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ON THE
COVER

Anti-Aging Research Advances

- A remarkable number of **healthy-longevity** findings have been published over the past 18 months.
- **Life Extension®** is funding a major study that aims to **reverse aging** in old **monkeys** using a **gene** therapy proven effective in mice.
- In the meantime, a more bioavailable **plant extract** has emerged to help fight **degenerative processes**.

26 HOW MAGNESIUM HELPS YOU SLEEP

In **human** trials, **magnesium** improved **sleep** quantity and quality and increased daytime productivity.



38 LOW LITHIUM IN PEOPLE WITH DEMENTIA

A major **2025** study found that **brain** tissue from people with **dementia** was **low** in **lithium**. The same study showed that low-dose **lithium** nearly *restored* **memory** in aging mice.



50 ACTIVATE AMPK

Activated **AMPK** may *delay* certain **aging** processes. In separate **clinical trials**, two AMPK-activating plant extracts trimmed **belly fat**, lowered blood glucose, and improved blood vessel activity.



60 WHAT TO LOOK FOR IN A MULTIVITAMIN

Millions of Americans take a **multivitamin**. Many commercial multivitamin formulas, however, contain **low** **potencies** and fail to utilize *enzymatically active* nutrients.



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17 IN THE NEWS

Creatine improved cognition in Alzheimer's patients; **melatonin** improved multiple sclerosis symptoms; how **statins** help prevent cancer; **curcumin** improved GI symptoms in obese women.



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73 RESEARCH UPDATE: LINK BETWEEN GLUCOSAMINE AND REDUCED MORTALITY RISK

Two large observational studies found an association between **glucosamine**, commonly used to support joint and cartilage health, with a **15-27%** *reduced* risk of **mortality** from *any cause*.



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Anti-Aging Research Advances



WILLIAM FALOON



A remarkable number of healthy-longevity findings have been published over the past 18 months.

I presented much of this data at a scientific conference in July 2025. The audience was thrilled to learn how close we may be to significantly **extending** our **lifespans**.

In upcoming issues of **Life Extension Magazine** I will provide easy-to-understand advances rapidly occurring in the **regenerative medicine** arena.

The good news is that scientists are further validating much of what most of you do now to live longer.

And the progress being made in the fields of **age-delay** and **age-reversal** gives us all hope of longevity **enhancements** that were previously unimaginable.

Our **regenerative research** projects are funded solely from proceeds of **blood tests** and **nutritional supplements** you obtain from us.

Unlike early decades (1970s-1990s) when we were ridiculed for suggesting **humans** could **live** much *longer*, the most influential people today are also pursuing initiatives to restore *youthful* functionality to our **aged** bodies.

In preclinical studies, a plant extract called **luteolin** has demonstrated potential to fight the **aging** process.¹⁻³

As you will learn on the next page, a more **bioavailable** form of **luteolin** may enable greater systemic effects.

My gratitude to **Life Extension** supporters who enable us to fund pioneering projects aimed at whole-body **rejuvenation**.



Luteolin and Cellular Integrity

Luteolin is a polyphenol found in foods such as fruits, flowers, and herbs.⁴

It was identified by **Life Extension®** in 1985 and made available as part of a multi-ingredient formula shortly after.

Luteolin may exert its anti-aging benefits by modulating **autophagy**,^{3,5} aka **cellular housekeeping**, or the body's ability to remove intracellular waste products.⁶

With age, the cell's ability to clear out its damaged components declines. This results in the accumulation of debris inside our cells that interferes with healthy function.⁷

Autophagy deficits have been implicated in neurodegenerative disorders, cardiovascular diseases, cancer, and more.^{7,8}

Luteolin boosts **autophagy** and may also engage the molecular machinery that improves **mitophagy**, which is the selective removal of degraded or damaged **mitochondria**.⁹

Boosting **autophagy** and **mitophagy** has been shown to increase or extend **lifespan** in yeast, nematodes, fruit flies, and mice.¹⁰

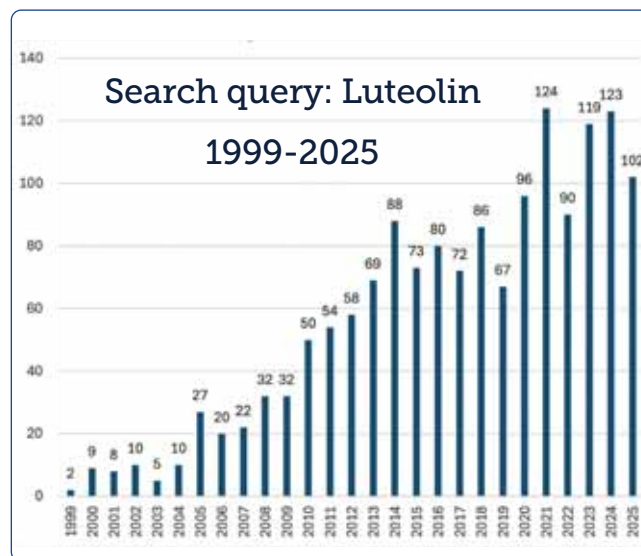
It may do the same in **humans**.

Preclinical research suggests that **luteolin** may provide some protective effects against the following conditions:

- Cancer (liver, breast, lung, GI, bladder, pancreatic)^{4,11,12}
- Cardiovascular/Atherosclerosis⁴
- Obesity⁴
- Insulin Resistance^{11,13}
- Liver disorders⁴
- Kidney disorders⁴
- Brain injury¹⁴
- Neurodegenerative disorders^{4,15}
- Asthma^{4,11,16,17}
- Gastrointestinal (GI) disorders^{4,18}
- Depression¹⁹

The question is whether this preclinical evidence translates into real-world benefits for **aging** humans.

This growing body of data on luteolin has spurred increasing interest from the scientific community. A search for "**luteolin**" in titles on the **National Library of Medicine** (PubMed) returns over **1,300 new results**, with exponentially greater results since the year 2009.



Luteolin Research²⁰

The major dilemma with **luteolin** has been its poor **bioavailability**.

In an artificial environment, like a cell culture, luteolin can reach and penetrate cells, but it doesn't do this well when ingested orally. In animal research, its bioavailability is around **26%**.²¹

Researchers have found that the **bioavailability** can be enhanced significantly when **luteolin** is combined with fibers from the **fenugreek plant**.

In fact, in a **human** trial, this **formulated luteolin** achieved "**nearly 14**" times greater bioavailability than an unformulated version.²²

Thanks to this bioavailability enhancement, some of the benefits of luteolin observed in preclinical studies may now be replicated in **humans**.

Higher dosages around **500 mg** have been clinically shown to improve testosterone and libido in men, but lower dosages with *higher* bioavailability may be all that's needed to provide benefits for men and women without affecting sex hormones.²² (More on this will be published in a future issue of *Life Extension®* Magazine.)

Summary

The **longevity sciences** are advancing at a rapid pace.

Our supporters take advantage of interventions available today to live long enough to benefit from discoveries that have *already* occurred in the laboratory.

This may soon include **cellular reprogramming** that has reversed certain molecular and physiological hallmarks of aging in mice.

We at **Life Extension®** are now testing this in **aged monkeys**. (Look forward to research updates on this primate study in future issues of Life Extension magazine.)

In the meantime, I am adding **100 mg/day** of bioavailable **luteolin** to my personal program based on evidence that it may help protect against a range of degenerative processes.

For longer life,



William Faloon, Co-Founder
Life Extension® Group

Luteolin: $C_{15}H_{10}O_6$



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Summary of Noteworthy Preclinical Research Findings on **LUTEOLIN**

CARDIOVASCULAR

- Exerted **anti-fibrotic** effects in the **heart**. **Fibrosis** is the thickening and scarring of connective tissue that inflicts tissue damage and loss of function.²³
- Inhibited platelet activation, oxidative stress, and thrombosis in **human platelets**.²⁴
- Restored *nitric oxide* production and supported **vascular function** in mice with diet-induced **obesity**.²⁵
- Promoted autophagy and cleared out **intracellular cholesterol** from **macrophages**, preventing them from turning into **pro-atherogenic foam cells**, which contributes to the clogging of arteries that causes heart disease.²⁶
- Reduced **cardiac damage** caused by hyperlipidemia in rats.²⁷

CANCER

- Favorably regulated signaling pathways that suppress **cancer cell survival** and **proliferation**.²⁸
- Sensitized tumors to **chemotherapeutic agents** such as cisplatin, oxaliplatin, doxorubicin, and Taxol, while potentially reducing their toxicity.^{29,30}
- Disrupted cancer cells' adaptation to **hypoxia**, limiting their ability to survive in low-oxygen environments.³¹
- Had **anti-inflammatory** activity in **keratinocytes** (primary cells in the outer skin layer) and **fibroblasts** (most common cells of connective tissue) as well as several immune cells.³²
- In plants, flavonoids protect against UV radiation.

