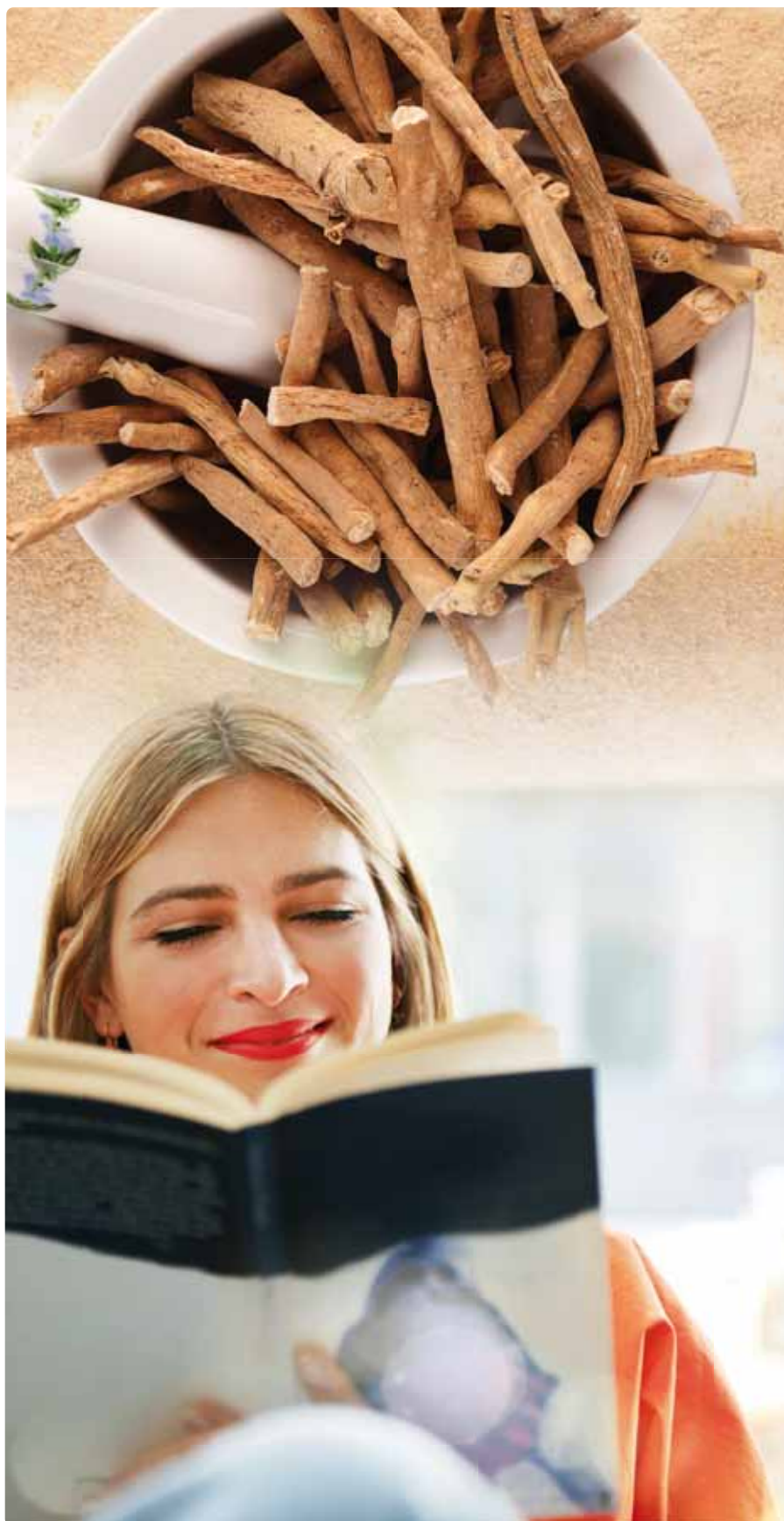
The treatment group received **300 mg** of ashwagandha root extract twice daily, and the control group received a placebo.

After eight weeks, the ashwagandha group experienced significantly greater improvements in **general memory** (recall of items such as geometric designs and faces) and **immediate memory** (the ability to recall information over a few seconds, such as a person's name or a telephone number), compared to the placebo group.

The ashwagandha group also experienced greater improvements in executive function, sustained attention, and information processing speed.

Editor's Note: The researchers concluded, "Ashwagandha may be effective in enhancing both immediate and general memory in people with mild cognitive impairment as well as improving executive function, attention, and information processing speed."

* *J Diet Suppl.* 2017 Nov 2;14(6):599-612.





Shiitake Mushrooms Boost Immunity

Eating shiitake mushrooms on a regular basis improves immune function, according to a study published in the *Journal of the American College of Nutrition*.*

For the study, 52 healthy adults between 21 and 41 years old were given a four-week supply of either **5 grams** or **10 grams** of dry shiitake mushrooms.

They cooked the mushrooms at home and consumed a serving every day as instructed.

After **four weeks**, compared to baseline, researchers observed increases in:

- **Gamma delta T cells**, thought to serve as one of the immune system's first lines of defense in epithelial and mucosal tissues,
- **NK-T** (natural killer-T) cells, a type of immune cell which promotes the activity that helps defend against infection, and
- **Secretory IgA** (sIgA) production, which protects the nasal mucosa and respiratory tract mucosal surfaces from infection.

Reductions in **C-reactive protein** (CRP) and *increases* in **anti-inflammatory cytokines** were also seen, suggesting lower **inflammation**.

The researchers concluded that regular consumption of shiitake mushrooms resulted in improved immunity.

Editor's Note: Shiitake mushrooms could also boost heart health, as they contain beta glucans, a type of fiber that can help lower cholesterol.

**J Am Coll Nutr.* 2015;34(6):478-87.

FISETIN

The Longevity Flavonoid



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

In preclinical studies, fisetin:

- Mimics effects of **calorie reduction**²
- Targets longevity pathways²⁻⁶
- Extends lifespan of mice by about **10%**⁷
- Removes **senescent** cells through **senolytic** action⁷
- Suppresses excess **mTOR** activation⁸

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

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

References

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



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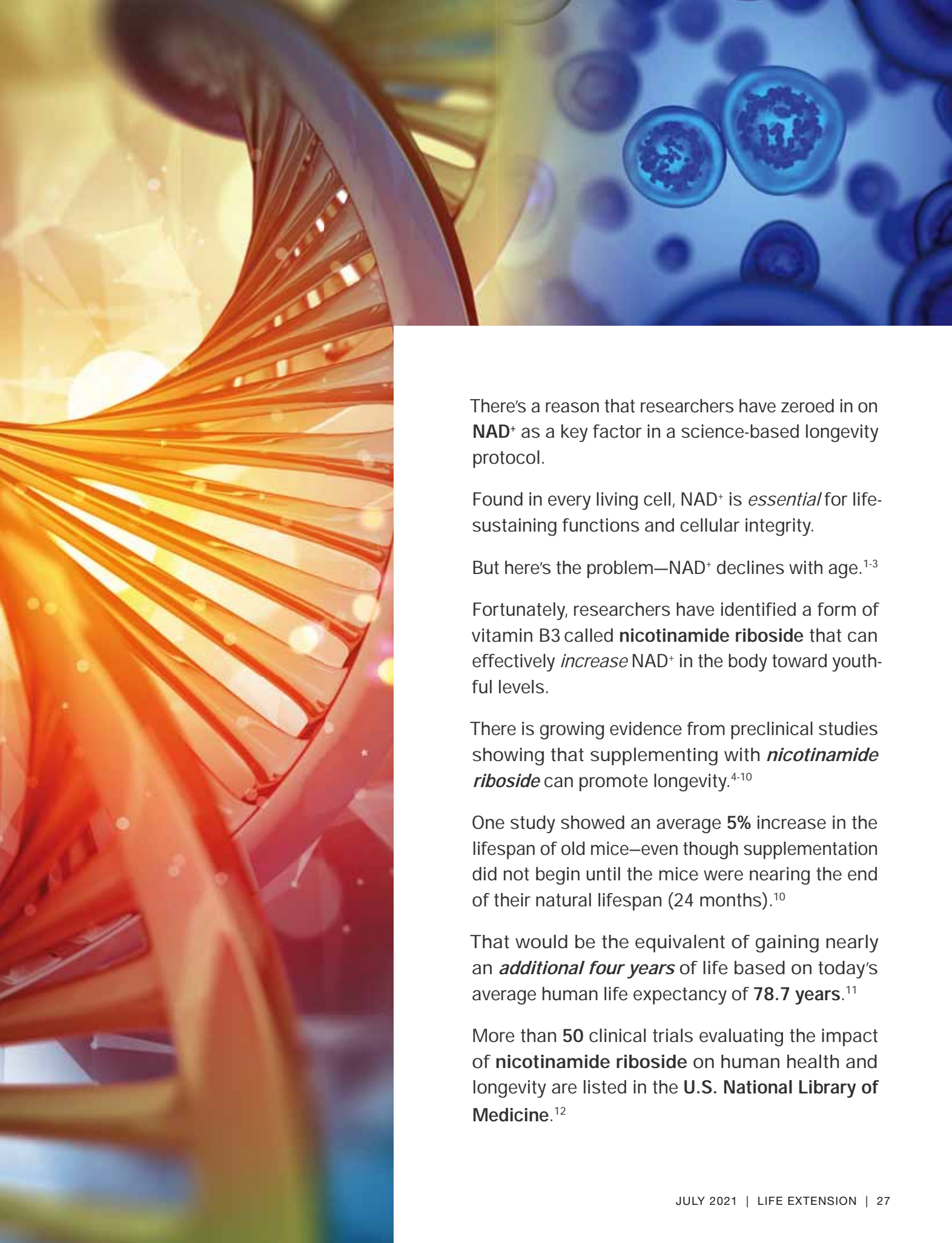
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What has Scientists Excited About NAD^+

BY JEFF SIMMONS





There's a reason that researchers have zeroed in on **NAD⁺** as a key factor in a science-based longevity protocol.

Found in every living cell, NAD⁺ is *essential* for life-sustaining functions and cellular integrity.

But here's the problem—NAD⁺ declines with age.¹⁻³

Fortunately, researchers have identified a form of vitamin B3 called **nicotinamide riboside** that can effectively *increase* NAD⁺ in the body toward youthful levels.

There is growing evidence from preclinical studies showing that supplementing with **nicotinamide riboside** can promote longevity.⁴⁻¹⁰

One study showed an average **5%** increase in the lifespan of old mice—even though supplementation did not begin until the mice were nearing the end of their natural lifespan (24 months).¹⁰

That would be the equivalent of gaining nearly an **additional four years** of life based on today's average human life expectancy of **78.7 years**.¹¹

More than **50** clinical trials evaluating the impact of **nicotinamide riboside** on human health and longevity are listed in the **U.S. National Library of Medicine**.¹²

Boosting NAD⁺ Levels

One of the problems for aging individuals trying to restore NAD⁺ levels is that it is unstable and is not effective when taken orally.

Researchers have discovered a compound called **nicotinamide riboside** that is a **precursor** to NAD⁺.

This means that taking nicotinamide riboside orally can help jump-start NAD⁺ production. Cells can then use nicotinamide riboside to produce more NAD⁺ on their own, effectively boosting levels even into older age.

In both animal and human studies, nicotinamide riboside **quickly boosts** cellular NAD⁺ levels and stimulates NAD⁺ metabolism in cells.¹³⁻¹⁵

Anti-Aging Benefits of Raising NAD⁺

A number of studies confirm that replenishing NAD⁺ levels can prevent or even *reverse* many of the changes associated with aging. It also shields against many of the chronic diseases of age.

Various lab and animal studies show that increasing NAD⁺ levels with nicotinamide riboside:

- Protects against metabolic abnormalities induced by a high-fat diet,¹⁶
- Helps preserve cognition in models of Alzheimer's disease,¹⁷⁻¹⁹

- Reduces fasting and non-fasting blood glucose in a mouse model of type II diabetes, while protecting against diabetic neuropathy and preventing fatty liver disease,¹⁵ and
- Extends lifespan.^{4,7,10}

NAD⁺ Boosts Sirtuins

In so many ways, **NAD⁺** is essential to the functioning and rejuvenation of the body.

Several important **proteins**, such as **sirtuins**, that regulate cellular repair and defenses, require NAD⁺ to function.

Sirtuins are an important target for **anti-aging** interventions.^{1,2,20-22}

Sirtuins are dependent on NAD⁺ to **function**.

NAD⁺ levels markedly **decline** with age, creating an energy deficit that decreases the body's ability to retain **youthful function**.²³

Multiple animal studies have demonstrated that **increasing sirtuin activity** leads to longer life and reduction in age-related loss of function.^{4,7,10}

Rejuvenating Stem Cells

As in humans, NAD⁺ levels drop in older mice. This leads to a *decline* in organ function, including in the ovaries.





WHAT YOU NEED TO KNOW

Boost NAD⁺ For Health and Longevity

One of the most recent studies of **nicotinamide riboside** evaluated its effect in the **ovaries** of middle-aged mice.²⁴

These older mice suffer from a loss of **ovarian follicles** (which contain the egg cells released during ovulation), poor egg quality, infertility, and frequent miscarriages or stillbirths.

A similar decline in human **reproductive function** occurs with age in women.

But when these older mice were given **nicotinamide riboside**, the health of the ovaries *and* reproductive function improved.

Ovarian follicles *increased* in number, and the mice were able to **reproduce** more easily and with a higher live birth rate. When scientists examined the ovaries, they saw markers of more youthful biology—healthier cells and improved cellular metabolism.

This improvement in organ function may be largely due to **rejuvenation of stem cells**.

In adult tissues, **stem cells** are meant to replace old, dysfunctional, and dying cells with healthy young ones. This maintains the health and youthful function of the tissue. But stem cells themselves age and stop working properly, causing the whole organ to fail.

- **Nicotinamide adenine dinucleotide (NAD⁺)** is a crucial cofactor for many different enzymes in all cells.
- NAD⁺ is *required* for the activity of **sirtuin** proteins, which help regulate metabolism and aging.
- NAD⁺ levels drop significantly with age, contributing to more accelerated aging, loss of function, and risk for chronic disease.
- **Nicotinamide riboside**, a form of vitamin B3, is a NAD⁺ precursor. Taking it orally has been found to rapidly and safely replenish bodily levels of NAD⁺.
- In many studies, nicotinamide riboside reduces markers of aging in tissues, rejuvenates organ function, revitalizes old stem cells, lowers risk for common chronic diseases, and **extends lifespan**.



Replenishing **NAD⁺ levels** with nicotinamide riboside rejuvenated muscle **stem cells** of aged mice.¹⁰

This study showed that boosting NAD⁺ improved **mitochondrial** function in muscle stem cells and inhibited stem cell senescence.

The researchers also showed that boosting NAD⁺ decreased senescence of brain and skin stem cells.

Aged stem cells from diverse tissues have been shown to be made more youthful with increased cellular NAD⁺ levels.^{25,26}

Longer, Healthier Life

Studies have consistently shown that increasing NAD⁺ levels improves **overall health** and **extends lifespan** in a range of preclinical models.

Longevity is difficult to study in humans because of our long lives. But boosting NAD⁺ has been shown to extend life in several other organisms, including yeast, worms, and mice.^{4,7,10,27}

Yeast grown with nicotinamide riboside have an increase in lifespan.⁴ In **worms**, this NAD⁺ precursor extends life by at least **10%**.⁷

In elderly **mice** the **human equivalent** of about **70 years** of age, **nicotinamide riboside** extended lifespan by roughly **5%** compared to untreated animals.¹⁰

In human terms, this is the equivalent of gaining nearly **four additional years of life** based on today's average human life expectancy of **78.7 years**.¹¹

These studies and others show why scientists and doctors are so excited about raising NAD⁺ levels as one key to anti-aging efforts, and to promoting longevity.

Summary

The compound **NAD⁺ (nicotinamide adenine dinucleotide)** plays a critical role in fighting aging and possibly preventing degenerative disease risk.

NAD⁺ is required for cellular enzymes and proteins to work properly. The **sirtuin** proteins, which are promising targets for life-extending interventions, need NAD⁺ to **function**.

NAD⁺ levels decline with advancing age.

Nicotinamide riboside, a precursor to NAD⁺, rapidly increases **NAD⁺** blood levels.

Boosting NAD⁺ to more youthful levels with **nicotinamide riboside** has been shown to prolong life and reverse loss of function in animal models.

Life Extension[®] continues to monitor ongoing trials on the impact that **nicotinamide riboside** could have on **human health** and **longevity**. •

Nicotinamide Riboside and Resveratrol

Resveratrol is a plant compound found in red grapes, red wine, and other darkly colored fruits.

Among its many benefits, it *activates sirtuins*, defender proteins linked to longer, healthier life.²⁸⁻³⁰

But resveratrol can't do this if cells are low in **NAD⁺**, which is required for sirtuins to work properly. It would be like pressing the accelerator in your car when your gas tank is empty.

The solution is to increase intake of **nicotinamide riboside** to boost **NAD⁺** levels at the same time as stimulating sirtuin activity with **resveratrol**. This combination can promote optimal sirtuin activity, which can translate to better health and greater longevity.

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

References

1. Imai S, Guarente L. NAD⁺ and sirtuins in aging and disease. *Trends Cell Biol.* 2014 Aug;24(8):464-71.
2. Johnson S, Imai SI. NAD⁺ biosynthesis, aging, and disease. *F1000Res.* 2018;7:132.
3. Zhou CC, Yang X, Hua X, et al. Hepatic NAD⁺ deficiency as a therapeutic target for non-alcoholic fatty liver disease in ageing. *Br J Pharmacol.* 2016 Aug;173(15):2352-68.
4. Belenky P, Racette FG, Bogan KL, et al. Nicotinamide riboside promotes Sir2 silencing and extends lifespan via Nrk and Urrh1/Pnp1/Meu1 pathways to NAD⁺. *Cell.* 2007 May 4;129(3):473-84.
5. Denu JM. Vitamins and aging: pathways to NAD⁺ synthesis. *Cell.* 2007 May 4;129(3):453-4.
6. Lu SP, Kato M, Lin SJ. Assimilation of endogenous nicotinamide riboside is essential for calorie restriction-mediated life span extension in *Saccharomyces cerevisiae*. *J Biol Chem.* 2009 Jun 19;284(25):17110-9.
7. Mouchiroud L, Houtkooper RH, Moullan N, et al. The NAD⁺/Sirtuin Pathway Modulates Longevity through Activation of Mitochondrial UPR and FOXO Signaling. *Cell.* 2013 Jul 18;154(2):430-41.
8. Poljsak B, Milisav I. NAD⁺ as the Link Between Oxidative Stress, Inflammation, Caloric Restriction, Exercise, DNA Repair, Longevity, and Health Span. *Rejuvenation Res.* 2016 Oct;19(5):406-15.