BRAIN HEALTH AND COGNITION

- Inhibited **amyloid-beta** (protein associated with Alzheimer's), induced cell death and oxidative stress.³³
- Suppressed the neuroinflammatory response from **microglia** (immune cells of the brain) and **astrocytes** (helper cells of neurons).¹⁴
- Protected against **glutamate-induced** neuronal cell death by regulating **autophagy** and **mitochondrial dynamics**,⁹ and it may promote the growth of new **astrocytes**.³⁴
- *Glutamate is an excitatory neurotransmitter; in excessive amounts it can negatively impact neuronal health and contribute to brain injury.*

OBESITY AND INSULIN RESISTANCE

- Luteolin improved **insulin resistance**, suppressed **obesity**, and reduced inflammatory **macrophage infiltration** in mice fed a high-fat diet.¹³
- Upregulated the expression of genes controlling lipolysis (the breakdown of fat).³⁵

AUTOIMMUNE

- Regulated macrophage oxidative stress, which may improve symptoms associated with **lupus**.³⁶
- Inhibited mast cells as well as mast cell-dependent T cell activation which is implicated in **multiple sclerosis** pathogenesis.¹⁵
- *Mast cells play a pro-inflammatory and modulatory role in the pathogenesis of multiple sclerosis.*

KIDNEY

- Delayed the progression of IgA **nephropathy** (the main cause of end stage kidney disease) by attenuating inflammation, oxidative stress, and reducing extracellular matrix accumulation.³⁷
- Improved **renal function** in rats with renal injury by reducing oxidative stress, neutrophil infiltration, inflammation, and renal cell apoptosis.³⁸

LIVER

- Reduced **liver lesions** (abnormal growth) through various mechanisms including inhibiting inflammatory factors, reducing oxidative stress, regulating lipid balance, slowing down aggregation of extracellular matrix, and induced both apoptosis and autophagy in liver cells.³⁹
- Relieved metabolic dysfunction-associated **fatty liver disease** in rats caused by high-fat diets and reduced levels of markers of oxidative stress.¹⁸

GI DISORDERS

- Reduced the incidence of **colitis** in a mouse model of disease and demonstrated anti-inflammatory activity.⁴⁰
- Alleviated ulcerative colitis by restoring **intestinal barrier integrity** and inhibiting pro-inflammatory cytokine production in colonic tissues.⁴⁰

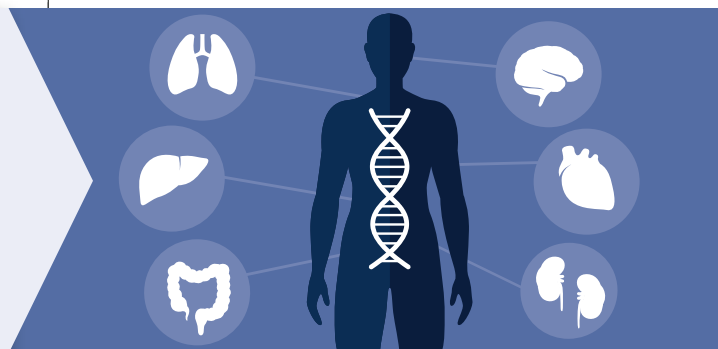
ASTHMA

- Attenuated airway inflammation, hyperresponsiveness, and mucus production in experimental **asthma** models.¹⁷

DEPRESSION

- Ameliorated chronic stress-induced **depressive-like behaviors** in mice.¹⁹

Clinical trials urgently needed to see if these laboratory findings translate into people.



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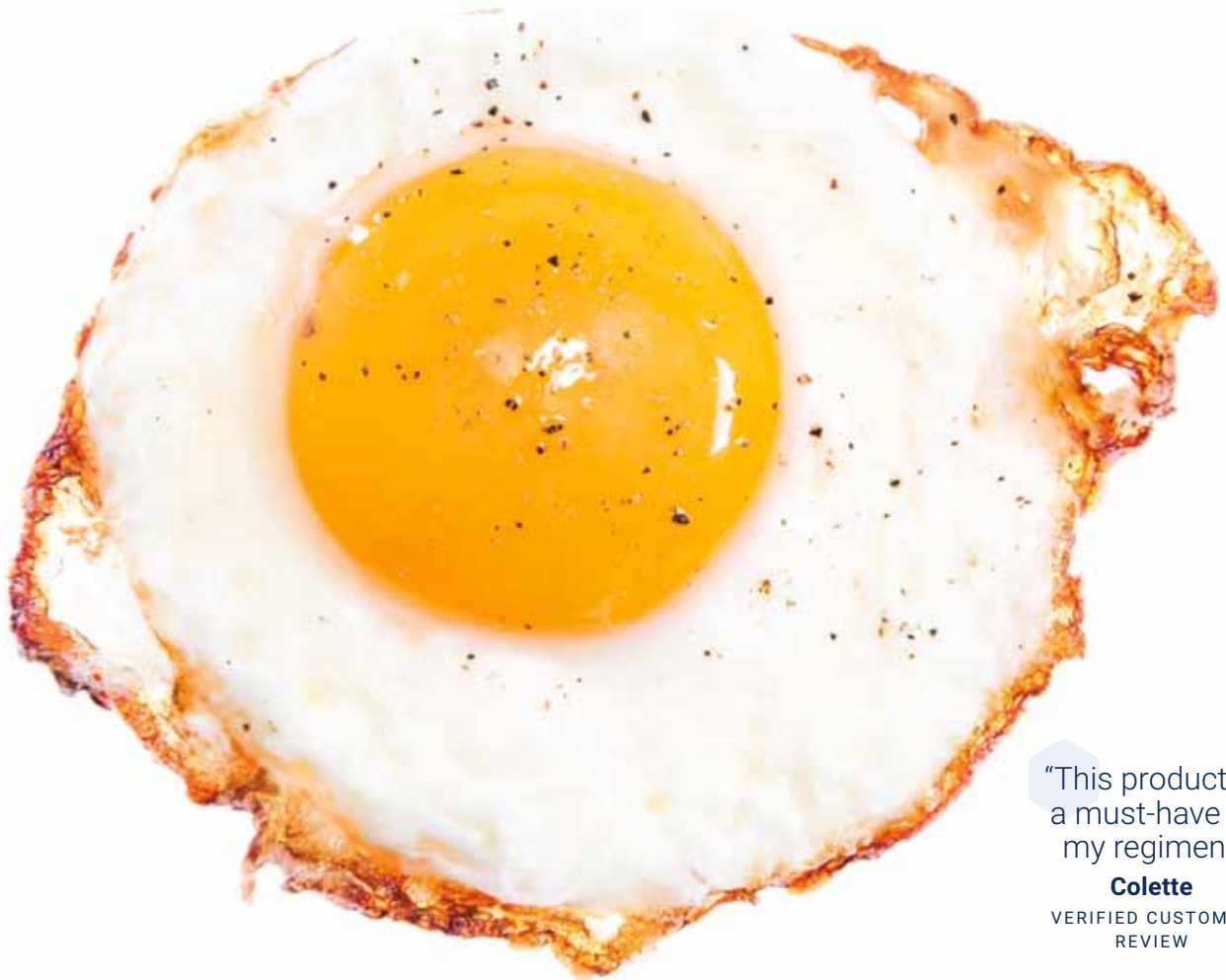
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Bioavailability refers to the proportion of an orally administered compound that reaches the bloodstream intact and becomes available to produce effects in the body.²

Luteolin occurs naturally in foods such as celery, broccoli, peppers, and artichokes, but because it's metabolized in the intestines, it's not easily absorbed by the body.

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* Regular luteolin defined as 98% pure powder luteolin

1. Akay. Data on file. Bio-Luteolin pharmacokinetics study. 2025. 2. Molecules. 2023;28(24):8038.

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In the News



Creatine May Improve Cognition in Alzheimer's Patients

The first pilot study to evaluate the effects of supplemental creatine monohydrate in people with dementia produced positive results that open the door for further investigation.¹

In a single-arm pilot trial, 20 patients with Alzheimer's disease took **20 grams** per day of creatine monohydrate (donated by **Life Extension**) for eight weeks, split into **two 10-gram** doses. A research dietitian provided oral and written education to participants and study partners on taking it and called the study partner weekly to encourage compliance with the intervention. At the end of the study, total creatine in the brain increased by **11%**.

The participants also experienced improvements in working memory and executive function, as demonstrated by scores on the National Institutes of Health Toolbox and the Mini-Mental State Examination (MMSE) assessments.

Editor's note: The standard dose of creatine is **3-5 grams** per day. While this amount is adequate for reaching muscles, higher or more prolonged dosing strategies may be required to significantly increase brain creatine content.² This study demonstrated that **20 grams** of creatine not only reached the brain, but that it was safe and well tolerated.

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Melatonin Improves Multiple Sclerosis Symptoms

A clinical study found that people with multiple sclerosis who received melatonin experienced significant improvements in muscle strength, hand control (manual dexterity), postural balance, cognition, and mood compared with those given a placebo.*

The trial included 27 participants: 15 received **3 mg** of melatonin nightly and 12 received a placebo, both for 12 weeks.

Compared to placebo, the melatonin group showed greater knee muscle strength, enhanced manual dexterity, better static postural balance, and improved cognitive function. They also reported reduced anxiety and depression.

Editor's Note: Melatonin is neuroprotective in people with multiple sclerosis due to its ability to lower oxidative damage and support a healthy inflammatory response and nervous system health, the authors explained.

* *J Diet Suppl.* 2025;22(2):236-261.





How Statins May Help Prevent Cancer

The human body has a gene called **p53** that fights against cancer by regulating cell growth. When p53 becomes damaged, instead of preventing cancer, it can *accelerate* it. About half of human cancer contains damaged p53.

Previous research on mice revealed that **statins**, which are cholesterol-lowering drugs such as Lipitor (atorvastatin), Crestor (rosuvastatin) and Zocor (simvastatin) can help reduce levels of these damaged p53 proteins. A study published in *Nature Cell Biology* reveals *how*.¹

When p53 genes become mutated, enzymes target their proteins for destruction. But when a protein called **DNAJA1** *binds* to these damaged p53 proteins, it prevents them from getting flagged for elimination. This latest research shows that statins stop DNAJA1 from binding to damaged p53 proteins, allowing them to be targeted for destruction. Since this process only occurs in misfolded p53 proteins, the *healthy* p53 proteins are not affected.

Editor's note: Researcher Tomoo Iwakuma, M.D., Ph.D, stated, "Mutant p53 makes human cancer cells more metastatic and resistant to chemotherapy. That's a primary reason to get rid of it—to improve survival in cancer patients."²

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Curcumin Improves GI Symptoms Among Obese Women

Severely obese women experienced a reduction in gastrointestinal (GI) symptoms and body mass index (BMI) after consuming curcumin daily for 13 weeks compared with those who received a placebo.*

The study followed 24 women with severe obesity. Half of the participants took **six curcumin capsules** each day (**250 mg** each, three with lunch and three with dinner) for 13 weeks, while the other half received a placebo.

By the end of the trial, women in the curcumin group reported fewer digestive issues, including less constipation and belching. They also showed measurable reductions in neck size and a significant drop in BMI, an average decrease of **4.0 kg/m**. None of these changes were seen in the placebo group.

Editor's Note: People with severe obesity often experience gastrointestinal (GI) effects such as bloating, indigestion, stomach pain, acid reflux and altered bowel patterns.

* *Nutrients*. 2025 Jun 20;17(13):2064.



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For full product description and to order **Creatine Powder**, **Creatine Capsules**, or **Creatine & Acetyl-L-Carnitine Energy Plus**, call 1-800-544-4440 or visit www.LifeExtension.com

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3. Eur J Appl Physiol. 2013 Apr;113(4):987-96. 4. Curr Opin Gastroenterol. 2023;39(2):125-8.

* When combined with a regular resistance training/exercise program.

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BY RYAN SHORE

How MAGNESIUM Helps You SLEEP

Sleep problems are frustratingly common in Americans.

One in three adults gets less regular quality sleep than the recommended amount.¹

If this sounds familiar, **magnesium** might help.

This essential mineral supports relaxation, enhances sleep quality and duration,^{2,4} and promotes more restorative sleep^{5,6} and daytime performance.^{2,7}

In a clinical study, elderly adults with insomnia taking **500 mg** of elemental magnesium reported increased overall **sleep time** and **sleep efficiency** (the percentage of time spent asleep while in bed) and decreased **time to fall asleep** and **insomnia severity**.²

In another clinical study, adults with sleep problems who took **1,000 mg** of **magnesium-L-threonate** had better **sleep quality** than those taking a placebo, and reported improved **energy**, mood, **mental alertness**, and daytime productivity.

Other forms of magnesium may work similarly.



The Importance of Sleep

Getting enough high-quality **sleep** is essential for maintaining overall health and well-being.

Chronic sleep deprivation doesn't just leave people feeling fatigued, it's also linked to a *higher* risk of serious health issues. Regular sleep duration of less than six hours has been associated with:

- Cognitive decline,⁸
- Increased risk of falls in the elderly,⁹
- Chronic diseases including type 2 diabetes, high blood pressure, and cardiovascular disease,^{3,8}
- Depression and anxiety,⁹ and
- Overall mortality.⁸

In an observational study of community-dwelling older adults followed for nine years, elderly men experiencing both insomnia and daytime sleepiness had up to a **three times greater risk of death from any cause**, compared to those without these symptoms.¹⁰



Insomnia is characterized by persistent problems with sleep. This may include difficulty falling asleep, difficulty staying asleep, or early awakening.

Age-related sleep changes can also harm **sleep quality**, with reductions in deep sleep and REM sleep.¹¹

Magnesium and Healthy Sleep

Magnesium is an essential nutrient that is required for the healthy functioning of neurons in the brain and hundreds of enzymes in the body.¹²

In animals, magnesium has been shown to play a role in cellular **timekeeping**.¹³

In the brain, magnesium is essential for maintaining a healthy balance of **excitatory** and **inhibitory** neurotransmission.

It acts as a natural *inhibitor* of **NMDA** channels, one of the most abundant excitatory receptors in the nervous system. And it *boosts* the activity of the neurotransmitter **GABA**, the most abundant relaxation-associated hormones in the brain.⁴

Together, these effects may help reduce anxiety and promote a feeling of **calm**, which may help support sleep.

More Magnesium, Better Sleep

Magnesium deficiency can negatively impact sleep, especially in older adults. It may lead to disorganized sleep patterns and disrupted **sleep-wake cycles**.¹⁴ Chronic insomnia, in turn, may affect mood and contribute to depression and anxiety.^{15,16}

One possible explanation is that magnesium deficiency negatively affects hormones that regulate sleep. For example, studies in rodents show that low magnesium levels decrease melatonin—a “sleep hormone”³ and increase secretion of **cortisol**, the “stress hormone.”¹⁶

These changes can have a drastic negative impact on sleep.

In an observational study of nearly **4,000** adults, those with the *greatest* intake of magnesium had better **sleep quality** and were more likely to sleep at least **seven hours** a night compared to those with the lowest intake.³



A systematic review of multiple human studies found that low magnesium levels are associated with increased rates of **daytime drowsiness**, snoring, and **shorter sleep duration**.⁴

In older adults, magnesium supplementation helps improve sleep quality and helps regulate sleep-related hormones by increasing melatonin and reducing cortisol levels.²

What Clinical Studies Show

The majority of older adults have lower than the recommended daily intake of **magnesium**.^{17,18}

The benefits of magnesium have been shown in additional clinical trials.