9. Tsang F, James C, Kato M, et al. Reduced Ssy1-Ptr3-Ssy5 (SPS) signaling extends replicative life span by enhancing NAD⁺ homeostasis in *Saccharomyces cerevisiae*. *J Biol Chem*. 2015 May 15;290(20):12753-64.
10. Zhang H, Ryu D, Wu Y, et al. NAD⁽⁺⁾ repletion improves mitochondrial and stem cell function and enhances life span in mice. *Science*. 2016 Jun 17;352(6292):1436-43.
11. Available at: https://www.cdc.gov/nchs/data/factsheets/factsheet_NVSS.pdf. Accessed December 14, 2020.
12. Available at: <https://www.clinicaltrials.gov/ct2/results?cond=&term=%22nicotinamide+ribose%22&cntry=&state=&city=&dist=>. Accessed December 15, 2020.
13. Airhart SE, Shireman LM, Risler LJ, et al. An open-label, non-randomized study of the pharmacokinetics of the nutritional supplement nicotinamide riboside (NR) and its effects on blood NAD⁺ levels in healthy volunteers. *PLoS One*. 2017;12(12):e0186459.
14. Martens CR, Denman BA, Mazzo MR, et al. Chronic nicotinamide riboside supplementation is well-tolerated and elevates NAD⁽⁺⁾ in healthy middle-aged and older adults. *Nat Commun*. 2018 Mar 29;9(1):1286.
15. Trammell SA, Weidemann BJ, Chadda A, et al. Nicotinamide Riboside Opposes Type 2 Diabetes and Neuropathy in Mice. *Sci Rep*. 2016 May 27;6:26933.
16. Canto C, Houtkooper RH, Pirinen E, et al. The NAD⁽⁺⁾ precursor nicotinamide riboside enhances oxidative metabolism and protects against high-fat diet-induced obesity. *Cell Metab*. 2012 Jun 6;15(6):838-47.
17. Gong B, Pan Y, Vempati P, et al. Nicotinamide riboside restores cognition through an upregulation of proliferator-activated receptor-gamma coactivator 1alpha regulated beta-secretase 1 degradation and mitochondrial gene expression in Alzheimer's mouse models. *Neurobiol Aging*. 2013 Jun;34(6):1581-8.
18. Fang EF, Hou Y, Palikaras K, et al. Mitophagy inhibits amyloid-beta and tau pathology and reverses cognitive deficits in models of Alzheimer's disease. *Nat Neurosci*. 2019 Mar;22(3):401-12.
19. Xie X, Gao Y, Zeng M, et al. Nicotinamide ribose ameliorates cognitive impairment of aged and Alzheimer's disease model mice. *Metab Brain Dis*. 2019 Feb;34(1):353-66.
20. Grabowska W, Sikora E, Bielak-Zmijewska A. Sirtuins, a promising target in slowing down the ageing process. *Biogerontology*. 2017 Aug;18(4):447-76.
21. Satoh A, Stein L, Imai S. The role of mammalian sirtuins in the regulation of metabolism, aging, and longevity. *Handb Exp Pharmacol*. 2011;206:125-62.
22. Watroba M, Dudek I, Skoda M, et al. Sirtuins, epigenetics and longevity. *Ageing Res Rev*. 2017 Nov;40:11-9.
23. Imai SI, Guarente L. It takes two to tango: NAD⁽⁺⁾ and sirtuins in aging/longevity control. *NPJ Aging Mech Dis*. 2016;2:16017.
24. Yang Q, Cong L, Wang Y, et al. Increasing ovarian NAD⁽⁺⁾ levels improve mitochondrial functions and reverse ovarian aging. *Free Radic Biol Med*. 2020 Aug 20;156:1-10.
25. Igarashi M, Miura M, Williams E, et al. NAD⁽⁺⁾ supplementation rejuvenates aged gut adult stem cells. *Aging Cell*. 2019 Jun;18(3):e12935.
26. Moon J, Kim HR, Shin MG. Rejuvenating Aged Hematopoietic Stem Cells Through Improvement of Mitochondrial Function. *Ann Lab Med*. 2018 Sep;38(5):395-401.
27. Fang EF, Scheibye-Knudsen M, Brace LE, et al. Defective mitophagy in XPA via PARP-1 hyperactivation and NAD⁽⁺⁾/SIRT1 reduction. *Cell*. 2014 May 8;157(4):882-96.
28. Huang JP, Hsu SC, Li DE, et al. Resveratrol Mitigates High-Fat Diet-Induced Vascular Dysfunction by Activating the Akt/eNOS/NO and Sirt1/ER Pathway. *J Cardiovasc Pharmacol*. 2018 Nov;72(5):231-41.
29. Gomes BAQ, Silva JPB, Romeiro CFR, et al. Neuroprotective Mechanisms of Resveratrol in Alzheimer's Disease: Role of SIRT1. *Oxid Med Cell Longev*. 2018;2018:8152373.
30. Kim EN, Lim JH, Kim MY, et al. Resveratrol, an Nrf2 activator, ameliorates aging-related progressive renal injury. *Aging (Albany NY)*. 2018 Jan 11;10(1):83-99.

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Immune-Boosting Properties of MEDICINAL MUSHROOMS

BY RONNIE CORTEZ



Shiitake

Mushrooms have been used medicinally around the world for centuries.

They contain compounds called **beta glucans** that are responsible for many of their health benefits, including **antiviral** and **immune-boosting** effects.¹⁻⁴

Studies of **mushroom extracts** *and* isolated **beta glucans** show that these nutrients can help bolster **immune** defenses against infectious diseases.



What Are Beta glucans?

Beta glucans are a group of polysaccharides naturally occurring in cell walls of seaweed, whole grains, fungi, and mushrooms.

Mushrooms, yeast, and other **fungi** are particularly rich in **beta glucans** because their cell walls are made up primarily of these compounds.

Beta glucans can help nourish healthy gut bacteria and augment the action of **immune cells** throughout the body.⁵



Chaga

Mushrooms as Medicine

There are thousands of species of **mushrooms**, and many have health benefits.

Three have been found to be particularly effective at supporting **immune health**.

Shiitake

Shiitake mushrooms are a staple of East Asian cuisine and have long been used in traditional Chinese medicine.

In an animal model of severe **bacterial lung infection**, shiitake mushrooms significantly decreased the number of bacteria in the lungs and improved the animals' condition.⁶

Other studies have shown **antiviral** effects against several types of viruses, both by directly inactivating them and by blocking viral replication.⁷⁻⁹

Shiitake mushrooms bolster immune defenses by increasing the number of immune system cells, including **T-cells** (which fight specific kinds of viruses) and **natural killer (NK) cells** (which can kill a wide variety of virally infected cells and tumors).¹⁰

Shiitake also boosts secretion of **antibodies** that protect the digestive tract and reduce **C-reactive protein**, a marker of harmful **chronic inflammation**.¹⁰

Maitake

Maitake mushrooms grow in various parts of the world and are commonly used in cuisine.

In preclinical studies, maitake was shown to activate immune cells such as **NK cells** and **macrophages** (which are among the *first* immune cells to fight an infection).^{11,12}

Extracts of these mushrooms also induce the secretion of **interferons**, proteins that improve the body's ability to defend against infection.¹²

Chaga

Chaga mushrooms grow primarily on birch trees in cold climates, including in northern Europe, Asia, and North America. They are powerful **immunomodulators**.

In a study of mice treated with a drug that *inhibits* **immune system** activity, chaga extract returned levels of immune cells almost back to normal.¹³ It also kept down the levels of **tumor necrosis factor**, a marker of potentially harmful inflammation.

This mushroom has been shown in various preclinical studies to have **antiviral** activity against a wide range of viruses. These include various forms of influenza, herpes, hepatitis C, the human immunodeficiency virus (HIV), and others.¹⁴⁻¹⁶

Natural Immune Support

Mushrooms contain many different compounds. But when it comes to supporting the immune system, **beta glucans** are considered their single most bioactive component.

These polysaccharide compounds can also be isolated from **yeast**.

They work by binding to receptors on an assortment of cells important for **immunity**.^{2,3} That activates pathways in the cells that boost their function and help them defend against infection and other threats.

Immune responses can be divided into two types: **innate immunity** and **adaptive immunity**.¹⁷

1. Innate immunity is the body's first line of defense. It is comprised of sentinel cells that detect and attack a wide range of different viruses and pathogens. Cells of innate immunity include macrophages, neutrophils, NK cells, and others.

2. Adaptive immunity types are the “big guns” that are brought in later to fight off *specific* threats—a particular bacteria or virus, for example—once they have been identified. This also helps the body develop **long-term immunity** to a pathogen. The most important of these cell types are **lymphocytes**, including various B-cells and T-cells.

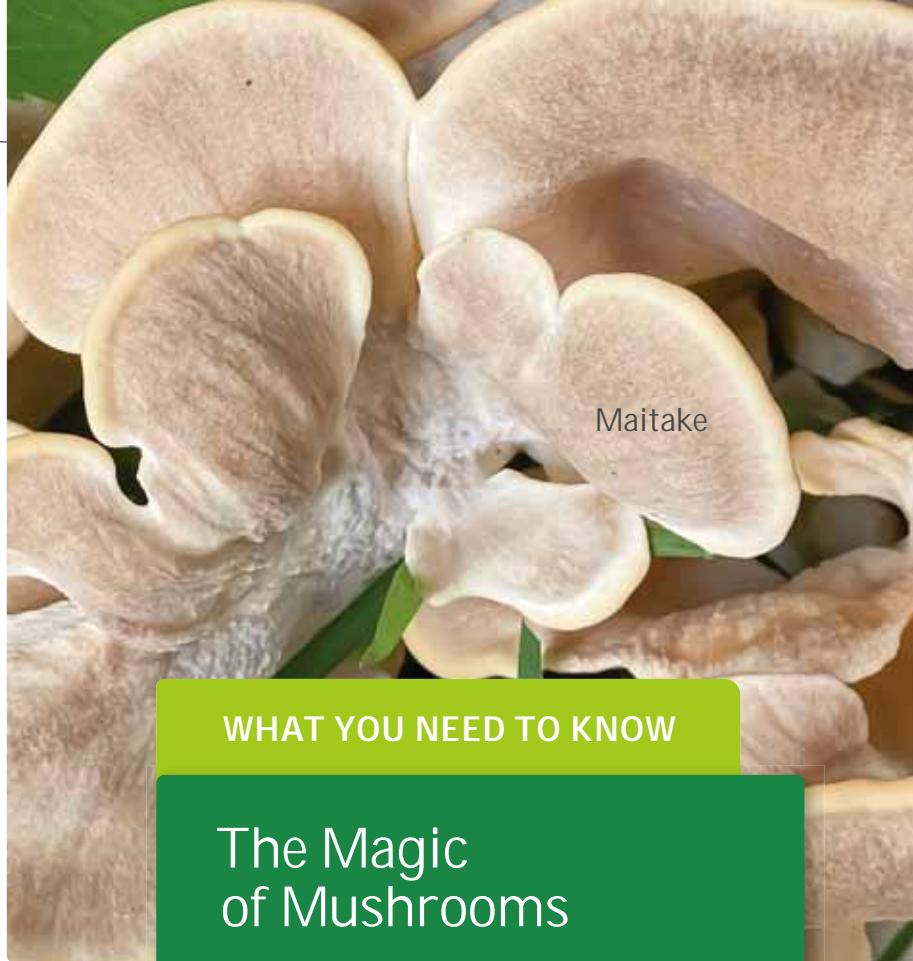
Beta glucans have a remarkable ability to activate and stimulate *both* **innate** and **adaptive immunity**.^{2,3,10,18,19}

They can also help block dangerous inflammation. For example, **endotoxin** is a compound produced by disease-causing bacteria. Endotoxin is often used to induce excess, harmful inflammation in experimental animals. Beta glucans *block* this form of inflammation.²⁰⁻²²

A Healthy Gut

A healthy **gut microbiota** (the population of intestinal microorganisms) is also critical to optimal health and fighting **infection**.

In studies, **beta glucans** and **mushrooms** have been shown to encourage the growth of healthy microbiota.^{2,23-25} That's because beta glucans serve as **pre-biotics**, a source of nutrition for beneficial **bacteria**.²



WHAT YOU NEED TO KNOW

The Magic of Mushrooms

- Various **mushrooms** have long been used for their medicinal properties.
- These medicinal mushrooms, along with **baker's yeast**, contain compounds called **beta glucans**. These nutrients are responsible for many of the health benefits of mushrooms.
- In studies, mushrooms and beta glucans help strengthen the **immune system** in several different ways, boosting healthy immune responses.
- Along with direct **antiviral** activity, this immune system enhancement helps the body defend against infection and more rapidly eliminate infections that do occur.
- A combination of **beta glucans** from **yeast** along with **shiitake**, **maitake**, and **chaga** mushrooms provides a wide range of compounds to help boost immunity.

These **prebiotics** stimulate the growth and survival of *healthy* bacteria while blocking the growth and development of *disease-causing* bacteria.²

As an added bonus, when beneficial bacteria consume beta glucans, they produce **short-chain fatty acids** as a byproduct.^{23,25} These compounds support a healthy gut lining, help regulate appetite and metabolism, reduce harmful inflammation, defend against cancer, and more.²⁶⁻²⁹

Countering Immune Senescence

As we age, our **immune system** weakens, a process known as **immunosenescence**.³⁰

With the deterioration of immune function, the elderly become more susceptible to infectious disease and cancer.

Studies in animal models of aging have shown that intake of **beta glucans** can help *prevent* or even *reverse* these age-related changes.^{18,31}

One study on mice found that by enhancing immune-cell numbers and function, mushroom-derived beta glucans had a **rejuvenating effect** on immune system responses. They had a similar effect on the gut microbiota, reversing negative age-related changes.³¹

Fighting Infectious Disease

The effects of **mushroom** and **beta glucans** have on the immune system can help prevent and treat infection by a range of pathogens.

In animal models, beta-glucan use dramatically **improves survival rates** after infection by various bacteria and parasites.³²⁻³⁵

Even in cases of infection that are notoriously difficult to eradicate, beta glucans have shown great promise.

For example, in **hepatitis B** infection of the liver, the virus can actively suppress the body's immune response. That leads to chronic infection that can destroy liver function. But in a mouse study, **beta-glucans** isolated from yeast helped the animals to recruit immune cells to the area and clear the virus.³⁶

Several human trials of beta glucans have been performed as well.³⁷⁻⁴² Most used a dose of **250 mg** of **beta glucans** isolated from yeast. Subjects were randomized to receive the beta glucans or a placebo.

A number of benefits were observed, particularly in **upper respiratory tract infections** such as the common **cold** and **flu**.



Maitake



Subjects receiving the **beta glucans** had:

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

One study looked at a *non*-infectious disorder: **ragweed allergy**. People suffering from this common allergy were randomized to receive either **250 mg** of **beta glucans** or a placebo for four weeks.⁴³

Those receiving **beta glucans** had significant *reductions* in total allergy symptoms and symptom severity. Measures of mood, energy, vigor, sleep, and overall quality of life were all improved as well.



Chaga

Shiitake

This suggests that beta glucans can help improve immune responses not only to infection, but to other forms of inflammation as well.

Summary

Various **mushrooms** have long been used for their medicinal properties.

Compounds contained in their cell walls, called **beta glucans**, are most responsible for these benefits.

Medicinal mushrooms and beta glucans can improve **immune** responses, helping to fight various types of **infection** and reduce unwanted **inflammation**.

Beta glucans also help cultivate a healthy **gut microbiota** while resisting the growth of pathogenic bacteria.

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

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

Higher Mushroom Consumption is Associated with Lower Cancer Risk

Scientists continue to explore the multiple health benefits of mushrooms.

Researchers at **Penn State University** performed a systemic review and meta-analysis of observational studies published between 1966 and 2020.*

Data from more than **19,500** cancer patients was analyzed specifically for the connection between mushroom consumption and cancer risk. Researchers found that *higher* mushroom intake was associated with *lower* risk of cancer.

Further analysis showed that a *higher* intake of **18 grams** per day was associated with a **45% lower** risk of **total cancer** compared to an intake of **0 grams** per day.

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

Mushrooms, which are low in calories, can be eaten raw as a healthy snack, mixed into a salad, or cooked into different dishes.⁴⁴

References

1. Blagodatski A, Yatsunskaya M, Mikhailova V, et al. Medicinal mushrooms as an attractive new source of natural compounds for future cancer therapy. *Oncotarget*. 2018 Jun 26;9(49):29259-74.
2. Ciecierska A, Drywień ME, Hamulka J, et al. Nutraceutical functions of beta glucans in human nutrition. *Rocz Panstw Zakl Hig*. 2019;70(4):315-24.
3. Jin Y, Li P, Wang F. beta glucans as potential immunoadjuvants: A review on the adjuvanticity, structure-activity relationship and receptor recognition properties. *Vaccine*. 2018 Aug 23;36(35):5235-44.
4. Zhang M, Zhang Y, Zhang L, et al. Mushroom polysaccharide lentinan for treating different types of cancers: A review of 12 years clinical studies in China. *Prog Mol Biol Transl Sci*. 2019;163:297-328.
5. Kim HS, Hong JT, Kim Y, et al. Stimulatory Effect of beta glucans on Immune Cells. *Immune Netw*. 2011 Aug;11(4):191-5.
6. Masterson CH, Murphy EJ, Gonzalez H, et al. Purified beta glucans from the Shiitake mushroom ameliorates antibiotic-resistant *Klebsiella pneumoniae*-induced pulmonary sepsis. *Lett Appl Microbiol*. 2020 Oct;71(4):405-12.
7. Avtonomova AV, Krasnopolskaya LM. [Antiviral properties of basidiomycetes metabolites]. *Antibiot Khimioter*. 2014;59(7-8):41-8.
8. Ren G, Xu L, Lu T, et al. Structural characterization and antiviral activity of lentinan from *Lentinula edodes* mycelia against infectious hematopoietic necrosis virus. *Int J Biol Macromol*. 2018 Aug;115:1202-10.
9. Rincão VP, Yamamoto KA, Ricardo NM, et al. Polysaccharide and extracts from *Lentinula edodes*: structural features and antiviral activity. *Virology*. 2012 Feb 15;9:37.
10. Dai X, Stanilka JM, Rowe CA, et al. Consuming *Lentinula edodes* (Shiitake) Mushrooms Daily Improves Human Immunity: A Randomized Dietary Intervention in Healthy Young Adults. *J Am Coll Nutr*. 2015;34(6):478-87.