In one **clinical trial**, elderly adults with insomnia took either **500 mg** of elemental magnesium in the form of magnesium oxide or a placebo daily for eight weeks. Those taking magnesium had the following results:²

- Higher melatonin levels,
- Lower cortisol levels,
- Increased overall sleep time,
- Improved sleep efficiency,
- Reduced time to fall asleep, and
- Lower **insomnia severity index** score.

In this randomized controlled trial of 43 older adults with sleep difficulties, participants who took **500 mg** of elemental magnesium daily (administered as two doses of **magnesium oxide**) for eight weeks, showed increased blood melatonin levels, reduced cortisol concentrations, and also reported improvements in total sleep time, sleep efficiency, and sleep onset latency.²

A recent study assessed **magnesium-L-threonate** intake in 80 adults aged between 35 to 55 years with self-assessed sleep problems.^{5,6} This form of magnesium has been shown to effectively deliver magnesium into the brain.¹⁹

In the clinical trial, subjects received either **1,000 mg** of **magnesium-L-threonate** (providing **72 mg** of elemental magnesium) or a placebo daily for 21 days. At the end of the study, compared to the placebo, those receiving magnesium showed improved **sleep quality**, including more time spent in restorative **deep** and **REM sleep** and less time in light sleep.⁵



What You
Need
To Know

A Better Night's Sleep with Magnesium

- Getting enough high-quality **sleep** is essential to health and quality of life.
- Sleep problems like insomnia are common, affecting up to **50%** of older adults.
- The mineral **magnesium** plays a critical role in sleep regulation, maintaining healthy levels of hormones that impact sleep such as melatonin and cortisol.
- In **clinical trials**, magnesium intake increased sleep time, reduced the time it takes to fall asleep, decreased insomnia severity, and improved energy, mood, mental alertness, and daytime productivity.

Those taking magnesium also reported improved **energy, mood, mental alertness**, and daytime **productivity**.

In another study focusing on patients recovering from open-heart surgery, those receiving **500 mg of magnesium oxide** daily had improved sleep quality and lower levels of anxiety and depression, compared to patients receiving standard care without magnesium.²⁰

Summary

Sleep problems like **insomnia** are very common in adults.

Magnesium is critical to healthy sleep, helping to regulate sleep-wake cycles and balance hormones that affect sleep like melatonin and cortisol.

In clinical trials, magnesium intake improved **sleep quantity** and **quality**, leading to more energy and alertness during the day. ■

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

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Forms of Magnesium

Life Extension has long emphasized to its readers the importance of this key mineral. While all forms of magnesium are absorbed well, maintaining healthy blood levels depends on consistent intake rather than relying on a single form. The goal should be to ensure daily replenishment through both diet and supplementation.

Magnesium supplements are available in various forms, each offering distinct properties. When selecting a magnesium supplement, the choice depends on individual preference, tolerance, cost, quality brand, and health goals. Oral magnesium comes in a variety of different formulations which are commonly included but are not limited to:

- **Magnesium glycinate** is a well absorbed form of magnesium to support whole-body health.²¹ It combines magnesium with the amino acid glycine.²² Individuals who tend to experience occasional gastrointestinal discomforts when using magnesium supplements prefer magnesium glycinate over others.
- **Magnesium citrate** is another well absorbed form of magnesium.²³ This affordable form is also a good choice for those who experience occasional gastrointestinal discomfort when taking other magnesium supplements.
- **Magnesium oxide** offers a higher percentage of elemental magnesium per single dose. It is often found in multi-ingredient products as it delivers a greater concentration of elemental magnesium without increasing the number of capsules.²⁴
- **Magnesium-L-threonate** is a formulation developed by a team of scientists at the **Massachusetts Institute of Technology (MIT)**. It has been shown to effectively deliver magnesium into the body.²⁵ It is a better option if you are looking for brain health benefits. It has been clinically studied to support quick thinking and working memory, and it promotes overall cognitive health.¹⁹
- **Magnesium Acetyl-Taurate** combines magnesium with the acetylated form of the amino acid taurine. Preliminary evidence suggests it may help support relaxation and manage occasional anxiety.²⁶



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		4+ units	—	\$24.30 ea.	17%
		10+ units	—	\$22.50 ea.	23%
00335	DHEA • 25 mg • 100 capsules For hormone balance, muscle mass and sexual function.	1 unit	\$11.25	\$10.13	10%
		4+ units	—	\$9.23 ea.	18%
01778	Super Selenium Complex • 200 mcg • 100 vegetarian capsules Three different forms of selenium that support healthy aging, thyroid and immune function.	1 unit	\$10.50	\$9.45	10%
		4+ units	—	\$8.10 ea.	23%
02500	Testosterone Elite† • 30 vegetarian capsules Promotes healthy testosterone production.	1 unit	\$42.75	\$38.48	10%
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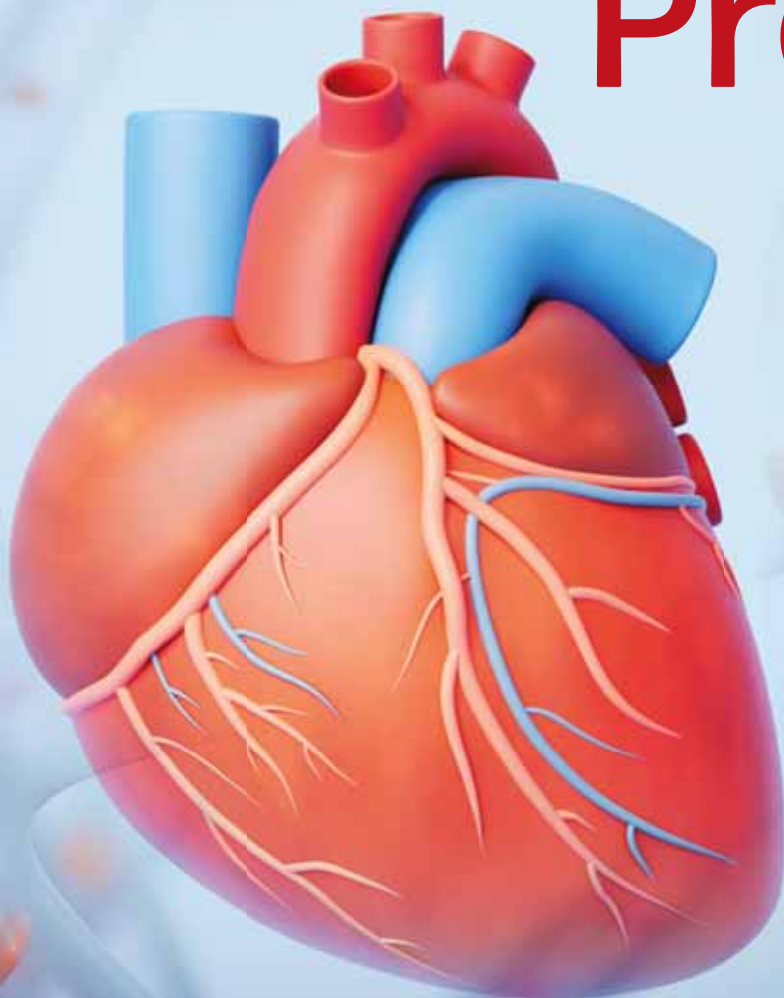
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MICRODOSING LITHIUM





BY MARSHA MCCULLOCH, MS, RD

Life Extension has reported for years on the benefits of low-dose **lithium**, including the mineral's potential to reduce **dementia risk**.

In preclinical models, lithium has been shown to favorably modulate several biological processes involved in **aging** and **disease**.^{1,2}

A **human** interventional study suggests that it may help reduce depression and anxiety in individuals genetically predisposed to psychiatric conditions such as depression, bipolar disorder, and schizophrenia.³

An observational study in Japan found that trace amounts of **lithium** in **drinking water** are associated with lower all-cause mortality.⁴

A groundbreaking experimental study published in the prestigious journal **Nature** provides some of the strongest evidence that **lithium** may help **prevent dementia**.

In the study, low-dose **lithium orotate** nearly restored memory in both normal **aging mice** and in mice with an inbred susceptibility to **Alzheimer's**-like changes.⁵

This multi-part study also found that **human brain tissue** from people with dementia was low in **lithium**.⁵

Dietary intake of lithium is considered insufficient in many regions of the world.⁶

An oral **microdose** of **300 mcg** to **2,000 mcg** a day and higher may provide a wide range of potential health benefits.

An Underappreciated Mineral

High-dose prescription lithium has long been a treatment for mood disorders, particularly bipolar disorder.⁷

These doses generally range from **600 to 1,200 mg** of lithium carbonate daily. This is many hundreds of times more lithium than the amounts people get in their diet or take as a supplement.⁷

Some experts have suggested a recommended intake of roughly **1,000 mcg**, or just **1 mg** of lithium daily for most adults.⁷

Lithium is found in very small amounts in water and some foods (like grains, legumes, nuts, and leafy vegetables), depending on the soil content of the mineral in the region.⁸

Because the earth's surface lithium content varies from region to region, food and water lithium content also vary, making them unreliable sources of the mineral. Given the growing evidence of lithium's health benefits and psychiatric applications, it has been suggested that international health agencies consider developing guidelines for its recommended daily intake.⁶

Oral **microdoses (1 mg/day)** can be taken daily to ensure adequate intake.

New Evidence: Lithium Fights Dementia

Observational studies have linked long-term exposure to higher levels of lithium in drinking water with lower dementia risk^{9,10} and **Alzheimer's mortality**.¹¹

In small clinical trials, long-term low-dose lithium use (in the gluconate or carbonate form, rather than orotate) has been shown to slow cognitive and functional decline in participants with mild cognitive impairment.¹²⁻¹⁴ These **human** studies found that lithium favorably affected Alzheimer's-related biomarkers¹³ and may offer disease-modifying benefits in early Alzheimer's.¹³⁻¹⁵

A recent multi-part study published in **2025** provides powerful new evidence that lithium could play a role in dementia prevention.⁵

Scientists measured **27** minerals in the brain tissue from hundreds of older adults who died with or without **mild cognitive impairment** or **Alzheimer's**. Lithium was the *only* mineral tested that was significantly reduced in the **brains** of those with mild **cognitive impairment** or **Alzheimer's**, compared to healthy brains.⁵

Neurological Dangers of Lithium Deficiency

The same scientists put aging mice on a **lithium-deficient diet** to see how that affected their brain tissue. Some of the mice were genetically altered to develop amyloid plaques and Alzheimer's-like symptoms.⁵

Both the dementia-prone *and* normal mice had significant impairments in some measures of **learning** and **memory** after the deficient lithium diet.

Brain changes in lithium-deficient mice compared to mice on a regular diet included:⁵

- Accelerated buildup of **amyloid plaque**,
- Abnormal accumulation of **phosphorylated tau**, which can lead to nerve fiber tangles,
- Increased **neuroinflammation**, impairing the ability to clear amyloid, and
- Loss of **synapses**, **axons**, and **myelin** needed for the transmission of nerve cell messages.





What You
Need
To Know

Lithium Orotate Superior to Carbonate

Next, the scientists gave the mice small amounts of either **lithium orotate**, sodium orotate (to test whether it was lithium or orotate that explained any effects), or lithium carbonate (the form commonly used to treat bipolar disorder).^{5,16}

Lithium orotate was significantly more effective than **lithium carbonate** in raising lithium levels in needed areas of the brain while avoiding getting trapped in amyloid plaque.⁵

Remarkably, **lithium orotate** greatly reduced plaque buildup, prevented pathological changes and nearly restored memory in dementia-prone mice.

In normal mice, **lithium orotate** treatment similarly improved **memory performance** and reduced **neuro-inflammation**. Mice that were treated with either lithium carbonate or sodium orotate had no improvement.⁵

Lithium Protects Aging Brains

- **Lithium** is a trace mineral involved in biological processes related to aging and disease.
- A study published in 2025 provides new insight into the potential for micro-doses of lithium to stave off **Alzheimer's** and other forms of dementia.⁵
- In the study, **human brain tissue** of people who died with Alzheimer's or mild cognitive impairment was found to have low lithium levels.⁵
- In the same study, mice fed a lithium-deficient diet developed impaired learning and memory. Low doses of lithium orotate nearly **restored memory** in the rodents.
- **Lithium orotate** was shown to deliver lithium more efficiently to the brain in preclinical research.

Lithium and GSK-3

One key way lithium may benefit the brain is by inhibiting the activity of **glycogen synthase kinase-3 (GSK-3)**, a signaling molecule.¹⁷

Overactivation of **GSK-3** can trigger **cognitive decline**.^{18,19}

In the mouse study, **lithium depletion** led to increased activity of **GSK-3**. This led to pathological brain changes, including increased amyloid plaque and phosphorylated tau.⁵

Previous studies have shown increased **GSK-3** expression and activity in the brains of people with **Alzheimer's**.^{19,20}

People with **glaucoma**, a major cause of blindness in older people and around the world, also have increased activation of GSK-3. Preclinical research suggests GSK-3 overactivity can lead to **elevated** intra-ocular **eye pressure**, which damages the optic nerve.²¹



People with glaucoma have a higher risk of developing **dementia**.²²⁻²⁴ This could mean that low-dose lithium intake may have multiple benefits in this population.²⁵

Other Effects of Lithium

Preclinical and observational research shows **low-dose oral lithium** may have several other benefits, including:

- Providing **anti-inflammatory** and **antioxidant** protection,^{26,27}
- Supporting **blood vessels**,²⁸ and **heart function**,^{26,29}
- Protecting **bone density** and **muscle mass**,^{26,30}
- Promoting **metabolic health**,²⁶ and
- Reducing **all-cause mortality**.⁴

A daily **microdose of lithium** may provide cognitive benefits and promote overall healthy aging.

Summary

Lithium prescribed in high doses is used to treat bipolar disorder. Emerging evidence suggests that **microdoses** of the mineral may help support brain health in aging adults.

A major multi-part study published in **2025** found that brain tissue from people who died with **dementia** was low in **lithium** and that mice given a **lithium-deficient** diet developed Alzheimer's-like memory problems.

The **lithium orotate** form of the mineral raised lithium levels in the rodents' brains and nearly **restored their memory**.

Taking oral microdoses of **lithium orotate** provides a consistent, dependable source of the mineral. ■

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



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Restore Youthful Cellular Energy with PQQ

This formulation contains 20 mg of PQQ per capsule, which is the recommended daily dose.



PQQ helps support mitochondrial health, which produces cellular energy.¹⁻⁴

Studies show PQQ supports heart health and cognitive function, complementing CoQ10.⁵⁻⁸

PQQ helps protect against oxidative stress and encourages whole-body health.⁹

SUPER SALE PRICE

Item #01647

30 vegetarian capsules

1 bottle \$21.60

4 bottles \$16.20 each



Also available are 10 mg PQQ caps (Item #01500) and 100 mg Super Ubiquinol CoQ10 with PQQ (Item #01733).

For full product description and to order PQQ or any other PQQ-containing formulas, call 1-800-544-4440 or visit www.LifeExtension.com

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MACUGUARD® OCULAR SUPPORT PROVIDES:

- **Lutein, zeaxanthin, and meso-zeaxanthin** to help maintain structural integrity of the **macula** and **retina**.¹⁻⁵
- **Saffron** to help support **vision** as demonstrated by doctors' eye exams.¹
- **Alpha-carotene** to further help support **macular density**.¹

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

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**MacuGuard® Ocular Support
with Saffron + Astaxanthin**
SUPER SALE PRICE
Item #01993 • 60 softgels
1 bottle **\$29.03**
4 bottles \$26.10 each

"This is a
great item
for me."

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VERIFIED
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REVIEW



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MacuGuard® Ocular Support with Saffron has met ConsumerLab.com standards for ingredient and product quality for Lutein and Zeaxanthin in independent testing. More information at www.consumerlab.com.



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Support Healthy Aging with Benfotiamine

"Love this supplement!"

Sarah

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REVIEW



Mega Benfotiamine provides a fat-soluble form of thiamine (vitamin B1) known as benfotiamine.