11. Hou L, Meng M, Chen Y, et al. A water-soluble polysaccharide from *Grifola frondosa* induced macrophages activation via TLR4-MyD88-IKKbeta-NF-kappaB p65 pathways. *Oncotarget*. 2017 Oct 17;8(49):86604-14.

12. Vetvicka V, Vetvickova J. Immune-enhancing effects of Maitake (*Grifola frondosa*) and Shiitake (*Lentinula edodes*) extracts. *Ann Transl Med*. 2014 Feb;2(2):14.

13. Kim YR. Immunomodulatory Activity of the Water Extract from Medicinal Mushroom *Inonotus obliquus*. *Mycobiology*. 2005 Sep;33(3):158-62.

14. Pan HH, Yu XT, Li T, et al. Aqueous extract from a Chaga medicinal mushroom, *Inonotus obliquus* (higher Basidiomycetes), prevents herpes simplex virus entry through inhibition of viral-induced membrane fusion. *Int J Med Mushrooms*. 2013;15(1):29-38.

15. Shibnev VA, Garaev TM, Finogenova MP, et al. [Antiviral activity of aqueous extracts of the birch fungus *Inonotus obliquus* on the human immunodeficiency virus]. *Vopr Virusol*. 2015;60(2):35-8.

16. Shibnev VA, Mishin DV, Garaev TM, et al. Antiviral activity of *Inonotus obliquus* fungus extract towards infection caused by hepatitis C virus in cell cultures. *Bull Exp Biol Med*. 2011 Sep;151(5):612-4.

17. Chaplin DD. Overview of the immune response. *J Allergy Clin Immunol*. 2010 Feb;125(2 Suppl 2):S3-23.

18. Song L, Yuan J, Ni S, et al. Enhancement of adaptive immune responses of aged mice by dietary intake of beta glucans, with special emphasis on anti-aging activity. *Mol Immunol*. 2020 Jan;117:160-7.

19. Zheng X, Zou S, Xu H, et al. The linear structure of beta-glucan from baker's yeast and its activation of macrophage-like RAW264.7 cells. *Carbohydr Polym*. 2016 Sep 5;148:61-8.

20. Ryan MT, Collins CB, O'Doherty JV, et al. Effects of dietary beta glucans supplementation on cytokine expression in porcine liver. *J Anim Sci*. 2012 Dec;90 Suppl 4:40-2.

21. Smiderle FR, Alquini G, Tadra-Sfeir MZ, et al. *Agaricus bisporus* and *Agaricus brasiliensis* (1-->6)-beta-D-glucans show immunostimulatory activity on human THP-1 derived macrophages. *Carbohydr Polym*. 2013 Apr 15;94(1):91-9.

22. Wang J, Yuan Y, Yue T. Immunostimulatory activities of beta-D-glucan from *Ganoderma lucidum*. *Carbohydr Polym*. 2014 Feb 15;102:47-54.

23. Jayachandran M, Chen J, Chung SSM, et al. A critical review on the impacts of beta glucans on gut microbiota and human health. *J Nutr Biochem*. 2018 Nov;61:101-10.

24. Jayachandran M, Xiao J, Xu B. A Critical Review on Health Promoting Benefits of Edible Mushrooms through Gut Microbiota. *Int J Mol Sci*. 2017 Sep 8;18(9).

25. Mitsou EK, Saxami G, Stamoulou E, et al. Effects of Rich in Beta glucans Edible Mushrooms on Aging Gut Microbiota Characteristics: An In Vitro Study. *Molecules*. 2020 Jun 18;25(12).

26. Byrne CS, Chambers ES, Morrison DJ, et al. The role of short chain fatty acids in appetite regulation and energy homeostasis. *Int J Obes (Lond)*. 2015 Sep;39(9):1331-8.

27. Gill PA, van Zelm MC, Muir JG, et al. Review article: short chain fatty acids as potential therapeutic agents in human gastrointestinal and inflammatory disorders. *Aliment Pharmacol Ther*. 2018 Jul;48(1):15-34.

28. Hijoja E, Chmelarova A. Short chain fatty acids and colonic health. *Bratisl Lek Listy*. 2007;108(8):354-8.

29. Sivaprakasam S, Prasad PD, Singh N. Benefits of short-chain fatty acids and their receptors in inflammation and carcinogenesis. *Pharmacol Ther*. 2016 Aug;164:144-51.

30. Aiello A, Farzaneh F, Candore G, et al. Immunosenescence and Its Hallmarks: How to Oppose Aging Strategically? A Review of Potential Options for Therapeutic Intervention. *Front Immunol*. 2019;10:2247.

31. Xu X, Yang J, Ning Z, et al. *Lentinula edodes*-derived polysaccharide rejuvenates mice in terms of immune responses and gut microbiota. *Food Funct*. 2015 Aug;6(8):2653-63.

32. Ji L, Sun G, Li J, et al. Effect of dietary beta-glucan on growth, survival and regulation of immune processes in rainbow trout (*Oncorhynchus mykiss*) infected by *Aeromonas salmonicida*. *Fish Shellfish Immunol*. 2017 May;64:56-67.

33. Udayangani RMC, Dananjaya SHS, Fronte B, et al. Feeding of nano scale oats beta-glucan enhances the host resistance against *Edwardsiella tarda* and protective immune modulation in zebrafish larvae. *Fish Shellfish Immunol*. 2017 Jan;60:72-7.

34. Yun CH, Estrada A, Van Kessel A, et al. Beta-glucan, extracted from oat, enhances disease resistance against bacterial and parasitic infections. *FEMS Immunol Med Microbiol*. 2003 Jan 21;35(1):67-75.

35. Sado RY, Gimbo RY, Salles FB. Routes of beta-glucan administration affect hematological and immune responses of *Oreochromis niloticus*. *Archivos De Zootecnia*. 2016;65:519-24.

36. Yu X, Zhang D, Shi B, et al. Oral administered particulate yeast-derived glucan promotes hepatitis B virus clearance in a hydrodynamic injection mouse model. *PLoS One*. 2015;10(4):e0123559.

37. Carpenter KC, Breslin WL, Davidson T, et al. Baker's yeast beta-glucan supplementation increases monocytes and cytokines post-exercise: implications for infection risk? *Br J Nutr*. 2013 Feb 14;109(3):478-86.

38. Mah E, Kaden VN, Kelley KM, et al. Beverage Containing Dispersible Yeast beta-Glucan Decreases Cold/Flu Symptomatic Days After Intense Exercise: A Randomized Controlled Trial. *J Diet Suppl*. 2020;17(2):200-10.

39. McFarlin BK, Carpenter KC, Davidson T, et al. Baker's yeast beta glucan supplementation increases salivary IgA and decreases cold/flu symptomatic days after intense exercise. *J Diet Suppl*. 2013 Sep;10(3):171-83.

40. McFarlin BK, Venable AS, Carpenter KC, et al. Oral Supplementation with Baker's Yeast Beta Glucan Is Associated with Altered Monocytes, T Cells and Cytokines following a Bout of Strenuous Exercise. *Front Physiol*. 2017;8:786.

41. Talbott S, Talbott J. Effect of BETA 1, 3/1, 6 GLUCAN on Upper Respiratory Tract Infection Symptoms and Mood State in Marathon Athletes. *J Sports Sci Med*. 2009;8(4):509-15.

42. Feldman S, Schwartz HI, Kalman DS, et al. Randomized phase II clinical trials of wellmune WGP(R) for immune support during cold and flu season. *Journal of Applied Research*. 2009;9(1-2):30+.

43. Talbott SM, Talbott JA, Talbott TL, et al. beta-Glucan supplementation, allergy symptoms, and quality of life in self-described ragweed allergy sufferers. *Food Sci Nutr*. 2013 Jan;1(1):90-101.

44. Ba DM, Ssentongo P, Beelman RB, et al. Higher Mushroom Consumption Is Associated with Lower Risk of Cancer: A Systematic Review and Meta-Analysis of Observational Studies. *Adv Nutr*. 2021 Mar 16.

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* *PLoS Med.* 2005 Sep;2(9):e307;author reply e309.

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A close-up photograph of an Ashwagandha plant. The central focus is a single, bright yellow star-shaped flower with a dark center, surrounded by several unopened buds. The leaves are green and have a slightly fuzzy texture. The background is softly blurred, showing more of the plant and some light-colored fabric on the right side.

ASHWAGANDHA'S Brain Benefits

BY RICK WILSON

Ashwagandha has been used in traditional Indian medicine for thousands of years.¹

Scientists have identified specific effects that ashwagandha has on **brain activity**.¹⁻⁴

In human studies, ashwagandha intake:^{5,6}

- Improved **cognitive performance** in healthy adults.
- Reduced **anxiety** and **stress**.

Lab studies show that it may also help protect against structural changes that can lead to **Alzheimer's** and other forms of **dementia**.⁷⁻¹⁰



A Staple of Ancient Medicine

Extracts of ashwagandha's roots and leaves contain a mixture of bioactive compounds, including **withaferin A**, **withanolides**, **withanosides**, and others.²

These compounds function as **antioxidants** and **anti-inflammatory** agents. They also act in other ways to protect the **brain** from disease.

They cross the **blood-brain barrier** and enter brain tissue, where they can exert beneficial actions.^{11,12}

In healthy adults, ashwagandha taken daily has been shown to **improve cognitive performance**—with boosts in reaction time, discrimination, vigilance, and other tests of brain function.⁵

Relieving Anxiety and Depression

Nearly **10%** of American adults suffer from **mood disorders** like anxiety, depression, and bipolar disorder in any given year.¹³

Stress and anxiety are often treated with **drugs** that stimulate the receptor for a neurotransmitter called **GABA (gamma aminobutyric acid)**. These drugs have side effects, including fatigue and cognitive impairment.

Ashwagandha stimulates these *same* GABA receptors, *without* the side effects.^{14,15} Rather than causing fatigue or cognitive impairment, ashwagandha is known to **enhance** cognitive performance.⁵

Ashwagandha has long been used to reduce stress and support a healthy mood.¹⁴ A review of human trials found that it **improved anxiety** symptoms, compared to a placebo.⁶



In animal models of **depression**, ashwagandha extracts *reverse* signs of behavioral despair and other abnormalities and improve cognitive function.¹⁶⁻¹⁹

In two studies in rodents, the magnitude of this impact was comparable to the effects of **imipramine** and **fluoxetine** (Prozac®), two drugs used in humans to treat depression and other disorders.^{16,17}

In patients with schizophrenia, who are prone to **anxiety and depression**, an ashwagandha extract reduced symptoms of *both*.²⁰

Protecting Brain Cells

Ashwagandha may protect against various forms of **dementia**.

In laboratory studies of animal models of **Alzheimer's disease**, ashwagandha displays various mechanisms known to reduce its progression.

One of the primary features of Alzheimer's is the accumulation of an abnormal protein called **beta-amyloid**.

This buildup inflicts toxic effects on brain cells and incites aggressive chronic inflammation, which leads to further deterioration of brain function.

Preclinical studies have shown that ashwagandha:

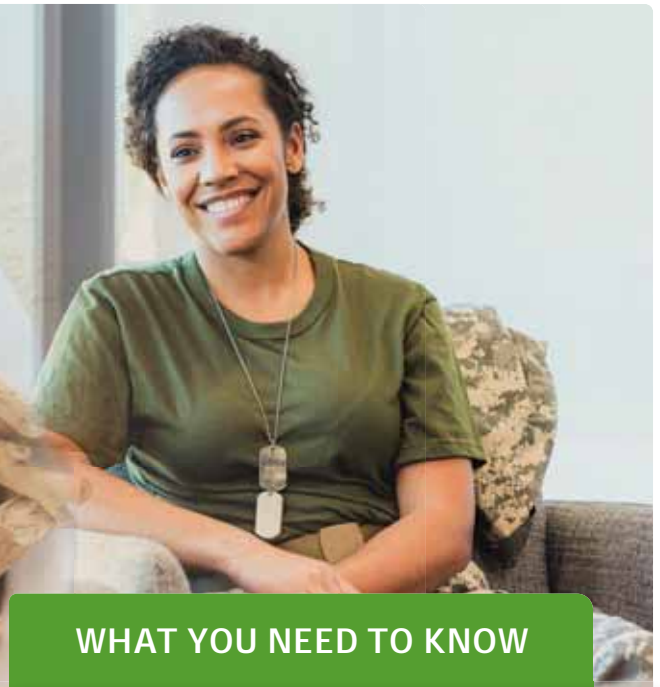
- Reduces the *formation* of amyloid in the brain and brain cells,^{21,22}
- Prevents the *accumulation* and aggregation of amyloid,²³
- Reduces the *toxic impact* of existing amyloid, protecting brain cells from injury and inflammation, and^{21,22,24}
- Aids in *removing* existing amyloid deposits, *reversing* Alzheimer's disease pathology.²⁵

Animal models of Alzheimer's also show a drop in two key proteins associated with brain maintenance and repair: **brain-derived neurotrophic factor (BDNF)** and **glial fibrillary acidic protein (GFAP)**. Ashwagandha helps maintain *higher* levels of both these protective proteins.^{26,27}

Boosting Acetylcholine

One effect of memory loss caused by Alzheimer's disease is a loss of **acetylcholine** function.

Acetylcholine is a neurotransmitter used for cell-to-cell communication in the brain. It is vital to normal cognitive function.



WHAT YOU NEED TO KNOW

Brain Benefits of Ashwagandha

- **Ashwagandha** is a plant native to India and surrounding parts of Asia. It has been used in traditional Indian medicine for millennia to promote overall health.
- Modern science has found that ashwagandha promotes healthy functioning of the **brain**.
- Extracts of ashwagandha may protect the brain from damage caused by a wide range of **toxins**, injuries, and **stroke**.
- Oral intake improves **cognitive performance** in healthy adults and in those with signs of cognitive decline.
- Ashwagandha reduces stress and anxiety, and relieves symptoms of depression.
- Research shows that ashwagandha may help protect against forms of dementia, including **Alzheimer's disease**.

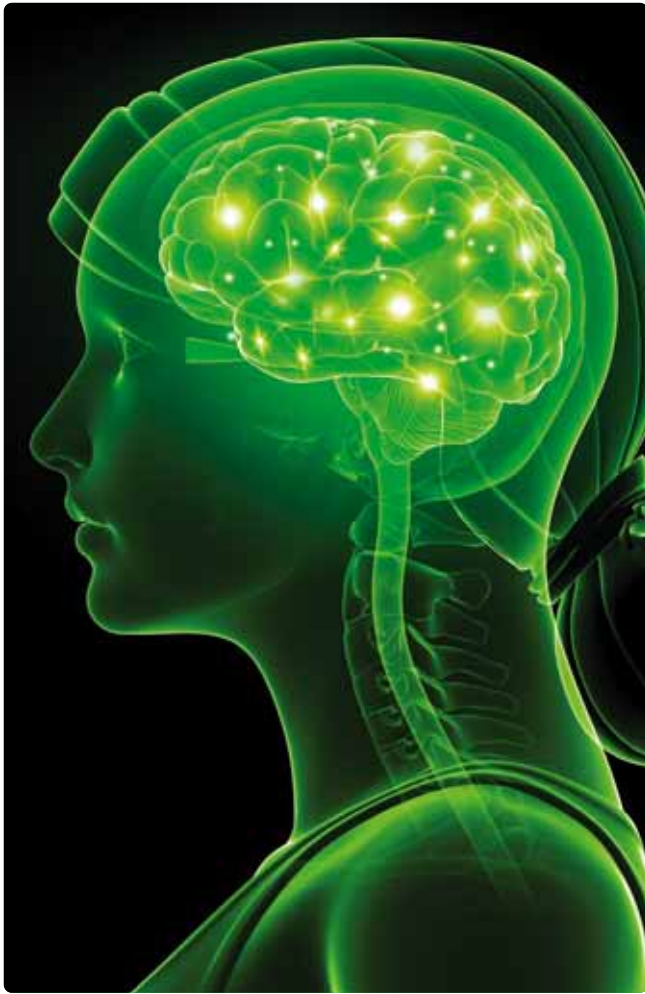
Some medications used to treat Alzheimer's *inhibit* the enzyme that breaks down acetylcholine, boosting its levels. Ashwagandha also blocks this enzyme, increasing acetylcholine levels.⁸⁻¹⁰

Together, these actions suggest that ashwagandha could help fight some of the primary damage that is among the causes of Alzheimer's disease, while also supporting healthy brain function.