Benfotiamine helps support cellular health by impeding formation of **advanced glycation end products (AGES)**.^{1,2,3}

References

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SUPER SALE PRICE

Item #00925

120 vegetarian capsules

1 bottle **\$20.93**

4 bottles \$18 each



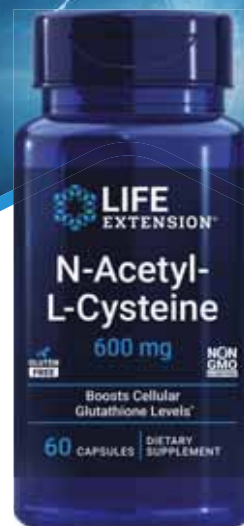
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ARMOR UP

Protect your cells with this powerful antioxidant and glutathione precursor

Help your body fight back against free radicals—and encourage your liver and respiratory health—with this easily absorbed immune health all-star.



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FOR DAILY HEALTH

Strong bones and a healthy heart are two benefits of adding vitamin K to your routine.

This essential vitamin helps maintain your body's calcium balance and, in turn, supports everything from your arterial health to healthy bone density.

Fortunately, you can ensure you're getting enough of this important nutrient by supplementing with exactly as much—or as little—vitamin K as you need.



Super K*

Vitamin K (as phytonadione) 2,000 mcg

Vitamin K2 (Mk-4) 1,000 mcg

Vitamin K2 (as MenaQ7® trans menaquinone-7) 180 mcg

SUPER SALE PRICE

Item #02334 • 90 softgels

1 bottle **\$21.60**

4 bottles \$19.80 each

(Each bottle lasts 3 months)



Low Dose Vitamin K*

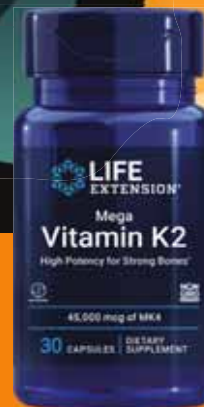
45 micrograms

SUPER SALE PRICE

Item #01936 • 90 softgels

1 bottle **\$12.15**

4 bottles \$10.80 each



Mega Vitamin K2*

45 milligrams

SUPER SALE PRICE

Item #02417 • 30 capsules

1 bottle **\$25.65**

4 bottles \$23.40 each

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

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

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"Works well!"

Ana

VERIFIED CUSTOMER
REVIEW

A Bodyguard for Your Brain



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

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

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



SUPER SALE PRICE

(1000 mcg of lithium per tiny cap)

Item #02403 | 100 vegetarian capsules

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

Each bottle lasts 100 days.



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

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

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

Activate AMPK For Optimal Metabolic Health





BY ROBERT FRIEDMAN

AMPK is an *enzyme* found in nearly every cell.¹

In youth, AMPK is more active than in older age.

Activated **AMPK** promotes vital processes such as:

- Healthy metabolism of lipids (fats) and glucose (sugars),^{2,3}
- Cellular housekeeping (autophagy),^{2,4}
- Insulin sensitivity (glucose control),³ and
- Mitochondrial function.^{2,3}

The age-related decline in **AMPK activity**^{5,6} can increase risks of metabolic disorders, cardiovascular disease, and other chronic illnesses.^{4,7}

Two nutrients have each been shown in separate **human** trials to activate **AMPK**.

What is AMPK?

The enzyme AMPK (AMP-activated protein kinase) acts as a master controller of cellular metabolism.⁸ It regulates over 100 critical proteins that affect nearly all aspects of cell function.⁹

AMPK activity declines significantly with age, leading to impaired cellular function and a higher risk of degenerative illnesses

Preclinical studies have shown that when activated, AMPK helps:

- Maintain cellular energy balance,⁹⁻¹¹
- Regulate lipid metabolism, including fat oxidation,^{3,9,12}
- Improve insulin sensitivity and glucose uptake by cells, lowering blood sugar,¹³
- Process and extract energy from carbohydrates,⁹
- Promote autophagy, or “cellular housekeeping,”^{2,3}
- Promote the replacement of old mitochondria with new ones, the energy-generating “powerhouses” of the cell,³
- Activate sirtuins, signaling proteins that play critical roles in regulating metabolism,¹⁴ and
- Reduce harmful inflammation.¹⁵

AMPK activation in animals has been shown to contribute to longer lifespans.⁴ Scientists believe that AMPK activation is capable of **delaying the aging process**.⁶

The Problem with Low AMPK Activity

For many modern humans, periods of nutrient scarcity (calorie reduction) that boost **AMPK** activity are rare.

Instead, constant access to calories causes AMPK activity to remain chronically low.

Impaired AMPK activity is associated with disrupted cellular metabolism, obesity, and inflammation¹⁶ Preclinical evidence suggests it also plays a role in the development of **type 2 diabetes**,^{5,16} **cardiovascular disease**,^{5,16} and **osteoarthritis**.⁵

Fortunately, there are ways to increase AMPK activity.

Boosting AMPK

Caloric restriction or **intermittent fasting** are effective AMPK activators. In animal models, restricting calories extends lifespan.¹⁷ However, these types of restrictive diets are difficult for people to maintain.

Exercise is another AMPK activator known to prolong healthy life.¹⁸

Scientists have discovered that some plant-derived compounds act as caloric restriction or exercise **mimetics**, mimicking their biological effects, including by activating AMPK. These include:

- Hesperidin, and
- *Gynostemma pentaphyllum* extract.

Hesperidin Helps Blood Vessels

Hesperidin is a flavonoid found in citrus fruits.¹⁹

In mice fed a high-fat diet, hesperidin intake for 16 weeks led to improvements in **metabolic health**, including reduced body weight and fat, improved blood glucose and lipid levels, lower insulin levels, and enhanced insulin sensitivity.²⁰

The effectiveness of hesperidin has also been validated in human trials.^{19,21}

In one clinical study, 24 adults with **metabolic syndrome** took **500 mg** of **hesperidin** or a placebo daily for three weeks. Those receiving hesperidin had improved **blood vessel reactivity** (the ability of vessels to constrict or relax when needed) and reduced systemic inflammation.¹⁹



Support Healthy Metabolism

- **AMPK** is a master regulator of cellular metabolism. It is activated when nutrient availability is scarce and inhibited when calories are abundant.
- Modern diets and advancing age tend to keep AMPK activity low, contributing to poor **metabolic health** and increased risk of disease.
- In separate human trials, the plant compounds **hesperidin** and an extract of the herb ***Gynostemma pentaphyllum*** have been shown to boost AMPK activity, leading to improvements in metabolic and overall health.

Gynostemma Targets Fat

Gynostemma pentaphyllum is a plant native to Asia²² that is sometimes referred to as the “immortality herb” in local cultures. It contains beneficial compounds called **saponins**.²³

Animal and cell studies show that **Gynostemma extract** can activate AMPK and lead to weight loss and improved cholesterol levels.^{22,24-27}

Human studies confirm these findings. One study randomized obese adults to receive **450 mg** of **Gynostemma** extract or a placebo daily for 12 weeks, with *no changes to diet or exercise*. Compared to placebo, those taking Gynostemma had declines in:^{22,28}

- Body mass index (BMI),
- Body weight,
- Body fat mass,
- Percent body fat, and
- Total abdominal fat area.



Abdominal fat is considered particularly dangerous and is associated with chronic inflammation and poor metabolic health. In this study, Gynostemma led to a remarkable **11%** reduction in **abdominal fat** deposits.

Those receiving Gynostemma also lost an average of **one inch** off their waistline, equal to roughly one belt notch.

In another clinical trial, 16 healthy young untrained men took **450 mg** of Gynostemma extract or a placebo daily for four weeks and were tested during exercise. Results indicated that the extract improved exercise performance, activated **muscle AMPK** (after 60-minute exercise), slowed the fat-associated hormone **leptin**, and improved blood glucose levels.²⁹

These two nutrients can be taken as part of a balanced diet and regular exercise routine to achieve optimal results.

Summary

AMPK is a master regulator of cellular metabolism. Aging is associated with reduced AMPK activity, driving metabolic disease, and risk for age-related disorders.