Ashwagandha has also shown promise in preclinical studies of other neurodegenerative diseases, including Parkinson's disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease.^{1,2,28,29}

Defense Against Neurotoxins

Ashwagandha has been found, in preclinical models, to shield against a range of neurotoxins, including lead, aluminum chloride, streptozotocin, scopolamine, kainic acid, and bisphenol A (**BPA**, a common additive in plastics).^{1,30,31}



One example is **glutamate**. Glutamate is an amino acid that acts as a neurotransmitter in the brain. Normal levels of glutamate are vital to brain communication.⁴

But very *high* levels of glutamate can cause **excitotoxicity**—overstimulation of brain cells that can cause them to go haywire, and even die. Some brain injuries, such as **traumatic head injuries** and **stroke**, cause a huge release of glutamate that results in further cell death.⁴

Glutamate excitotoxicity has been found to be a component of the pathology seen in neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, ALS, and multiple sclerosis.⁴

Ashwagandha defends the brain against this damage. In lab studies, pretreatment with ashwagandha extracts *before* exposure to high levels of glutamate markedly **inhibit cell death** and other changes associated with excitotoxicity.^{1,32,33}

Helping Stroke Victims

The most common forms of **stroke** result from a lack of oxygen and blood to the brain, leading to cell dysfunction and death.

In several animal studies of experimental stroke, **ashwagandha** intake prevented much of this brain damage.³⁴⁻³⁸ It reduced the size of the brain injury and the biochemical changes that typically accompany stroke.

This helped prevent the behavioral, motor, and cognitive dysfunction that would otherwise have occurred.

These actions, along with its other benefits, make **ashwagandha** a powerful neuroprotective nutrient.

Summary

The herb **ashwagandha** has been used for its diverse health benefits for thousands of years.

Ashwagandha extract appears to be beneficial to the **brain**.

It may shield the brain from damage resulting from exposure to **toxins**, physical injury, and **stroke**.

It helps relieve stress and improves symptoms of **anxiety** and **depression**.

Ashwagandha also improves **cognitive performance** and may defend against cognitive decline and dementia. •

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

References

1. Dar NJ, MuzamilAhmad. Neurodegenerative diseases and Withania somnifera (L.): An update. *J Ethnopharmacol*. 2020 Jun 28;256:112769.
2. Zahiruddin S, Basist P, Parveen A, et al. Ashwagandha in brain disorders: A review of recent developments. *J Ethnopharmacol*. 2020 Jul 15;257:112876.
3. Ng QX, Loke W, Foo NX, et al. A systematic review of the clinical use of Withania somnifera (Ashwagandha) to ameliorate cognitive dysfunction. *Phytother Res*. 2020 Mar;34(3):583-90.
4. Wadhwa R, Konar A, Kaul SC. Nootropic potential of Ashwagandha leaves: Beyond traditional root extracts. *Neurochem Int*. 2016 May;95:109-18.
5. Pingali U, Pilli R, Fatima N. Effect of standardized aqueous extract of Withania somnifera on tests of cognitive and psychomotor performance in healthy human participants. *Pharmacognosy Res*. 2014 Jan;6(1):12-8.
6. Pratte MA, Nanavati KB, Young V, et al. An alternative treatment for anxiety: a systematic review of human trial results reported for the Ayurvedic herb ashwagandha (Withania somnifera). *J Altern Complement Med*. 2014 Dec;20(12):901-8.

ADDITIONAL BRAIN-BOOSTING NUTRIENTS

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Researchers have identified a unique form of sage that improves cognitive function.

Clinical evidence demonstrated that this proprietary extract increased **memory performance** in older adults by nearly **60%** and improved **attention** by **250%**—*within hours* of ingestion.³⁹

In addition to enhancing **cognitive function** in humans, this unique **sage extract** has been shown to increase **lifespan** by **12%** in a *C. elegans* model of aging.⁴⁰

PHOSPHATIDYLSERINE

Phosphatidylserine is a **phospholipid**, one of the structural components of the membranes that surround all cells in the body.^{41,42} This is especially critical for nerve cells in the brain, because it is their cell membranes that carry nerve impulses throughout the nervous system.⁴³ The **myelin** that surrounds nerve fibers and aids signal conduction also relies on phosphatidylserine for normal structure and function.

Aging is associated with structural deterioration in the nervous system, which may be reduced by phosphatidylserine's ability to preserve cognitive function.

BLUEBERRY

Blueberries are packed full of **anthocyanins**, powerful compounds that help protect the plant from oxidative stress. These compounds have been explored in the medical literature for years for their potential health benefits to humans.

Several recent trials in humans have demonstrated that blueberries enhance cognitive function. Not only has blueberry been found to enhance memory and other cognitive performance in older subjects, it improves mood and cognition in children and young adults as well.⁴⁴⁻⁴⁸

PREGNENOLONE

Pregnenolone, a hormone and hormone-precursor, as well as the derivatives it forms in the brain, have modulatory effects on nervous system function.

Several studies in animals and humans have reported beneficial effects for the brain.⁴⁹

Pregnenolone appears to be a neuroprotectant, defending the brain from various forms of injury. It has also been found to have positive effects on mood, memory, and other aspects of cognition.



SAGE



BLUEBERRY

7. Gautam A, Wadhwa R, Thakur MK. Involvement of hippocampal Arc in amnesia and its recovery by alcoholic extract of Ashwagandha leaves. *Neurobiol Learn Mem*. 2013 Nov;106:177-84.
8. Grover A, Shandilya A, Agrawal V, et al. Computational evidence to inhibition of human acetyl cholinesterase by withanolide a for Alzheimer treatment. *J Biomol Struct Dyn*. 2012;29(4):651-62.
9. Vinutha B, Prashanth D, Salma K, et al. Screening of selected Indian medicinal plants for acetylcholinesterase inhibitory activity. *J Ethnopharmacol*. 2007 Jan 19;109(2):359-63.
10. Yadav CS, Kumar V, Suke SG, et al. Propoxur-induced acetylcholine esterase inhibition and impairment of cognitive function: attenuation by Withania somnifera. *Indian J Biochem Biophys*. 2010 Apr;47(2):117-20.
11. Kumar G, Patnaik R. Exploring neuroprotective potential of Withania somnifera phytochemicals by inhibition of GluN2B-containing NMDA receptors: An in silico study. *Med Hypotheses*. 2016 Jul;92:35-43.
12. Vareed SK, Bauer AK, Nair KM, et al. Blood-brain barrier permeability of bioactive withanamide present in Withania somnifera fruit extract. *Phytother Res*. 2014 Aug;28(8):1260-4.
13. Available at: <https://www.nlm.nih.gov/health/statistics/any-mood-disorder.shtml>. Accessed March 31, 2021.
14. Candelario M, Cuellar E, Reyes-Ruiz JM, et al. Direct evidence for GABAergic activity of Withania somnifera on mammalian ionotropic GABAA and GABA_B receptors. *J Ethnopharmacol*. 2015 Aug 2;171:264-72.
15. Singh G, Sharma PK, Dudhe R, et al. Biological activities of Withania somnifera. *Ann Biol Res*. 2010;1(3):56-63.
16. Attari M, Jamaloo F, Shadvar S, et al. Effect of Withania somnifera Dunal Root Extract on Behavioral Despair Model in Mice: a Possible Role for Nitric Oxide. *Acta Med Iran*. 2016 Mar;54(3):165-72.
17. Bhattacharya SK, Bhattacharya A, Sairam K, et al. Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: an experimental study. *Phytomedicine*. 2000 Dec;7(6):463-9.
18. Jayanthi MK. Anti-depressant effects of withania somnifera fat (ashwagandha grutha) extract in experimental mice. *Int J Pharm Bio Sci*. 2012;3(1):33-42.
19. Maity T, Adhikari A, Bhattacharya K, et al. A study on evaluation of antidepressant effect of imipramine adjunct with Ashwagandha and Brahmi. *Nepal Med Coll J*. 2011 Dec;13(4):250-3.
20. Gannon JM, Brar J, Rai A, et al. Effects of a standardized extract of Withania somnifera (Ashwagandha) on depression and anxiety symptoms in persons with schizophrenia participating in a randomized, placebo-controlled clinical trial. *Ann Clin Psychiatry*. 2019 May;31(2):123-9.
21. Atluri VSR, Tiwari S, Rodriguez M, et al. Inhibition of Amyloid-Beta Production, Associated Neuroinflammation, and Histone Deacetylase 2-Mediated Epigenetic Modifications Prevent Neuropathology in Alzheimer's Disease in vitro Model. *Front Aging Neurosci*. 2019;11:342.
22. Pandey A, Bani S, Dutt P, et al. Multifunctional neuroprotective effect of Withanone, a compound from Withania somnifera roots in alleviating cognitive dysfunction. *Cytokine*. 2018 Feb;102:211-21.
23. Jayaprakasam B, Padmanabhan K, Nair MG. Withanamide in Withania somnifera fruit protect PC-12 cells from beta-amyloid response for Alzheimer's disease. *Phytother Res*. 2010 Jun;24(6):859-63.
24. Singh M, Ramassamy C. In vitro screening of neuroprotective activity of Indian medicinal plant Withania somnifera. *J Nutr Sci*. 2017;6:e54.
25. Sehgal N, Gupta A, Valli RK, et al. Withania somnifera reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in liver. *Proc Natl Acad Sci U S A*. 2012 Feb 28;109(9):3510-5.
26. Konar A, Shah N, Singh R, et al. Protective role of Ashwagandha leaf extract and its component withanone on scopolamine-induced changes in the brain and brain-derived cells. *PLoS One*. 2011;6(11):e27265.
27. Sangiovanni E, Brivio P, Dell'Agli M, et al. Botanicals as Modulators of Neuroplasticity: Focus on BDNF. *Neural Plast*. 2017;2017:5965371.
28. Dutta K, Patel P, Julien JP. Protective effects of Withania somnifera extract in SOD1(G93A) mouse model of amyotrophic lateral sclerosis. *Exp Neurol*. 2018 Nov;309:193-204.
29. Rajasankar S, Manivasagam T, Surendran S. Ashwagandha leaf extract: a potential agent in treating oxidative damage and physiological abnormalities seen in a mouse model of Parkinson's disease. *Neurosci Lett*. 2009 Apr 17;454(1):11-5.
30. Birla H, Keswani C, Rai SN, et al. Neuroprotective effects of Withania somnifera in BPA induced-cognitive dysfunction and oxidative stress in mice. *Behav Brain Funct*. 2019 May 7;15(1):9.
31. Kumar P, Singh R, Nazmi A, et al. Glioprotective effects of Ashwagandha leaf extract against lead induced toxicity. *Biomed Res Int*. 2014;2014:182029.
32. Kataria H, Wadhwa R, Kaul SC, et al. Water extract from the leaves of Withania somnifera protect RA differentiated C6 and IMR-32 cells against glutamate-induced excitotoxicity. *PLoS One*. 2012;7(5):e37080.
33. Shah N, Singh R, Sarangi U, et al. Combinations of Ashwagandha leaf extracts protect brain-derived cells against oxidative stress and induce differentiation. *PLoS One*. 2015;10(3):e0120554.
34. Baitharu I, Jain V, Deep SN, et al. Withanolide A prevents neurodegeneration by modulating hippocampal glutathione biosynthesis during hypoxia. *PLoS One*. 2014;9(10):e105311.
35. Chaudhary G, Sharma U, Jagannathan NR, et al. Evaluation of Withania somnifera in a middle cerebral artery occlusion model of stroke in rats. *Clin Exp Pharmacol Physiol*. 2003 May-Jun;30(5-6):399-404.
36. Mukherjee S, Kumar G, Patnaik R. Withanolide a penetrates brain via intra-nasal administration and exerts neuroprotection in cerebral ischemia reperfusion injury in mice. *Xenobiotica*. 2020 Aug;50(8):957-66.
37. Sood A, Kumar A, Dhawan DK, et al. Propensity of Withania somnifera to Attenuate Behavioural, Biochemical, and Histological Alterations in Experimental Model of Stroke. *Cell Mol Neurobiol*. 2016 Oct;36(7):1123-38.
38. Sood A, Mehrotra A, Dhawan DK, et al. Indian Ginseng (Withania somnifera) supplementation ameliorates oxidative stress and mitochondrial dysfunctions in experimental model of stroke. *Metab Brain Dis*. 2018 Aug;33(4):1261-74.
39. Scholey AB, Tildesley NT, Ballard CG, et al. An extract of Salvia (sage) with anticholinesterase properties improves memory and attention in healthy older volunteers. *Psychopharmacology (Berl)*. 2008 May;198(1):127-39.
40. Sibelius. Internal Report. Chronoscreen™ Analysis: Cognition Enhancing Drugs & Natural Extracts. 2018.
41. Available at: <https://www.drugbank.ca/drugs/DB00144>. Accessed April 1, 2021.
42. Glade MJ, Smith K. Phosphatidylserine and the human brain. *Nutrition*. 2015 Jun;31(6):781-6.
43. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK27954/>. Accessed April 1, 2021.
44. Whyte AR, Cheng N, Fromentin E, et al. A Randomized, Double-Blinded, Placebo-Controlled Study to Compare the Safety and Efficacy of Low Dose Enhanced Wild Blueberry Powder and Wild Blueberry Extract (ThinkBlue) in Maintenance of Episodic and Working Memory in Older Adults. *Nutrients*. 2018 May 23;10(6).
45. McNamara RK, Kalt W, Shidler MD, et al. Cognitive response to fish oil, blueberry, and combined supplementation in older adults with subjective cognitive impairment. *Neurobiol Aging*. 2018 Apr;64:147-56.
46. Whyte AR, Schafer G, Williams CM. Cognitive effects following acute wild blueberry supplementation in 7- to 10-year-old children. *Eur J Nutr*. 2016 Sep;55(6):2151-62.
47. Miller MG, Hamilton DA, Joseph JA, et al. Dietary blueberry improves cognition among older adults in a randomized, double-blind, placebo-controlled trial. *Eur J Nutr*. 2018 Apr;57(3):1169-80.
48. Khalid S, Barfoot KL, May G, et al. Effects of Acute Blueberry Flavonoids on Mood in Children and Young Adults. *Nutrients*. 2017 Feb 20;9(2).
49. Vallee M. Neurosteroids and potential therapeutics: Focus on pregnenolone. *J Steroid Biochem Mol Biol*. 2016 Jun;160:78-87.

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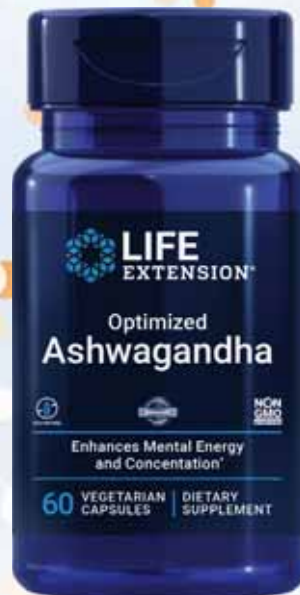


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The VITAMIN D-MAGNESIUM Connection

BY MARSHA MCCULLOCH, RD





The use of **vitamin D** has grown substantially over the past decade.¹

That's for good reason. Vitamin D is essential for immune function, heart health, and cognitive performance.^{2,3}

Unfortunately, many people aren't getting the *full* benefits of vitamin D because they have a low level of **magnesium**.

Researchers have documented the essential relationship between magnesium and vitamin D.⁴

It's estimated that **45%** of Americans are magnesium deficient.⁵

Magnesium is *essential* for converting vitamin D into its **active** form in the body.^{6,7} Magnesium also aids vitamin D **transport** in the blood.^{8,9}

At the same time, maintaining sufficient levels of vitamin D helps magnesium achieve *its* many benefits.¹⁰⁻¹²

A growing number of human studies focusing on the use of both vitamin D and magnesium are confirming their combined benefits for immunity, muscle strength, heart health, and more.¹³⁻¹⁵

The Importance of Vitamin D and Magnesium

Vitamin D and the mineral **magnesium** each have well-known health benefits.

Low levels of **vitamin D** can lead to weak bones, along with increased risk for cardiovascular disease, metabolic disorders, and cognitive decline.¹⁶⁻¹⁸

Magnesium deficiency can result in muscle spasms and cramps.¹⁹ Low magnesium can also contribute to osteoporosis, irregular heart rhythms, and migraines.²⁰

Oral intake of vitamin D and magnesium, *individually*, can help treat or lower risk for many of the same health concerns. These include:^{2,8,9,20,21}

- Musculoskeletal disorders,
- Type II diabetes,
- Cardiovascular disease,
- Some cancers,
- Immune system problems, and
- Neurological conditions, such as depression and dementia.

But for vitamin D and magnesium to work *optimally*, they need each other.



Magnesium Activates Vitamin D

Vitamin D consumed orally or made in the skin from sun exposure is **inactive**.¹⁰

This is also true of both vitamin **D2**, which is obtained from plant sources, and vitamin **D3**, which is made in the skin or found in oily fish and eggs.²²

Before vitamin D can perform its vital functions, it must be activated by a two-step process:^{10,23-25}

In the **liver**, an enzyme called *25-hydroxylase* converts vitamin D2 and D3 to **25-hydroxyvitamin D**. This is the major *circulating* form of vitamin D measured in blood tests to assess vitamin D levels.

In the **kidneys** (and other tissues) another enzyme, *1-alpha-hydroxylase*, converts 25-hydroxyvitamin D into **active vitamin D**.

Both of these enzymes **need magnesium** to function properly.^{6,7} Otherwise, vitamin D will remain in its *inactive* form, making it all but useless.

Magnesium also regulates **24-hydroxylase**, an enzyme that helps *inactivate* vitamin D when there's an excess supply.^{4,6}

Transport and Regulation of Vitamin D

Magnesium enables vitamin D to bind to a **carrier protein** that transports it through the blood.^{6,8}

Then, when active vitamin D arrives where it is needed, magnesium helps activate the **receptors** needed for cells to use vitamin D.²⁰

Magnesium deficiency *decreases* the number of vitamin D receptors in cells, limiting the vitamin's effects.²⁰ Aging leads to a decrease in vitamin D receptors.²⁶

Magnesium also boosts vitamin D activity by supporting synthesis and secretion of **parathyroid hormone**.^{4,8,10,11} This hormone stimulates the kidneys to convert vitamin D to its active form.²²

Vitamin D's Impact on Magnesium

The magnesium-vitamin D partnership isn't a one-way street.

Vitamin D can enhance intestinal **absorption** of magnesium, particularly in people with low magnesium levels.¹⁰⁻¹² This allows the mineral to be more efficiently used by the body.

In one human study, obese women given a **vitamin D** injection had a significant *increase* in their blood levels of **magnesium**.¹²

A Life-Saving Partnership

The link between vitamin D and magnesium can be seen in studies of **longevity**.

Vitamin D *deficiency* is known to be associated with a *higher* risk of death. In a large observational study, **low magnesium** levels made that risk even greater.²⁷

In this study, 1,892 men (ages 42-60 years) were followed for an average of 22 years.

In men with low vitamin D levels, a **lower magnesium** intake (less than **414 mg** per day) was associated with a **60% greater risk of death** than for those with a *higher* magnesium intake.²⁷

Further evidence of the link between the two nutrients comes from human studies of **rickets**, a softening or weakening of bones caused by severe and prolonged vitamin D deficiency.

In these studies, vitamin D intake *alone* failed to treat rickets. But adding **magnesium** to the regimen supported vitamin D activation and helped resolve the condition.⁴

In another recent study, 27 healthy, postmenopausal women were given **500 mg** of **magnesium** daily for two months, while 25 matched women received **placebo**. Most of the women were vitamin D deficient, and many were low in some measures of magnesium.

This study showed that in response to magnesium supplementation (with no vitamin D), the number of women deficient in **vitamin D** decreased by about **20%**.²⁸

Bone and Teeth Health

Both vitamin D and magnesium are important for healthy **bone mass** and **strength**.^{19,29}

Together, they are even more beneficial. Vitamin D promotes intestinal absorption of calcium and magnesium, which are vital components of bone that help prevent **osteoporosis**.

Insufficient magnesium can impair bone health by causing a reduction in **parathyroid hormone** levels and a *decrease* in active vitamin D levels.¹¹

Vitamin D and magnesium also play key roles in replenishing the minerals in teeth. This may help prevent **tooth loss**.^{29,30}

Optimizing vitamin D intake also promotes the success of **dental implant** surgery, an increasingly popular option for replacing missing teeth.³¹

Oral health has a wide impact on whole-body health due to the association between **periodontal disease** (gum inflammation) and **systemic disease**, including type II diabetes and cardiovascular disease.³⁰

Vitamin D and magnesium help combat oral inflammation to *prevent* periodontal disease.^{29,32}



WHAT YOU NEED TO KNOW

Vitamin D and Magnesium: Partners in Health

- The **vitamin D** produced from sun exposure and consumed in food or through direct oral intake is **inactive**.
- Enzymes that **activate** vitamin D require the mineral **magnesium** to work properly. Magnesium also supports the transport of vitamin D throughout the body.
- Vitamin D can enhance magnesium **absorption** in the intestines.
- By working in **partnership**, magnesium and vitamin D support musculoskeletal and heart health and promote proper metabolic function.



Muscle Strength and Function

One of the most significant challenges in aging is **sarcopenia**, the loss of muscle mass, strength, and function. It frequently leads to falls and fractures in older adults.³³

Chronic inflammation is one contributor to sarcopenia. Vitamin D and magnesium can help *reduce* inflammation and may *prevent* sarcopenia.¹⁴

Scientists have discovered that **muscles** have receptors for vitamin D. As people age, these tend to decline in number. Taking oral vitamin D *increases* the number of receptors in muscle tissue.³⁴

In a study of 83 healthy, middle-aged women deficient in vitamin D, half the group received **50,000 IU** of **vitamin D** weekly and **250 mg** of **magnesium** daily for eight weeks. The rest of the group received placebos.

Women who received the vitamin D and magnesium had a significant *increase* in **handgrip strength** and overall **mobility**, compared to the placebo group. The treatment group also had a *decrease* in an important inflammatory marker, compared to the beginning of the study.¹⁴

Cardiometabolic Health

In observational studies, *higher* intake and blood levels of both vitamin D and magnesium have been linked with a *lower* risk of **insulin resistance** and **type II diabetes**.^{35,36}

Vitamin D appears to improve **insulin secretion** from the pancreas, which has specific receptors for interacting with the vitamin.³⁵ Magnesium also supports insulin secretion.³⁷

Magnesium plays an important role in protecting cells from **oxidative stress** as well. Magnesium deficiency results in *decreased* production of **glutathione**, one of the body's most potent antioxidants.³⁷

Multiple studies conducted across several decades show that magnesium and vitamin D intake interacted in affecting vitamin D status.^{4,38,39}

The vitamin and mineral intake also interacted with circulating vitamin D levels in the risk of cardiovascular mortality.^{4,6}

Without enough magnesium and vitamin D, calcium isn't properly routed to the bones. Instead, calcium is more likely to deposit in arteries, increasing risk of **cardiovascular disease**.^{11,40}



Summary

The health benefits of **vitamin D** are well-established. But the *effectiveness* of vitamin D intake depends on getting enough **magnesium**, a nutrient on which nearly **half** of all Americans fall short.

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

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

Vitamin D and **magnesium** are clearly both vital for overall health. Taking one without the other fails to take advantage of their full benefits. •

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

References

1. Rooney MR, Harnack L, Michos ED, et al. Trends in Use of High-Dose Vitamin D Supplements Exceeding 1000 or 4000 International Units Daily, 1999-2014. *JAMA*. 2017 Jun 20;317(23):2448-50.
2. Cannell JJ, Hollis BW. Use of vitamin D in clinical practice. *Altern Med Rev*. 2008 Mar;13(1):6-20.
3. Hansdottir S, Monick MM, Hinde SL, et al. Respiratory epithelial cells convert inactive vitamin D to its active form: potential effects on host defense. *J Immunol*. 2008 Nov 15;181(10):7090-9.
4. Dai Q, Zhu X, Manson JE, et al. Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial. *Am J Clin Nutr*. 2018 Dec 1;108(6):1249-58.
5. Workinger JL, Doyle RP, Bortz J. Challenges in the Diagnosis of Magnesium Status. *Nutrients*. 2018 Sep 1;10(9):1202.
6. Deng X, Song Y, Manson JE, et al. Magnesium, vitamin D status and mortality: results from US National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 and NHANES III. *BMC Med*. 2013 Aug 27;11:187.

7. Available at: <https://lpi.oregonstate.edu/mic/vitamins/vitamin-D>. Accessed April 27, 2021.
8. Rosanoff A, Dai Q, Shapses SA. Essential Nutrient Interactions: Does Low or Suboptimal Magnesium Status Interact with Vitamin D and/or Calcium Status? *Adv Nutr*. 2016 Jan;7(1):25-43.
9. Erem S, Atfi A, Razzaque MS. Anabolic effects of vitamin D and magnesium in aging bone. *J Steroid Biochem Mol Biol*. 2019 Oct;193:105400.
10. Uwitonze AM, Razzaque MS. Role of Magnesium in Vitamin D Activation and Function. *J Am Osteopath Assoc*. 2018 Mar 1;118(3):181-9.
11. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and Human Health: Perspectives and Research Directions. *Int J Endocrinol*. 2018;2018:9041694.
12. Farhanghi MA, Mahboob S, Ostadrahimi A. Obesity induced magnesium deficiency can be treated by vitamin D supplementation. *J Pak Med Assoc*. 2009 Apr;59(4):258-61.
13. Abiri B, Vafa M. Effects of vitamin D and/or magnesium supplementation on mood, serum levels of BDNF, inflammatory biomarkers, and SIRT1 in obese women: a study protocol for a double-blind, randomized, placebo-controlled trial. *Trials*. 2020 Feb 26;21(1):225.
14. Kheyri F, Sarrafzadeh J, Hosseini AF, et al. Randomized Study of the Effects of Vitamin D and Magnesium Co-Supplementation on Muscle Strength and Function, Body Composition, and Inflammation in Vitamin D-Deficient Middle-Aged Women. *Biol Trace Elem Res*. 2020 Sep 21.
15. Danik JS, Manson JE. Vitamin d and cardiovascular disease. *Curr Treat Options Cardiovasc Med*. 2012 Aug;14(4):414-24.
16. Meehan M, Penckofer S. The Role of Vitamin D in the Aging Adult. *J Aging Gerontol*. 2014 Dec;2(2):60-71.
17. Bennett AL, Lavie CJ. Vitamin D Metabolism and the Implications for Atherosclerosis. *Adv Exp Med Biol*. 2017;996:185-92.
18. Annweiler C, Dursun E, Feron F, et al. Vitamin D and cognition in older adults: international consensus guidelines. *Geriatr Psychol Neuropsychiatr Vieil*. 2016 Sep 1;14(3):265-73.
19. Razzaque MS. Magnesium: Are We Consuming Enough? *Nutrients*. 2018 Dec 2;10(12):1863.



20. Reddy P, Edwards LR. Magnesium Supplementation in Vitamin D Deficiency. *Am J Ther*. 2019 Jan/Feb;26(1):e124-e32.
21. Wintermeyer E, Ihle C, Ehnert S, et al. Crucial Role of Vitamin D in the Musculoskeletal System. *Nutrients*. 2016 Jun 1;8(6).
22. Khundmiri SJ, Murray RD, Lederer E. PTH and Vitamin D. *Compr Physiol*. 2016 Mar 15;6(2):561-601.
23. Underland L, Markowitz M, Gensure R. Calcium and Phosphate Hormones: Vitamin D, Parathyroid Hormone, and Fibroblast Growth Factor 23. *Pediatr Rev*. 2020 Jan;41(1):3-11.
24. Heaney RP. Vitamin D in health and disease. *Clin J Am Soc Nephrol*. 2008 Sep;3(5):1535-41.
25. Saponaro F, Saba A, Zucchi R. An Update on Vitamin D Metabolism. *Int J Mol Sci*. 2020 Sep 8;21(18):6573.
26. Gallagher JC. Vitamin D and aging. *Endocrinol Metab Clin North Am*. 2013 Jun;42(2):319-32.
27. Mursu J, Nurmi T, Voutilainen S, et al. The association between serum 25-hydroxyvitamin D3 concentration and risk of disease death in men: modification by magnesium intake. *Eur J Epidemiol*. 2015 Apr;30(4):343-7.
28. Vazquez-Lorente H, Herrera-Quintana L, Molina-Lopez J, et al. Response of Vitamin D after Magnesium Intervention in a Postmenopausal Population from the Province of Granada, Spain. *Nutrients*. 2020 Jul 30;12(8).
29. Uwitonze AM, Rahman S, Ojeh N, et al. Oral manifestations of magnesium and vitamin D inadequacy. *J Steroid Biochem Mol Biol*. 2020 Jun;200:105636.
30. Uwitonze AM, Murererehe J, Ineza MC, et al. Effects of vitamin D status on oral health. *J Steroid Biochem Mol Biol*. 2018 Jan;175:190-4.
31. Nastri L, Moretti A, Migliaccio S, et al. Do Dietary Supplements and Nutraceuticals Have Effects on Dental Implant Osseointegration? A Scoping Review. *Nutrients*. 2020 Jan 20;12(1).
32. Meisel P, Schwahn C, Luedemann J, et al. Magnesium deficiency is associated with periodontal disease. *J Dent Res*. 2005 Oct;84(10):937-41.
33. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019 Jan 1;48(1):16-31.
34. Cruz-Jentoft AJ, Dawson Hughes B, Scott D, et al. Nutritional strategies for maintaining muscle mass and strength from middle age to later life: A narrative review. *Maturitas*. 2020 Feb;132:57-64.
35. Palacios C, Perez CM, Gonzalez-Sepulveda L, et al. Vitamin D, Calcium, Magnesium, and Potassium Consumption and Markers of Glucose Metabolism in the Hispanic Community Health Study/ Study of Latinos. *J Am Coll Nutr*. 2020 Nov 30:1-10.
36. Gandhe MB, Jain K, Gandhe SM. Evaluation of 25(OH) Vitamin D3 with Reference to Magnesium Status and Insulin Resistance in T2DM. *J Clin Diagn Res*. 2013 Nov;7(11):2438-41.
37. Kostov K. Effects of Magnesium Deficiency on Mechanisms of Insulin Resistance in Type 2 Diabetes: Focusing on the Processes of Insulin Secretion and Signaling. *Int J Mol Sci*. 2019 Mar 18;20(6):1351.
38. Rude RK, Adams JS, Ryzen E, et al. Low serum concentrations of 1,25-dihydroxyvitamin D in human magnesium deficiency. *J Clin Endocrinol Metab*. 1985 Nov;61(5):933-40.
39. Fatemi S, Ryzen E, Flores J, et al. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab*. 1991 Nov;73(5):1067-72.
40. Hiemstra T, Lim K, Thadhani R, et al. Vitamin D and Atherosclerotic Cardiovascular Disease. *J Clin Endocrinol Metab*. 2019 Apr 4.



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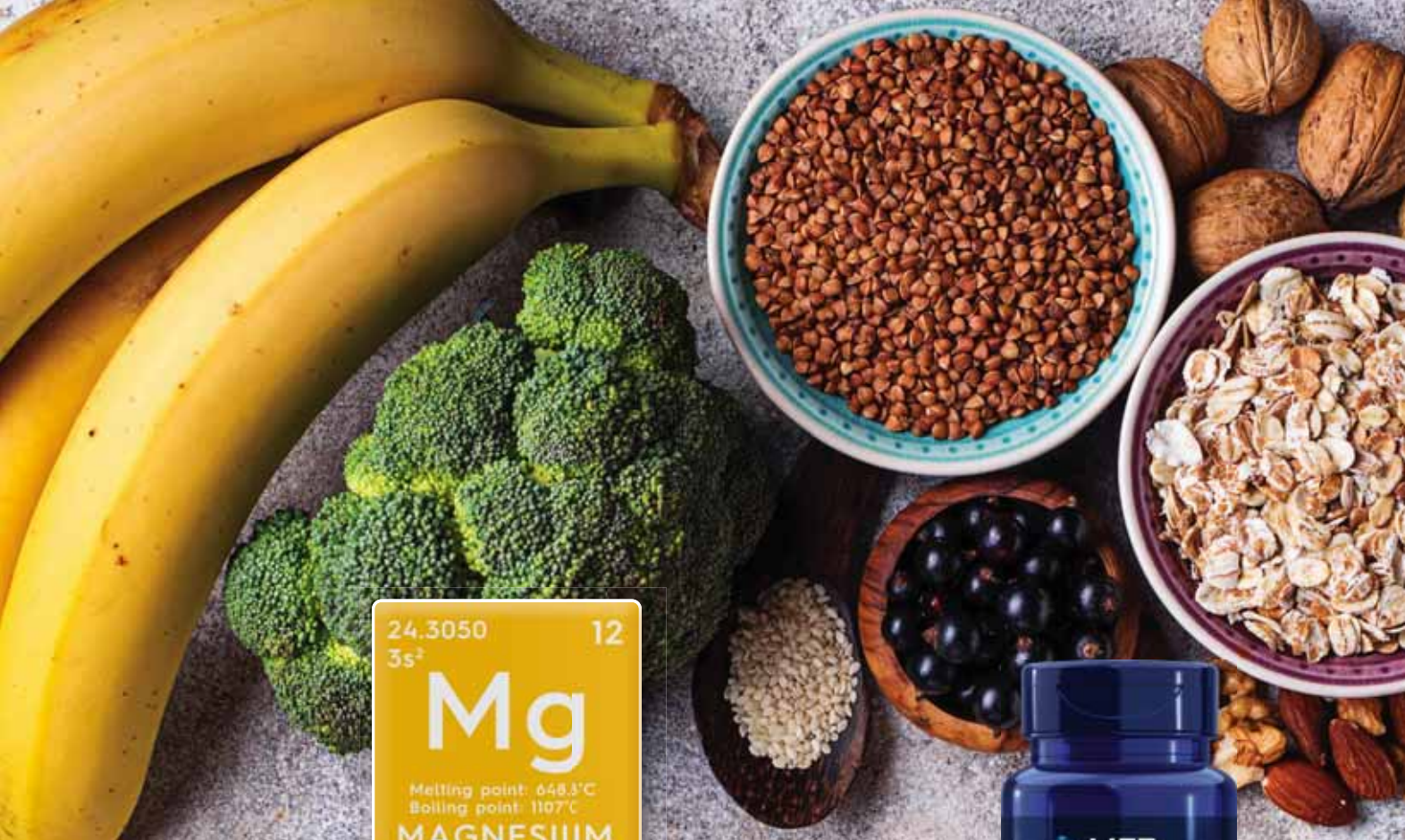
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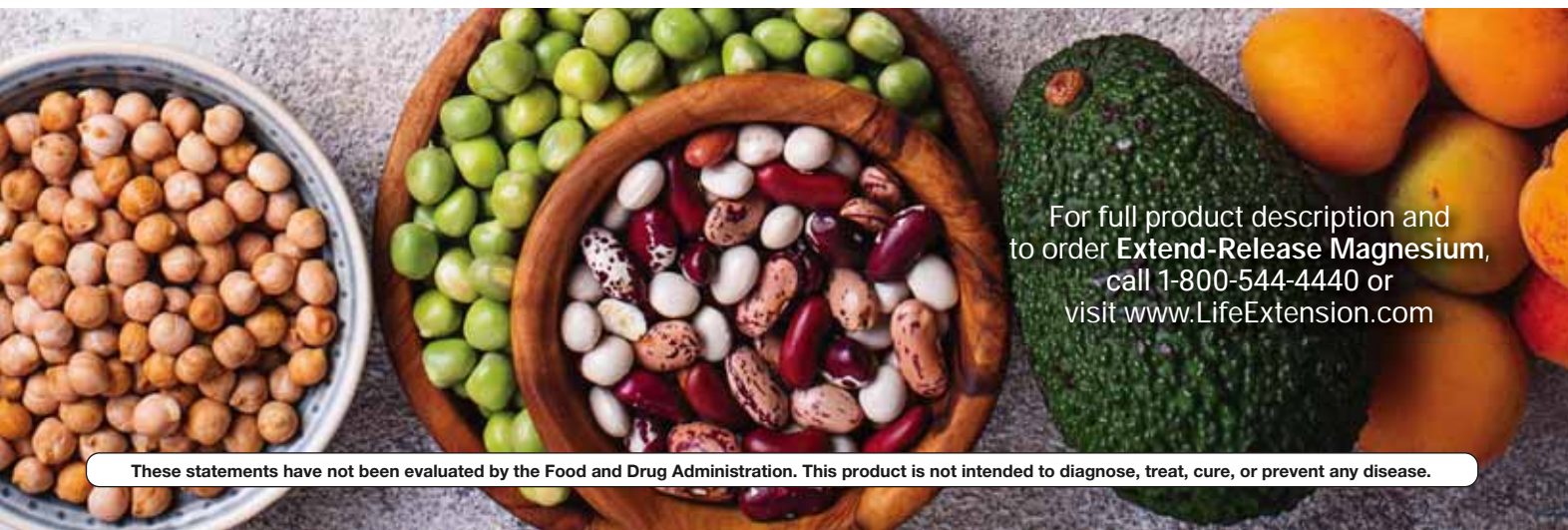
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Prevent Sun Damage from the Inside Out

BY MICHAEL DOWNEY



We all know the one surefire way to help protect against ultraviolet radiation that causes **skin cancer**: use sunscreen.