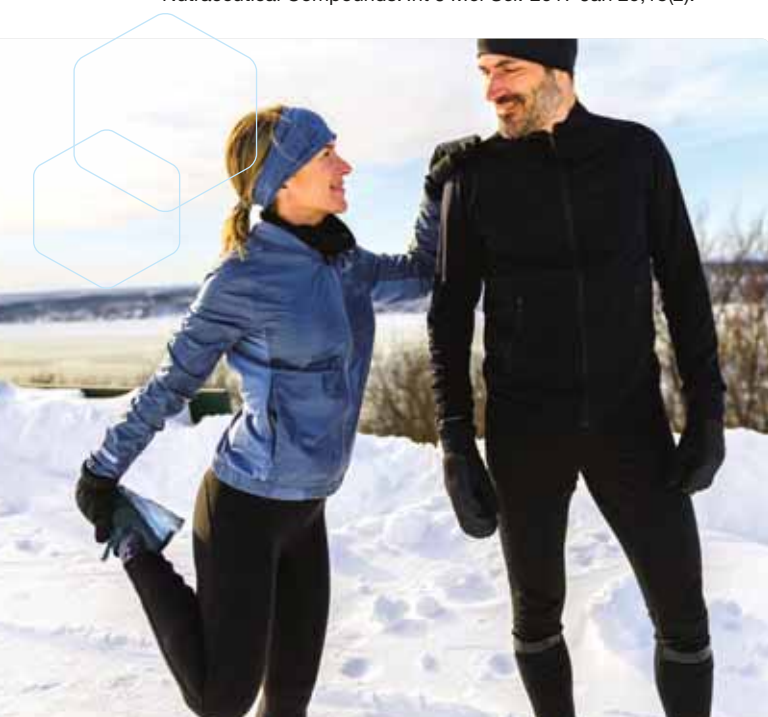
The polyphenol **hesperidin** and an extract of the herb **Gynostemma pentaphyllum** have each been found to boost **AMPK activity**, improving metabolic health markers. ■

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

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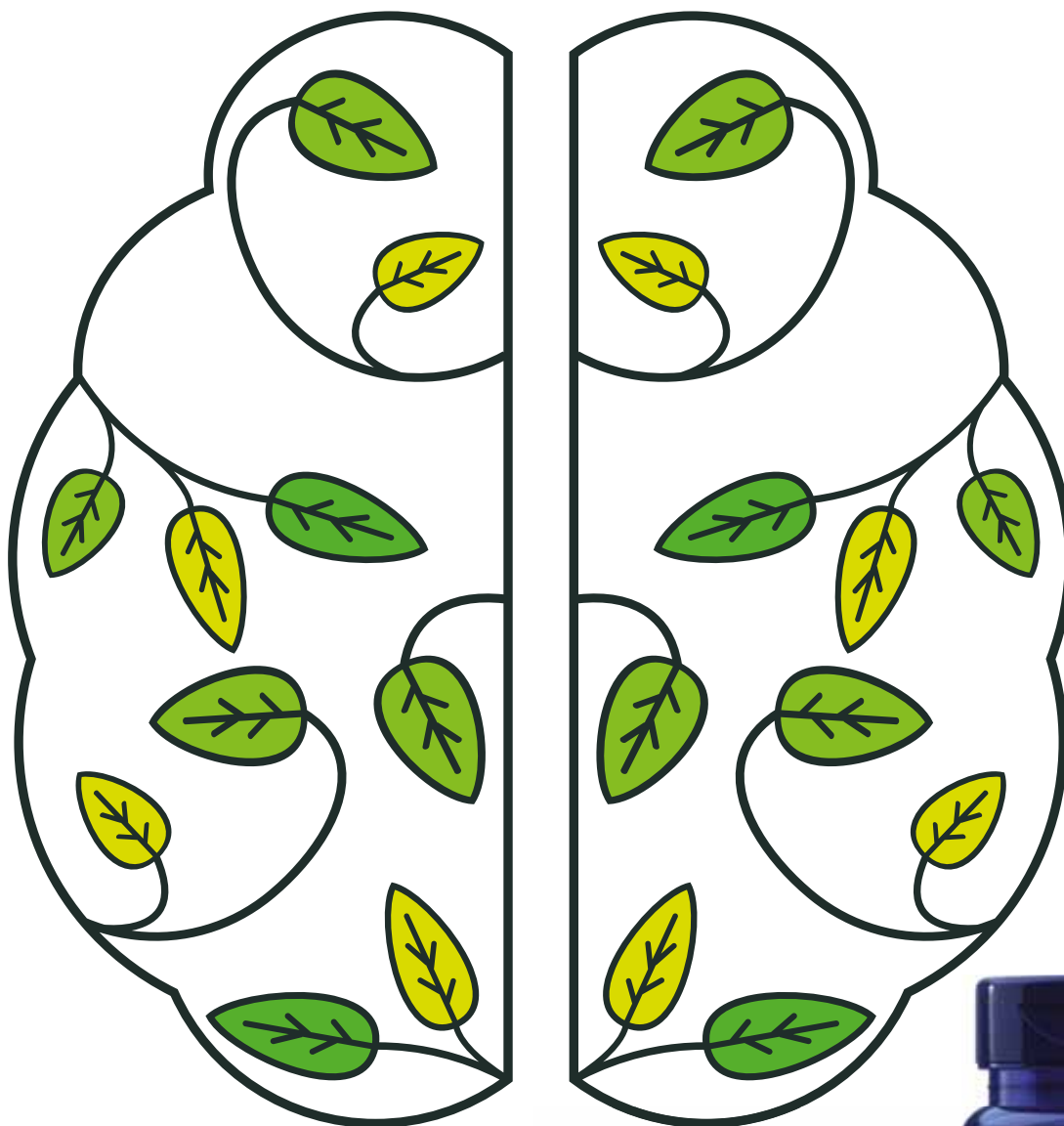
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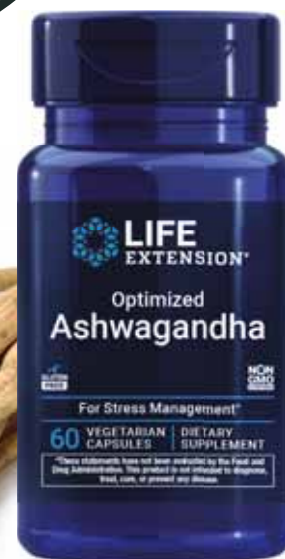
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A human trial showed **bioavailability** of this fisetin compound increased up to **25 times** compared to fisetin* by itself.²

"Good stuff."

Scott

VERIFIED CUSTOMER
REVIEW

References

1. *EBioMedicine*. 2018 Oct;36:18-28.
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* Studied against powder fisetin
(98% purity)

For full product description and to order Bio-Fisetin®,
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This supplement should be taken in conjunction with a healthy diet and regular exercise program. Individual results are not guaranteed, and results may vary.

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What to Look for in a **MULTI- VITAMIN**

BY HEATHER L. MAKAR

Reports from 2017–2018 show that nearly **40%** of U.S. adults aged 60 and older took a daily multivitamin.¹

Many commercial formulas, however, fall short of the benefits possible from obtaining *higher* potencies and **bioactive** forms of certain vitamins.^{2,3}

Most consumers don't know the difference.

When selecting a multivitamin, both dosage and bioavailability are crucial factors, particularly as nutrient absorption and utilization become less efficient with **age**.⁴



Deficiency is Widespread

Many adults do not get enough of key vitamins, minerals, and other nutrients. For example:

- According to the National Health and Nutrition Examination Survey (NHANES), about **50%** of Americans have **insufficient** levels of **vitamin D**.⁵ Low levels of vitamin D are linked to chronic diseases such as bone, heart, and metabolic disorders, as well as mental and autoimmune conditions.⁶
- **Human** studies show that even many people in developed countries are deficient or insufficient in one or more forms of **B vitamins**, which can negatively affect brain health.⁷

Vitamins and essential minerals are critical to health. The body and mind can't function properly without them, and when they aren't supplied in adequate amounts, health suffers – sometimes seriously.

These and other vital nutrients enable essential functions like DNA repair, supporting immune function, reducing oxidative damage, maintaining cardiovascular health, and much more. When levels are **low**, many different symptoms can occur, notably **fatigue**, slow healing, and **poor cognition**.⁸

In short, a lack of essential vitamins and minerals increases the risk of many different ailments, including premature aging.⁹ Taking a science-based multivitamin can help cover many essential nutritional bases.

Nutrients in the Right Form

Not every multivitamin provides optimal potencies. Some contain **forms** of nutrients that may be difficult to use.