But a recent study by the U.S. Food and Drug Administration (FDA) reported alarming findings.¹

At least **six of the most common chemicals** used in most commercial sunscreens—the very chemicals that provide the UV protection—were absorbed into the bloodstream after just one application!

Not only that, but they were found in the bloodstream at levels that ranged from over six times to over **500 times greater** than the FDA's recommended safety threshold.

Every single sunscreen chemical tested, in every form of application (lotion and three different types of spray), ended up in the bloodstream in amounts considerably greater than what the FDA considers low risk.

No one should stop using sunscreen. But there are safer ways to protect yourself against the damage UV light can cause.

One option is to use **sunblock** containing **titanium dioxide** or **zinc oxide**, mineral compounds that *reflect* UV rays. This is different from the sunscreen chemicals mentioned above that *absorb* UV rays.²⁻⁵

Another option can be used along with sunblock: an **oral extract** of the fern ***Polypodium leucotomos***. Rather than blocking the sun's rays, it blocks the *damage* they can do.

A randomized controlled clinical trial showed that taking ***Polypodium extract*** before UV exposure led to a striking **84% decrease** in a UV-induced DNA mutation.⁶

For added sun protection, **nicotinamide** enhances DNA repair and reduces UV-induced immune suppression.⁷ An **orange extract** from select Sicilian red oranges boosts protection further, reducing sunburn intensity by about **35%**.^{8,9}

These nutrients work from the inside out to help protect against sun damage.



Sunscreen Chemicals in the Blood

Skin cancer affects over **three million** Americans each year.¹⁰⁻¹³

Using sunscreen is important. But most topical sunscreens block only a *portion* of harmful ultraviolet radiation from reaching the skin. They also break down over time, reducing their effectiveness.¹⁴

A new study by the U.S. Food and Drug Administration (FDA) raises another concern. After applying sunscreen to study subjects, and then testing their blood for **six chemicals** used in the sunscreens, scientists found blood levels of those chemicals ranging from over six to over **500 times greater** than the agency's recommended safety threshold.¹

Both the FDA and the American Academy of Dermatology stress that these chemicals have not been proven to be unsafe. However, they *have* been associated with possible hormone disruption and liver and kidney issues.¹⁵

Until the health effects of these ingredients are more fully understood, the FDA advises that people continue to use sunscreens.^{1,15}

Mineral-Based Sunblock: A Safer Option

Sunscreens come in two types. One contains chemicals and combinations of chemicals that *absorb* ultraviolet radiation. The other contains minerals, such as **zinc oxide** and **titanium dioxide**, that *block* UV rays.^{2,4}

Both the FDA and the Environmental Working Group have determined that **sunblocks** relying on a *mineral* ingredient like titanium dioxide are safe and effective.²⁻⁴ They sit on the skin's surface and act as a shield.

No matter what sunscreen you use, though, it can't provide *total* protection. Among the reasons:¹⁶

- Sunscreens don't protect the scalp or eyelids,
- Sunscreens may be rubbed off or washed off by perspiration or swimming,
- Most people don't apply nearly enough to block the sun's rays, and
- UV rays penetrate some fabrics in clothes, reaching areas where people have not applied sunscreen.

Scientists have discovered that an extract of a tropical fern called ***Polypodium leucotomos*** offers an ideal addition to topical sunscreens.

It protects the skin against ultraviolet damage caused by the sun. And because it is taken **orally**, it works on all skin areas evenly, and it won't wash or rub off.





WHAT YOU NEED TO KNOW

The Ultimate in Sun Protection

- **Ultraviolet radiation** is a major cause of skin cancer and premature skin aging.
- **Sunscreens** are the first line of defense against UV rays. But a new FDA study found that the chemicals used in most sunscreens are absorbed into the blood at alarmingly high levels after just one application.
- A **sunblock** that contains a *mineral* compound such as **zinc oxide** or **titanium dioxide** is considered safer, but still does not provide complete protection.
- Scientists have shown that a tropical fern extract called ***Polypodium leucotomos*** prevents the UV-induced DNA damage that leads to skin aging and skin cancer.
- Two other nutrients, **nicotinamide** (a form of vitamin B3) and **red orange extract**, further boost sun protection.
- These three ingredients reduce DNA mutations, support the repair of already damaged DNA, lower sunburn intensity and inflammation, and provide powerful protection against skin cancer and skin aging.

How *Polypodium* Works

The sun's ultraviolet radiation causes **premature skin aging** and **skin cancer** by:¹⁷⁻¹⁹

- Inducing DNA damage,
- Generating inflammation, and
- Increasing oxidative stress.

Research shows that the polyphenols in *Polypodium leucotomos* protect DNA and inhibit oxidative stress as well as inflammation.⁶

Clinically Validated in Humans

Scientists recruited healthy volunteers between ages 29 and 54 and divided them into control and treatment groups.

The treatment group took **240 mg** of ***Polypodium leucotomos*** extract orally, two times, eight and two hours *before* being exposed to UV rays.⁶

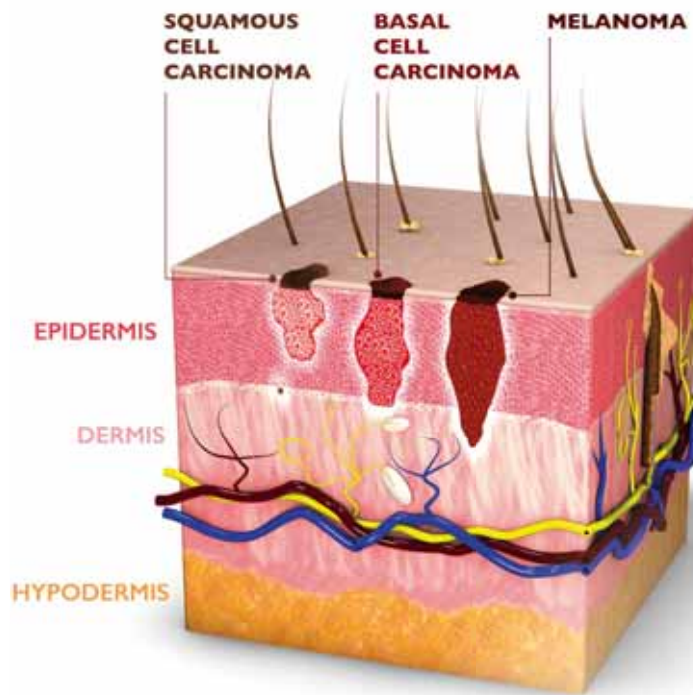
Subsequent skin biopsies showed significant **decreases** in DNA damage in the treated subjects.⁵

When subjected to a **low dose** of UV light,⁶

- **Placebo** participants had a **217% increase** in a damaging DNA mutation, while
- ***Polypodium***-taking participants had a striking **84% decrease** in that DNA mutation.



TYPES OF SKIN CANCER



When subjected to a *higher* dose of UV light,⁶

- The **DNA mutation** in the **placebo** group increased by a shocking **760%**, while
- The **DNA mutation** in the ***Polypodium*** group increased by only **61%**.

Since DNA mutations are a main cause of prematurely aged skin and skin cancer,^{18,20-23} *Polypodium leucotomos* has an enormous potential protective benefit.

Further Sun Defense with Nicotinamide

Two ingredients, **nicotinamide** and **red orange extract**, offer additional protection against sun damage.

Nicotinamide is a form of vitamin B3. Scientists recently completed a review study of its effects, and found that nicotinamide safely:⁷

- Enhances **DNA repair**,
- Reduces UV-induced suppression of **immunity**, and
- Acts as an **anti-inflammatory**.

Ultraviolet radiation normally causes the loss of **ATP** (adenosine triphosphate), the energy-carrying molecule that plays a role in DNA repair.²⁴ Nicotinamide *prevents* this loss, allowing DNA to be continuously repaired.²⁵

In a study that demonstrated this activity, scientists pretreated skin cells with nicotinamide and exposed them to UV radiation. The nicotinamide treatment increased the **removal and replacement of damaged DNA** and significantly increased the number of cells undergoing DNA repair.²⁶

A clinical trial further validated that nicotinamide protects against UV-induced **immune suppression**.²⁷

These two actions alone—repairing DNA and protecting against immune suppression—powerfully reduce the risk of **skin cancer**.²⁸

But **nicotinamide** goes even further. It also:^{7,25-30}

- Inhibits production of inflammatory proteins (cytokines), reducing inflammation,
- Regulates skin barrier function, which helps keep moisture in and harmful elements out, and
- Restores cellular energy levels after UV exposure.

Together, these actions can lead to a significant reduction in skin cancers.

In fact, in the randomized, controlled, clinical trials analyzed for the review study, nicotinamide was shown to *reduce* development of new, non-melanoma **skin cancers** in high-risk people.⁷

In one trial, scientists enlisted 386 healthy participants, all of whom had been diagnosed with at least two non-melanoma skin cancers in the previous five years.

This put them into the “**high-risk**” category for future skin cancers.

Twice a day, volunteers received either **500 mg of nicotinamide** or a **placebo**. After 12 months, the rate of new, non-melanoma skin cancers in the **nicotinamide** group was reduced by **23%** compared to placebo.³¹

Added Protection from Red Orange Extract

An **extract of Sicilian red oranges** provides an extra layer of protection against UV-induced **inflammation** and **oxidative stress**.

This extract is obtained from pigmented varieties of sweet oranges. Its benefits are due to its abundant **flavonoids** (health-promoting plant pigments) and **hydroxycinnamic acid**, another compound with anti-oxidant effects.³²⁻³⁵

Researchers applied this sweet red orange extract to human **keratinocytes**, the most common type of cell in the epidermis (the outermost layer of the skin). When they exposed these cells to UV radiation, the extract significantly *reduced* inflammation, cell damage, and cell death.³³

In a human clinical study, oral use of red orange extract **reduced sunburn intensity** by about **35%**.⁹ This is extremely significant, because the number of lifetime severe sunburns closely correlates with the development of skin cancers.³⁶⁻³⁸

In another clinical study, volunteers took red orange extract and were exposed regularly to a solar lamp.⁸

After 15 days, the extract had reduced age-spot pigmentation and decreased melanin content from **27%** to **7%**. It also decreased UV-induced sunburn.

The study concluded that **red orange extract** can improve skin appearance and protect the skin against sun damage and **photoaging**, aging of the skin caused by ultraviolet radiation.⁸

Summary

The sun’s ultraviolet rays cause DNA damage that accelerates aging of the skin and increases the risk of **skin cancer**.

Studies show that an extract of a fern called ***Polypodium leucotomos*** protects against this UV-induced damage to skin cells and supports DNA repair.

Nicotinamide and **red orange extract** provide additional support for sun protection.

These three nutrients protect skin from the inside out, extending to hard-to-reach areas of the body, and will not rub off.

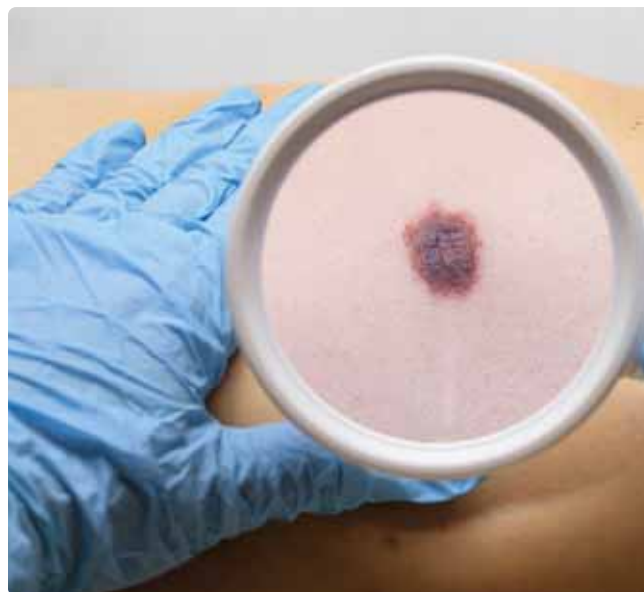
This potent defense should be combined with a high-quality, high-SPF topical sunscreen, preferably a **sunblock** that includes a safe mineral compound such as **zinc oxide** or **titanium dioxide** to reflect UV rays. •

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



References

- Matta MK, Florian J, Zusterzeel R, et al. Effect of Sunscreen Application on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. *JAMA*. 2020 Jan 21;323(3):256-67.
- Available at: <https://www.ewg.org/sunscreen/report/the-trouble-with-sunscreen-chemicals/>. Accessed April 22, 2021.
- Available at: <https://www.ewg.org/sunscreen/report/nanoparticles-in-sunscreen/>.
- Available at: <https://www.cnn.com/2020/01/21/health/sunscreen-dangers-chemicals-bloodstream-wellness/index.html>. Accessed April 22, 2021.
- Available at: <https://www.goodhousekeeping.com/beauty/anti-aging/g26541068/best-zinc-oxide-sunscreen/>. Accessed April 26, 2021.
- Villa A, Viera MH, Amini S, et al. Decrease of ultraviolet A light-induced "common deletion" in healthy volunteers after oral *Polypodium leucotomos* extract supplement in a randomized clinical trial. *J Am Acad Dermatol*. 2010 Mar;62(3):511-3.
- Snaird VA, Damian DL, Halliday GM. Nicotinamide for photoprotection and skin cancer chemoprevention: A review of efficacy and safety. *Exp Dermatol*. 2019 Feb;28 Suppl 1:15-22.
- Puglia C, Offerta A, Saija A, et al. Protective effect of red orange extract supplementation against UV-induced skin damages: photoaging and solar lentiginos. *J Cosmet Dermatol*. 2014 Jun;13(2):151-7.
- Bonina F, Puglia C. Effect of the supplementation with Red Orange Complex® on ultraviolet-induced skin damage in human volunteers. Italy: BIONAP Report.
- Available at: <https://www.aad.org/media/stats/conditions/skin-cancer>. Accessed April 22, 2021.
- Guy GP, Jr., Thomas CC, Thompson T, et al. Vital signs: melanoma incidence and mortality trends and projections - United States, 1982-2030. *MMWR Morb Mortal Wkly Rep*. 2015 Jun 5;64(21):591-6.
- Guy GP, Jr., Machlin SR, Ekwueme DU, et al. Prevalence and costs of skin cancer treatment in the U.S., 2002-2006 and 2007-2011. *Am J Prev Med*. 2015 Feb;48(2):183-7.
- Rogers HW, Weinstock MA, Feldman SR, et al. Incidence Estimate of Nonmelanoma Skin Cancer (Keratinocyte Carcinomas) in the U.S. Population, 2012. *JAMA Dermatol*. 2015 Oct;151(10):1081-6.
- Kabir Y, Seidel R, McKnight B, et al. DNA repair enzymes: an important role in skin cancer prevention and reversal of photodamage--a review of the literature. *J Drugs Dermatol*. 2015 Mar;14(3):297-303.
- Available at: <https://www.dailymail.co.uk/health/article-7911979/Sunscreen-chemicals-concentrations-blood-360-TIMES-higher-FDA-threshold.html>. Accessed April 22, 2021.
- Available at: <https://www.skincancer.org/skin-cancer-prevention/sun-protection/sun-protective-clothing/>. Accessed April 22, 2021.
- de Gruij FR, van Kranen HJ, Mullenders LH. UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer. *J Photochem Photobiol B*. 2001 Oct;63(1-3):19-27.
- Nishigori C. Cellular aspects of photocarcinogenesis. *Photochem Photobiol Sci*. 2006 Feb;5(2):208-14.
- Lohan SB, Muller R, Albrecht S, et al. Free radicals induced by sunlight in different spectral regions - in vivo versus ex vivo study. *Exp Dermatol*. 2016 May;25(5):380-5.
- Chen AC, Halliday GM, Damian DL. Non-melanoma skin cancer: carcinogenesis and chemoprevention. *Pathology*. 2013 Apr;45(3):331-41.
- Pfeifer GP, You YH, Besaratinia A. Mutations induced by ultraviolet light. *Mutat Res*. 2005 Apr 1;571(1-2):19-31.
- Sage E, Girard PM, Francesconi S. Unravelling UVA-induced mutagenesis. *Photochem Photobiol Sci*. 2012 Jan;11(1):74-80.
- Kim SI, Jin SG, Pfeifer GP. Formation of cyclobutane pyrimidine dimers at dipyrimidines containing 5-hydroxymethylcytosine. *Photochem Photobiol Sci*. 2013 Aug;12(8):1409-15.
- Lans H, Marteiin JA, Vermeulen W. ATP-dependent chromatin remodeling in the DNA-damage response. *Epigenetics & Chromatin*. 2012 2012/01/30;5(1):4.
- Park J, Halliday GM, Surjana D, et al. Nicotinamide prevents ultraviolet radiation-induced cellular energy loss. *Photochem Photobiol*. 2010 Jul-Aug;86(4):942-8.
- Surjana D, Halliday GM, Damian DL. Nicotinamide enhances repair of ultraviolet radiation-induced DNA damage in human keratinocytes and ex vivo skin. *Carcinogenesis*. 2013 May;34(5):1144-9.
- Yasemides E, Sivapirabu G, Halliday GM, et al. Oral nicotinamide protects against ultraviolet radiation-induced immunosuppression in humans. *Carcinogenesis*. 2009 Jan;30(1):101-5.
- Nazarali S, Kuzel P. Vitamin B Derivative (Nicotinamide) Appears to Reduce Skin Cancer Risk. *Skin Therapy Lett*. 2017 Sep;22(5):1-4.
- Damian DL. Nicotinamide for skin cancer chemoprevention. *Australas J Dermatol*. 2017 Aug;58(3):174-80.
- Minocha R, Damian DL, Halliday GM. Melanoma and non-melanoma skin cancer chemoprevention: A role for nicotinamide? *Photodermatol Photoimmunol Photomed*. 2018 Jan;34(1):5-12.
- Chen AC, Martin AJ, Choy B, et al. A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention. *N Engl J Med*. 2015 Oct 22;373(17):1618-26.
- Cardile V, Frasca G, Rizza L, et al. Antiinflammatory effects of a red orange extract in human keratinocytes treated with interferon-gamma and histamine. *Phytother Res*. 2010 Mar;24(3):414-8.
- Cimino F, Cristani M, Saija A, et al. Protective effects of a red orange extract on UVB-induced damage in human keratinocytes. *Biofactors*. 2007;30(2):129-38.
- Frasca G, Panico AM, Bonina F, et al. Involvement of inducible nitric oxide synthase and cyclooxygenase-2 in the anti-inflammatory effects of a red orange extract in human chondrocytes. *Nat Prod Res*. 2010 Sep;24(15):1469-80.
- Saija A, Tomaino A, Lo Cascio R, et al. In vitro antioxidant activity and in vivo photoprotective effect of a red orange extract. *Int J Cosmet Sci*. 1998 Dec;20(6):331-42.
- Calzavara-Pinton P, Ortel B, Venturini M. Non-melanoma skin cancer, sun exposure and sun protection. *G Ital Dermatol Venereol*. 2015 Aug;150(4):369-78.
- Wu S, Cho E, Li WQ, et al. History of Severe Sunburn and Risk of Skin Cancer Among Women and Men in 2 Prospective Cohort Studies. *Am J Epidemiol*. 2016 May 1;183(9):824-33.
- Available at: <https://www.nhs.uk/news/cancer/just-five-sunburns-increase-your-cancer-risk/>. Accessed April 22, 2021.



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References

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

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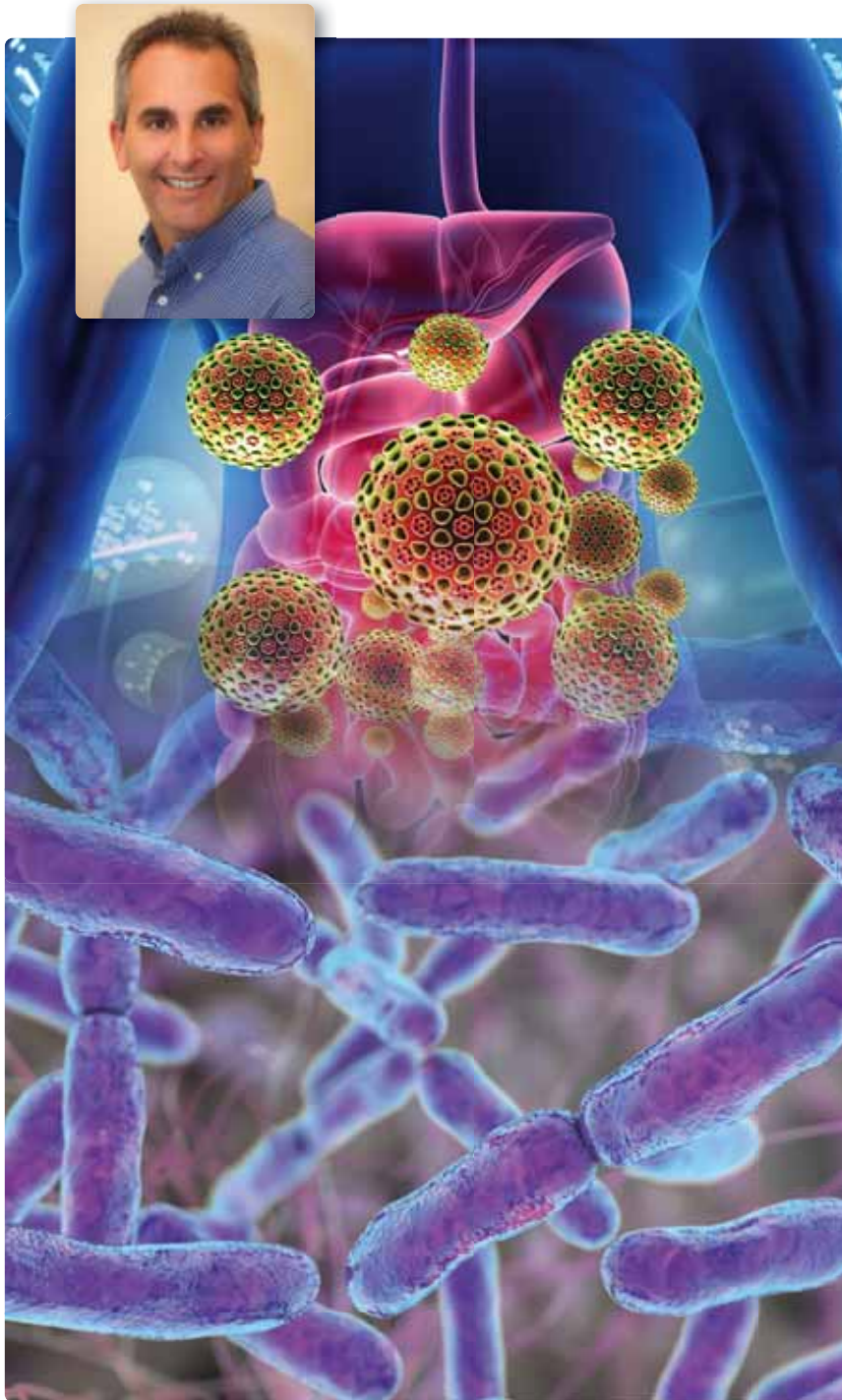
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Understanding Probiotics

BY ANDREW SWICK, MS, PhD



Scientific research has shown a wide range of benefits for **probiotics** in recent years.

As a result, there's now a glut of products on the market with probiotics added to them, from dietary supplements to breakfast cereals.

But probiotics aren't all the same, and it's important to take ones that have been tested and verified as effective in scientific studies.

In this interview with *Life Extension*[®], **Dr. Andrew Swick** talks about the benefits of different probiotic strains, how you can ensure you're getting the right kinds, and more.

LE: Probiotics are very popular now. What exactly are they?

Dr. Swick: Probiotics are live microorganisms that provide health benefits when consumed in appropriate amounts. The majority of probiotics are **healthy bacteria**. These "good" bacteria are beneficial in many ways, including some that help fight off "bad" bacteria. Probiotics take part in the larger community of microorganisms that live in many areas of your body, including your gut, skin, and mouth. This larger community is most commonly referred to as your "**microbiome.**"

LE: People often hear that fermented foods like yogurt contain probiotics. Is that correct?

Dr. Swick: Yogurt and other fermented foods, including kefir, kimchi, kombucha, sauerkraut, and pickles, *do* contain live microbes. These active cultures are popularly referred to as probiotics. But while these foods may provide some health benefits, they don't always meet the strict **scientific definition** of probiotics.

The International Scientific Association for Probiotics and Prebiotics (ISAPP) only designates **strains** that have been *characterized* (properly identified and named), scientifically studied, and demonstrated to provide health benefits, as **probiotics**. Fermented foods contain mixtures of microbes that are for the most part *uncharacterized*, and may not meet the level of scientific evidence required by the ISAPP to be considered probiotics.

LE: You mentioned strains. What are those and how do consumers know if they are getting the correct strain?

Dr. Swick: Consumers should look at the *full* name of each probiotic listed on a product label. Each probiotic has three names in the following order: **genus**, **species**, and **strain**. For example: In ***Lactobacillus rhamnosus* CRL1505**, *Lactobacillus* is the genus, *rhamnosus* is the species, and CRL 1505 is the strain.

Consumers sometimes overlook the **strain**, but it's very important. The specific strain is what was studied to determine the health benefits associated with the probiotic. Strains are not interchangeable, and they have specific benefits.

Think of it like this: All dogs are the same genus and species, *Canis familiaris*. But different breeds may



be nothing alike. For bacteria, **strain** can be thought of as the breed. Not knowing the strain would be like adopting a dog without knowing the breed. A Chihuahua is very different from a Great Dane!

LE: Probiotics sold as dietary supplements may contain different amounts of **colony forming units (CFUs)**, as well as a variety of strains. Is more always better?

Dr. Swick: No. That's a common misconception. The **amount** and **specific** strains listed on the label should be consistent with what was tested in a study. A larger amount or number of probiotic strains does not mean it's more effective.

LE: People mostly think of probiotics as helping with **digestive** health. But now there are targeted probiotics that can improve conditions as varied such as gum disease, depression, and allergies. How do these work?

Dr. Swick: Initially, probiotics were thought to be beneficial only for gastrointestinal health. We now know that specific strains of probiotics are helpful for a variety of conditions. Specific strains have been clinically demonstrated to support a healthy heart, throat, immune response, liver, and even mood.

In general, **condition-specific probiotics** work by supporting an overall healthier microbiome, producing substances that have specific effects,¹ and beneficially influencing immune responses. Targeted probiotics present a meaningful advance for supporting disease prevention and health.

LE: Can you give some examples of specific strains and the conditions they benefit?

Dr. Swick: Many human mouths are teeming with a type of bacteria, *Streptococcus mutans*, that is a cause of cavities, gingivitis (gum inflammation), and

periodontitis (gum disease).² Nearly a **third** of U.S. adults have untreated tooth decay, and nearly **half** of those 30 and older have periodontal disease.

In a clinical study, scientists demonstrated that ***Streptococcus salivarius M18*** was able to decrease the plaque index score and improve other measures of oral health. This is particularly important since we now know that gum disease is associated with other health conditions, including heart disease.

Another interesting application of condition-specific probiotics is in mitigating **depression** and **anxiety**. In two randomized controlled trials, participants taking a blend of ***Lactobacillus helveticus Rosell-52*** and ***Bifidobacterium longum Rosell-175*** reported significant improvements in mood, stress response, and emotional balance. One human study showed a **50%** improvement in depression scores with these two probiotics, and another showed a **55%** improvement in anxiety scores.^{3,4} The connection between the gut and brain is an exciting area of active research.

Scientists have also discovered and characterized a probiotic, ***Lactobacillus rhamnosus CRL 1505***, that stimulates the **immune system** in the respiratory tract and gut. In clinical studies, administration of this probiotic strain led to reduction in infection symptoms, infection incidence, and use of antibiotics. The data were so compelling that *Lactobacillus rhamnosus CRL 1505* was provided to schoolchildren as part of a national nutrition program in Argentina.

As research continues, new targeted probiotics are being developed for conditions such as constipation, and to support longevity.

LE: We also hear a lot lately about prebiotics. What are those?

Dr. Swick: Prebiotics are basically compounds that serve as “food” to support the growth of probiotics. Most prebiotics are dietary fibers, but not all dietary fibers are considered to be prebiotics.

LE: You’ve given us a lot of information. Can you provide the reader with some simple guidelines about how to select appropriate probiotic products?

Dr. Swick: Choosing a probiotic can be overwhelming! Here are a few key points to remember:

1. First and foremost, only purchase probiotics that are high quality and backed by science.
2. Ensure that the strain is clearly identified and appropriate for the specific conditions you want to address.
3. Remember that more is not better. The CFUs should be consistent with what was clinically studied.

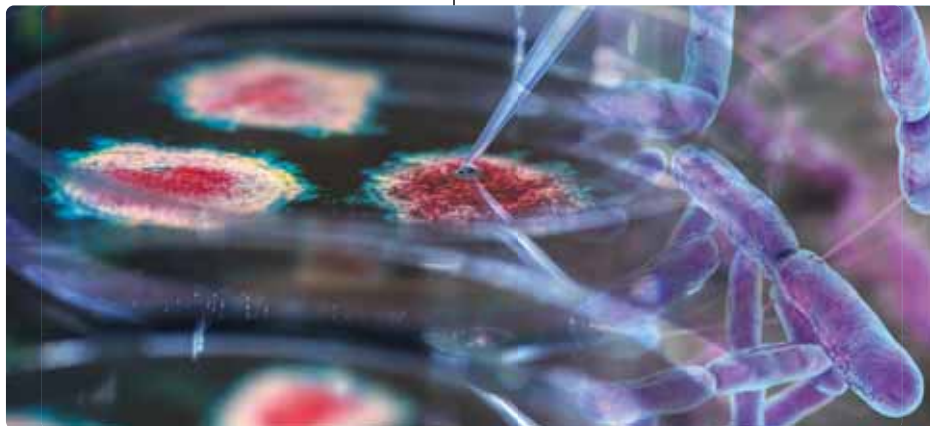
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Dr. Swick is the Chief Scientific Officer for Life Extension® and oversees all scientific and product development initiatives. Immediately prior, Dr. Swick was the Vice President of Nutrition Science at Metagenics. Dr. Swick also has deep pharmaceutical industry experience, having performed both scientific and managerial roles at Pfizer for more than 17 years, where he was responsible for drug discovery and research for obesity and atherosclerosis.

Previously, he also served as an Associate Professor at the Nutrition Research Institute at the University of North Carolina at Chapel Hill. Dr. Swick earned his PhD in Nutritional Biochemistry from the University of Wisconsin-Madison and was a Postdoctoral Research Fellow at the Johns Hopkins University School of Medicine and University of North Carolina Lineberger Comprehensive Cancer Center.

References

1. Galland L. The gut microbiome and the brain. *Journal of medicinal food*. 2014;17(12):1261-72.
2. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK8259/>. Accessed April 27, 2021.
3. Messaoudi M, Lalonde R, Violle N, et al. Assessment of psychotropic-like properties of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in rats and human subjects. *Br J Nutr*. 2011 Mar;105(5):755-64.
4. Messaoudi M, Violle N, Bisson JF, et al. Beneficial psychological effects of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in healthy human volunteers. *Gut Microbes*. 2011 Jul-Aug;2(4):256-61.



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* **EGCG** is the acronym for **epigallocatechin gallate**, which is the polyphenol in green tea that has demonstrated the most robust health benefits.

References

1. *Neuroscience*. 2016 May 13;322:208-20.
2. *J Neurosci*. 2010 Apr 14;30(15):5368-75.

3. *J Nutr Health Aging*. 2010 Jun;14(6):433-8.
4. *Appetite*. 2012 Apr;58(2):767-70.
5. *J Transl Med*. 2015;13:79.



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References

1. Preprints. 2020, 2020090564.
2. Myoceram Scientific Summary. Data on File. 2021.
3. *Jpn. Pharmacol. Ther.* 2013;41:1051-9.
4. *J Invest Dermatol.* 2005 Feb;124(2):304-7.
5. *Skin Pharmacol Physiol.* 2013;26(3):147-54.
6. *Nutrients.* 2017 Aug 12;9(8):866.

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1
DAILY

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4 bottles \$16 each



1
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- Positively influences the nervous system for healthy mood.

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1 box **\$15**

4 boxes \$13.50 each

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What is Tart Cherry?

BY CHANCELLOR FALOON



Tart cherries, also known as sour cherries, contain compounds, including a class of **polyphenols** known as **anthocyanins**, that help reduce inflammation and oxidative stress.^{1,2}

Research has shown that tart cherries can relieve arthritis pain, boost cognition, improve cardiovascular health, benefit endurance athletes, and target the underlying factors of gout.^{1,3}

Tart cherries have been widely used to boost recovery and performance for athletes.

A 2020 meta-analysis of trials on endurance athletes confirmed that tart cherry concentrate intake significantly improves **endurance exercise performance**.⁴

In recent randomized controlled trials, those drinking **tart cherry** juice had improvements in a variety of areas:

- Healthy older adults who drank **two cups (16 oz)** of tart cherry juice daily for 12 weeks had improved scores on tests of **cognitive abilities**, including reaction time, a learning task, and spatial working memory compared to baseline.⁵
- In subjects 50 and older suffering from **insomnia**, drinking **one cup (8 oz)** of tart cherry juice twice daily for two weeks led to increased sleep time and sleep efficiency. Researchers noted that tart cherry juice prevented the degradation of **tryptophan**, an essential amino acid that may help treat sleep disorders.⁶
- In overweight or obese individuals, **one cup (8 oz)/day** of tart cherry juice reduced serum **uric acid concentration** by **19.2%** and **C-reactive protein** (a marker of inflammation) by **19.4%**.⁷ Elevated blood uric acid is the underlying cause of gout, which is a painful form of arthritis.⁸

Tart cherries and their juice are naturally high in **sugar**. Many people prefer to avoid this sugar load and take **tart cherry extract** instead.

In one study, taking **tart cherry extract** was **15.4%** more effective at reducing the odds of a **gout attack** than eating cherries.⁹

A wealth of data shows that tart cherry extract can provide a wide range of health benefits.

A potential new use for tart cherry extract has been uncovered.

When components of tart cherry were tested on **oral epithelial cells** (cells that line the surfaces of the

mouth), they improved the protective **barrier function**. Tart cherry also reduced the ability of oral pathogens to clump together in sticky white plaque that forms on teeth and gums.¹⁰

In a different study, tart cherry extract reduced growth and activity of the bacteria that are the main cause of **gingivitis** (inflammation of the gums).^{11,12} These studies suggest that tart cherry extract fights oral pathogens and may help prevent and treat **oral plaque**. •

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

References

1. Mansoori S, Dini A, Chai SC. Effects of tart cherry and its metabolites on aging and inflammatory conditions: Efficacy and possible mechanisms. *Ageing Res Rev*. 2021 Mar;66:101254.
2. Kirakosyan A, Seymour EM, Llanes DEU, et al. Chemical profile and antioxidant capacities of tart cherry products. *Food Chemistry*. 2009 2009/07/01;115(1):20-5.
3. Kelley DS, Adkins Y, Laugero KD. A Review of the Health Benefits of Cherries. *Nutrients*. 2018 Mar 17;10(3).
4. Gao R, Chilibeck PD. Effect of Tart Cherry Concentrate on Endurance Exercise Performance: A Meta-analysis. *J Am Coll Nutr*. 2020 Sep-Oct;39(7):657-64.
5. Chai SC, Jerusik J, Davis K, et al. Effect of Montmorency tart cherry juice on cognitive performance in older adults: a randomized controlled trial. *Food Funct*. 2019 Jul 17;10(7):4423-31.
6. Losso JN, Finley JW, Karki N, et al. Pilot Study of the Tart Cherry Juice for the Treatment of Insomnia and Investigation of Mechanisms. *Am J Ther*. 2018 Mar/Apr;25(2):e194-e201.
7. Martin KR, Coles KM. Consumption of 100% Tart Cherry Juice Reduces Serum Urate in Overweight and Obese Adults. *Curr Dev Nutr*. 2019 May;3(5):nzz011.
8. Dalbeth N, Choi HK, Joosten LAB, et al. Gout. *Nat Rev Dis Primers*. 2019 Sep 26;5(1):69.
9. Zhang Y, Neogi T, Chen C, et al. Cherry consumption and decreased risk of recurrent gout attacks. *Arthritis Rheum*. 2012 Dec;64(12):4004-11.
10. Ben Lagha A, LeBel G, Grenier D. Tart cherry (*Prunus cerasus* L.) fractions inhibit biofilm formation and adherence properties of oral pathogens and enhance oral epithelial barrier function. *Phytother Res*. 2020 Apr;34(4):886-95.
11. Ben Lagha A, Pellerin G, Vaillancourt K, et al. Effects of a tart cherry (*Prunus cerasus* L.) phenolic extract on Porphyromonas gingivalis and its ability to impair the oral epithelial barrier. *PLoS One*. 2021;16(1):e0246194.
12. How KY, Song KP, Chan KG. Porphyromonas gingivalis: An Overview of Periodontopathic Pathogen below the Gum Line. *Frontiers in Microbiology*. 2016;7:53.



No **Pep** in Your **Step**?

GINSENG ENERGY BOOST

Ginseng has long been used to fight mental and physical fatigue.

One daily capsule of **Ginseng Energy Boost** delivers a **200 mg** dose of Asian ginseng, with no caffeine or other stimulant.

This proprietary ginseng extract is **fermented** to boost your body's absorption of its biologically active compounds.

Make every day a vibrant, high-energy day!*



Item #01805 • 30 vegetarian capsules
1 bottle **\$18** • 4 bottles \$16.50 each

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



* Ginseng is an adaptogenic herb that can promote healthy energy production, support endurance, balance oxidative processes, support the natural ability to manage stress, and encourage positive mood.



GS15-4™ is a trademark of ILHWA N.A.

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

YOUR BONE HEALTH ... NOW **BOOSTED**

Bone Restore with Vitamin K2 combines skeletal-strengthening nutrients in one highly absorbable formula.



Item #01727 • 120 capsules

1 bottle **\$18**

4 bottles \$16.50 each

For full product description and to order **Bone Restore with Vitamin K2**, call **1-800-544-4440** or visit **LifeExtension.com**

Caution: Those taking the anticoagulant drug Coumadin® (warfarin) should use Bone Restore without vitamin K2.

Fruitex B® and OsteoBoron® are registered trademarks of VDF Futureceuticals, Inc. U.S. patent #5,962,049. DimaCal® and TRAACS® are registered trademarks of Albion Laboratories, Inc., U.S. patent 6,706,904.



GLUTEN FREE



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.

STRONG SUPPORT FOR SORE MUSCLES

After Exercise and Everyday Exertion

Benefits of **TART CHERRY** include:¹⁻⁵

- **Rapid muscle recovery after exercise.**
- **Fast relief from the minor aches, discomfort, and stiffness following everyday activities.**

ANTHOCYANINS

Anthocyanins—the powerful flavonoids found in dark-pigmented fruit—have been studied for their many advantages, including **heart, cellular, and cognitive health.**⁶⁻⁸

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

Life Extension® offers **100% natural Tart Cherry with CherryPURE®.**

References

1. *J Int Soc Sports Nutr.* 2010 May 7;7:17.
2. *Scand J Med Sci Sports.* 2010 Dec;20(6):843-52.
3. *J Int Soc Sports Nutr.* 2016;13:26.
4. *J Int Soc Sports Nutr.* 2015;12:14.
5. *Am J Vet Res.* 2009 Jun;70(6):758-63.
6. *Mol Nutr Food Res.* 2007 Jun;51(6):675-83.
7. *Biochemistry (Mosc).* 2004 Jan;69(1):75-80.
8. *Adv Nutr.* 2011 Jan;2(1):1-7.

CherryPURE® is a registered trademark of Shoreline Fruit, LLC.

Item #02023 • 60 vegetarian capsules
1 bottle \$15 • 4 bottles \$14 each



For full product description and to order **Tart Cherry Extract with CherryPURE®**, 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.

ACTIVE LIFESTYLE & FITNESS

- 01529 Creatine Capsules
- 02318 Keto Brain and Body Boost
- 02020 Super Carnosine
- 02023 Tart Cherry with CherryPURE®
- 02146 Wellness Bar—Chocolate Brownie
- 02147 Wellness Bar—Cookie Dough
- 02246 Wellness Code® Advanced Whey Protein Isolate Vanilla
- 02221 Wellness Code® Muscle Strength & Restore Formula
- 02127 Wellness Code® Plant Protein Complete & Amino Acid Complex
- 02261 Wellness Code® Whey Protein Concentrate Chocolate
- 02260 Wellness Code® Whey Protein Concentrate Vanilla
- 02243 Wellness Code® Whey Protein Isolate Chocolate
- 02242 Wellness Code® Whey Protein Isolate Vanilla

AMINO ACIDS

- 01039 Arginine & Ornithine Capsules
- 00038 Arginine Ornithine Powder
- 01253 Branched Chain Amino Acids
- 01829 Carnosine
- 01671 D,L-Phenylalanine Capsules
- 01624 L-Arginine Caps
- 01532 L-Carnitine
- 00345 L-Glutamine
- 00141 L-Glutamine Powder
- 01678 L-Lysine
- 01827 Taurine
- 00133 Taurine Powder
- 00326 Tyrosine Tablets

BLOOD PRESSURE & VASCULAR SUPPORT

- 01824 Advanced Olive Leaf Vascular Support
- 02004 Arterial Protect
- 70000 Blood Pressure Monitor Arm Cuff
- 02497 Endothelial Defense™ Pomegranate Plus
- 02320 NitroVasc™ Boost
- 00984 Optimal BP Management
- 01953 Pomegranate Complete
- 00956 Pomegranate Fruit Extract
- 02024 Triple Action Blood Pressure AM/PM
- 02102 Venoflow™

BONE HEALTH

- 01726 Bone Restore
- 02123 Bone Restore Chewable Tablet
- 02416 Bone Restore Elite with Super Potent K2
- 01727 Bone Restore with Vitamin K2
- 01725 Bone Strength Collagen Formula
- 00313 Bone-Up™
- 01963 Calcium Citrate with Vitamin D
- 01506 Dr. Strum's Intensive Bone Formula
- 02417 Mega Vitamin K2
- 01476 Strontium Caps
- 02422 Vegan Vitamin D3

BRAIN HEALTH

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

- 02101 Memory Protect
- 00709 Migra-Eeze™
- 01603 Neuro-Mag® Magnesium L-Threonate Caps
- 02032 Neuro-Mag® Magnesium L-Threonate Powder
- 00888 Optimized Ashwagandha
- 01676 PS (Phosphatidylserine) Caps
- 02406 Quick Brain Nootropic
- 01327 Vinpocetine

CHOLESTEROL MANAGEMENT

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

DIGESTION SUPPORT

- 53348 Betaine HCl
- 54160 Black Vinegar
- 02412 Bloat Relief
- 30747 Digest RC®
- 07136 Effervescent Vitamin C - Magnesium Crystals
- 02021 Enhanced Super Digestive Enzymes
- 02022 Enhanced Super Digestive Enzymes and Probiotics
- 02033 EsophaCool™
- 01737 Esophageal Guardian
- 01706 Extraordinary Enzymes
- 02100 Gastro-Ease™
- 01122 Ginger Force™
- 00605 Regimint
- 01386 TruFiber®

ENERGY MANAGEMENT

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

EYE HEALTH

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

FISH OIL & OMEGAS

- 02311 Clearly EPA/DHA Fish Oil
- 00463 Flaxseed Oil
- 01937 Mega EPA/DHA
- 02218 Mega GLA Sesame Lignans
- 01983 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract
- 01988 Super Omega-3 Plus EPA/DHA Fish Oil, Sesame Lignans, Olive Extract, Krill & Astaxanthin

- 01982 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 softgels
- 01985 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 enteric coated softgels
- 01984 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 enteric coated softgels
- 01986 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 240 softgels
- 01812 Provinal® Purified Omega-7
- 01640 Vegetarian DHA

FOOD

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

GLUCOSE MANAGEMENT

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

HEART HEALTH

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

HORMONE BALANCE

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

IMMUNE SUPPORT

- 02411 5 Day Elderberry Immune
- 00681 AHCC®
- 02302 Bio-Quercetin®
- 02410 Black Elderberry + Vitamin C
- 01961 Enhanced Zinc Lozenges
- 01704 Immune Modulator with Tinofend®

- 00955 Immune Protect with PARACTIN®
- 02005 Immune Senescence Protection Formula™
- 29727 Kinoko® Gold AHCC
- 24404 Kinoko® Platinum AHCC
- 00316 Kyolic® Garlic Formula 102
- 00789 Kyolic® Reserve
- 01681 Lactoferrin (Apolactoferrin) Caps
- 02426 Mushroom Immune with Beta Glucans
- 01903 NK Cell Activator™
- 01394 Optimized Garlic
- 01309 Optimized Quercetin
- 01811 Peony Immune
- 00525 ProBoost Thymic Protein A
- 01708 Reishi Extract Mushroom Complex
- 01906 Standardized Cistanche
- 13685 Ten Mushroom Formula®
- 01097 Ultra Soy Extract
- 01561 Zinc Lozenges

INFLAMMATION MANAGEMENT

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

JOINT SUPPORT

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

KIDNEY & BLADDER SUPPORT

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

LIVER HEALTH & DETOXIFICATION

- 01922 Advanced Milk Thistle • 60 softgels
- 01925 Advanced Milk Thistle • 120 softgels
- 02240 Anti-Alcohol Complex
- 01651 Calcium D-Glucarate
- 00550 Chlorella
- 01571 Chlorophyllin
- 01522 Milk Thistle • 60 veg capsules
- 02402 FLORASSIST® Liver Restore™
- 01541 Glutathione, Cysteine & C
- 01393 HepatoPro
- 01608 Liver Efficiency Formula
- 01534 N-Acetyl-L-Cysteine
- 00342 PectaSol-C® Modified Citrus Pectin Powder
- 01080 PectaSol-C® Modified Citrus Pectin Capsules
- 01884 Silymarin
- 02361 SOD Booster

LONGEVITY & WELLNESS

- 00457 Alpha-Lipoic Acid
- 01625 AppleWise
- 02414 Bio-Fisetin
- 01214 Blueberry Extract
- 01438 Blueberry Extract and Pomegranate
- 02270 DNA Protection Formula
- 02405 Endocannabinoid System Booster
- 02119 GEROPROTECT® Ageless Cell™
- 02415 GEROPROTECT® Autophagy Renew
- 02133 GEROPROTECT® Longevity A.I.™
- 02401 GEROPROTECT® Stem Cell
- 02211 Grapeseed Extract
- 00954 Mega Green Tea Extract (decaffeinated)
- 00953 Mega Green Tea Extract (lightly caffeinated)
- 01513 Optimized Fucoidan with Maritech® 926
- 02230 Optimized Resveratrol
- 01637 Pycnogenol® French Maritime Pine Bark Extract
- 02210 Resveratrol
- 00070 RNA (Ribonucleic Acid)
- 02301 Senolytic Activator®
- 01208 Super R-Lipoic Acid
- 01919 X-R Shield

MEN'S HEALTH

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

MINERALS

- 01661 Boron
- 02107 Extend-Release Magnesium
- 30731 Ionic Selenium
- 01677 Iron Protein Plus
- 02403 Lithium
- 01459 Magnesium Caps
- 01682 Magnesium (Citrate)
- 01328 Only Trace Minerals
- 01504 Optimized Chromium with Crominex® 3+
- 02309 Potassium with Extend-Release Magnesium
- 01740 Sea-Iodine™
- 01879 Se-Methyl L-Selenocysteine
- 01778 Super Selenium Complex
- 00213 Vanadyl Sulfate
- 01813 Zinc Caps

MISCELLANEOUS

- 00577 Potassium Iodide
- 00657 Solarshield® Sunglasses

MOOD & STRESS MANAGEMENT

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

MULTIVITAMINS

- 02199 Children's Formula Life Extension Mix™
- 02498 Comprehensive Nutrient Packs ADVANCED
- 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

NERVE & COMFORT SUPPORT

- 02202 ComfortMAX™
- 02303 PEA Discomfort Relief

PERSONAL CARE

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

PET CARE

- 01932 Cat Mix
- 01931 Dog Mix

PROBIOTICS

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

SKIN CARE

- 80157 Advanced Anti-Glycation Peptide Serum
- 80165 Advanced Growth Factor Serum
- 80170 Advanced Hyaluronic Acid Serum
- 80154 Advanced Lightening Cream
- 80155 Advanced Peptide Hand Therapy
- 80175 Advanced Probiotic-Fermented Eye Serum
- 80177 Advanced Retinol Serum
- 80152 Advanced Triple Peptide Serum
- 80140 Advanced Under Eye Serum with Stem Cells
- 80137 All-Purpose Soothing Relief Cream
- 80139 Amber Self MicroDermAbrasion
- 80118 Anti-Aging Mask
- 80151 Anti-Aging Rejuvenating Face Cream
- 80153 Anti-Aging Rejuvenating Scalp Serum
- 80179 Brightening Peptide Serum
- 80176 Collagen Boosting Peptide Cream

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

SLEEP

- 01512 Bioactive Milk Peptides
- 02300 Circadian Sleep
- 01551 Enhanced Sleep with Melatonin
- 01511 Enhanced Sleep without Melatonin
- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 02308 Herbal Sleep PM
- 01722 L-Tryptophan
- 01668 Melatonin • 300 mcg, 100 veg capsules
- 01083 Melatonin • 500 mcg, 200 veg capsules
- 00329 Melatonin • 1 mg, 60 capsules
- 00330 Melatonin • 3 mg, 60 veg capsules
- 00331 Melatonin • 10 mg, 60 veg capsules
- 00332 Melatonin • 3 mg, 60 veg lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release
300 mcg, 100 veg tablets
- 01788 Melatonin 6 Hour Timed Release
750 mcg, 60 veg tablets
- 01786 Melatonin 6 Hour Timed Release 3 mg, 60 veg tablets
- 01721 Optimized Tryptophan Plus
- 01444 Quiet Sleep
- 01445 Quiet Sleep Melatonin

VITAMINS

- 01533 Ascorbyl Palmitate
- 00920 Benfotiamine with Thiamine
- 00664 Beta-Carotene
- 01945 BioActive Complete B-Complex
- 00102 Biotin
- 00084 Buffered Vitamin C Powder
- 02229 Fast-C® and Bio-Quercetin Phytosome
- 02075 Gamma E Mixed Tocopherol Enhanced with
Sesame Lignans
- 02070 Gamma E Mixed Tocopherol & Tocotrienols
- 01913 High Potency Optimized Folate
- 01674 Inositol Caps
- 02244 Liquid Vitamin D3 • 50 mcg (2000 IU)
- 02232 Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)
- 01936 Low-Dose Vitamin K2
- 00065 MK-7
- 00373 No Flush Niacin
- 01939 Optimized Folate (L-Methylfolate)
- 01217 Pyridoxal 5'-Phosphate Caps
- 01400 Super Absorbable Tocotrienols
- 02334 Super K
- 02335 Super K Elite
- 01863 Super Vitamin E
- 02028 Vitamin B5 (Pantothenic Acid)
- 01535 Vitamin B6
- 00361 Vitamin B12 Methylcobalamin
- 01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges
- 01537 Vitamin B12 Methylcobalamin • 5 mg, 60 veg lozenges
- 02228 Vitamin C and Bio-Quercetin Phytosome
1,000 mg, 60 veg tablets
- 02227 Vitamin C and Bio-Quercetin Phytosome
1,000 mg, 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

- 00658 7-Keto® DHEA Metabolite • 25 mg, 100 capsules
- 02479 7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules
- 01509 Advanced Anti-Adipocyte Formula
- 01807 Advanced Appetite Suppress
- 02207 AMPK Metabolic Activator
- 01492 Calorie Control Complex with Phase 3™ and
African Mango
- 02478 DHEA Complete
- 01738 Garcinia HCA
- 01292 Integra-Lean®
- 01908 Mediterranean Trim with Sinetrol™ -XPur
- 01432 Optimized Saffron
- 00818 Super CLA Blend with Sesame Lignans
- 01902 Waist-Line Control™
- 02151 Wellness Code® Appetite Control

WOMEN'S HEALTH

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

Regain Your *Youthful Energy*

Energize every cell in your body with
carnosine, R-lipoic acid, benfotiamine,
taurine, PQQ, and more.



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

Item #01868 • 120 vegetarian capsules

1 bottle **\$51** • 4 bottles **\$45** each



Bio-Enhanced® is a registered trademark of Geronova Research, Inc.

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.

PROSTATE HEALTH

The best way to keep You in the picture.

Ultra Prostate Formula was created to help maintain prostate health. It contains a dozen *standardized* ingredients to:

- Support healthy urination
- Promote healthy prostate function
- Support healthy prostate cell division

Ultra Prostate Formula is the most comprehensive *standardized*-ingredient prostate-health supplement.



Item #02029 • 60 softgels

1 bottle \$28.50 • 4 bottles \$26.25 each



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

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