For example, vitamin B9 (known as folate in its natural form) is needed to detoxify **homocysteine**, a risk factor for vascular disease. But first, it has to be converted into its **active** form, **5-MTHF**.¹⁰ Similarly, the methylated form of B12 may be more easily utilized, since it is already biologically active.¹¹ An optimal multivitamin provides these two B-vitamins in their **activated** form.

Vitamin B12 deficiency is more common in vegans, the elderly, and people with certain specific gastrointestinal disorders,¹¹ while people with some types of malabsorption and alcoholics can develop folate insufficiency.¹⁰

Other vitamins can also be delivered in advanced forms. For instance, vitamin E, when delivered as a combination of the four tocopherol forms alpha, beta, delta, and gamma,¹² may provide superior **antioxidant protection**, helping protect your cells from oxidative damage and inflammation.

Cutting-edge multivitamin formulas often also include certain **plant** and other **nutrient compounds** beyond basic vitamins/minerals, including:

- **LYCOPENE**, a carotenoid that supports prostate and cardiovascular health and protects against UV-induced skin damage,¹³
- **APIGENIN**, a flavone that provides cellular protection,¹⁴

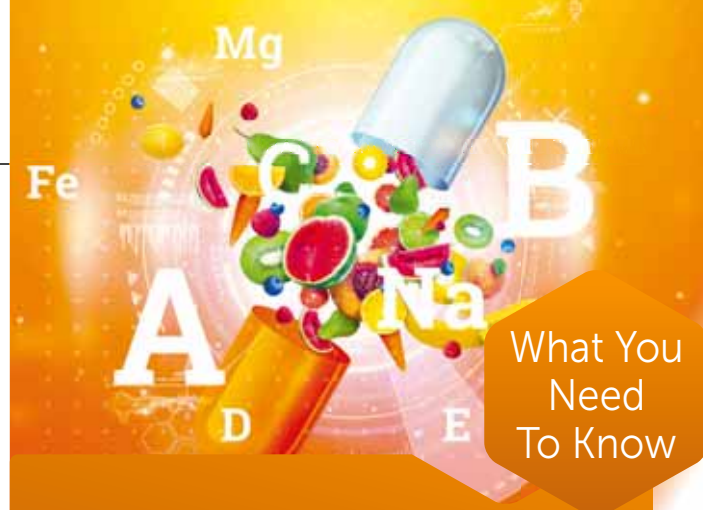


- **ALPHA-LIPOIC ACID**, a powerful antioxidant that helps regenerate *other* antioxidants and supports healthy glucose metabolism,¹⁵ and
- **LUTEIN AND ZEAXANTHIN**, carotenoids that concentrate in the eyes and brain, supporting visual health and cognitive function while protecting against blue-light damage.¹⁶

Valuable Vitamins

Multivitamins need to cover the basics:

- **VITAMIN B1: (THIAMINE)**, supports energy production, carbohydrate and protein metabolism, and proper nervous system function. Its deficiency disrupts mitochondrial activity and can cause severe neurological and cardiovascular disorders such as Wernicke's encephalopathy and heart failure.¹⁷
- **VITAMIN B3: (NIACIN/NIACINAMIDE)**, can be converted into NAD⁺, a molecule crucial for cellular energy and longevity. It also supports healthy energy and metabolism, as well as skin health and DNA repair.¹⁸
- **VITAMIN B6:** helps break down homocysteine, supports brain health, reduces inflammation, protects blood vessels and reduces glycation; deficiency can raise cardiovascular and neurological risks.¹⁹ Pyridoxine is the most common form of vitamin B6. Pyridoxal-5-phosphate is an active form that all forms of **vitamin B6** break down to, assuming there is sufficient *enzymatic* support to convert them to the biologically active (pyridoxal-5-phosphate) form.²⁰ By including pre-active B6 (pyridoxal-5-phosphate), a multivitamin can help ensure optimal benefits without relying on enzymatic conversion in our aging bodies.
- **VITAMIN C:** promotes immunity and is essential for collagen synthesis, supporting the strength of arteries, skin, bones, and teeth. It also aids in hormone production, iron absorption, and antioxidant defense, helping maintain overall health.²¹



Choose a Better Multivitamin

- Many **commercial multivitamins** are missing critical nutrients and provide others in low doses and poorly absorbed forms.
- An **optimal formula** should provide ample doses of crucial vitamins and minerals, often with additional plant extracts, in bioavailable forms.
- Taking a comprehensive multivitamin can support cardiovascular, metabolic, neurological, and immune health to promote overall **healthy aging**.

- **VITAMIN D3:** supports immune function and bone health. Its deficiency has been associated with an increased risk of various chronic conditions, including cardiovascular and metabolic diseases.⁶

Minerals for Maximum Absorption

In addition to the dose, the form of **minerals** can be important. Superior formulas use **bioavailable** forms of the following:

- **ZINC:** **zinc citrate** and **zinc mono-L-methionine sulfate** are recognized as well-absorbed forms of zinc.²² A combination of **zinc citrate** and **zinc mono-L-methionine sulfate** may support immune function, and over **300** enzymatic reactions.²³

- **SELENIUM:** Methylated seleno-cysteine as well as **sodium selenite** and **high-selenium yeast** provides broad-spectrum support. These three different forms of selenium have their own unique benefits.²⁴
- **CHROMIUM:** A stabilized form of this mineral using the compound **shilajit** improves bio-availability.²⁵ Chromium is a micronutrient that supports healthy glucose metabolism, insulin sensitivity, blood sugar, and lipid profile.²⁶
- **MOLYBDENUM:** This mineral is required for several enzyme activities, including those that detoxify alcohol and metabolize sulfur-containing amino acids.²⁷
- **MANGANESE:** Manganese is an essential mineral needed for immune function, energy production, blood sugar regulation, reproduction, digestion, bone growth, blood clotting, and protection against oxidative stress.²⁸ Using two bioavailable forms ensures adequate absorption of this mineral crucial for bone formation and antioxidant defense.
- **IODINE:** **Potassium iodide** provides consistent, contamination-free iodine for thyroid function and metabolic health.²⁹

- **BORON:** In an **amino acid chelate** form, boron supports bone health, cognitive function, and helps the body use other minerals more effectively.³⁰

Many of these vitamins, minerals, and other nutrients work together to support optimal health.

Summary

A superior **multivitamin** formula provides a broad range of pre-activated, **bioavailable** forms of vitamins, minerals, and plant extracts to help support cardiovascular, metabolic, neurological, and immune health. ■

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

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[†] This product is intended to support testosterone levels and does not contain testosterone.

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Chris

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24
HOURS
A DAY

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Buffered **ascorbate** encased in two plant extracts (liposomes plus hydrogel fenu-greek) increases blood (plasma) exposure nearly **seven times** more compared to an equivalent dose of vitamin C as calcium ascorbate.¹

It also maintains vitamin C levels throughout the day.²

Just one vegetarian tablet daily provides **around-the-clock** vitamin C support.

References 1. Akay Internal Study. Liposomal vitamin C (calcium ascorbate) pharmacokinetics. Data on file. 2021.
2. Akay Internal Study. Liposomal hydrogel vitamin C pharmacokinetics. Data on file. 2021.

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Vitamin B2 (riboflavin, riboflavin 5'-phosphate)	50 mg
Vitamin B3 (niacinamide, niacinamide ascorbate)	50 mg NE•
Vitamin B5 (D-calcium pantothenate)	50 mg
Vitamin B6 (pyridoxine HCl, pyridoxal 5'-phosphate)	75 mg
Folate (5-MTHF)	680 mcg DFE [°]
Vitamin B12 (methylcobalamin)	300 mcg
Biotin	300 mcg
Vitamin C (ascorbic acid, calcium and niacinamide ascorbates)	470 mg
Vitamin D3 (cholecalciferol)	(2,000 IU) 50 mcg
Vitamin E (D-alpha tocopheryl succinate, D-alpha tocopherol)	67 mg
Vitamin E (gamma, delta, alpha, beta tocopherols)	20 mg
Iodine (potassium iodide)	150 mcg
Magnesium (magnesium oxide)	100 mg
Zinc (zinc citrate, L-OptiZinc [®] zinc mono-L-methionine sulfate)	25 mg
Manganese (manganese citrate, gluconate)	2 mg
Chromium [Crominex [®] 3+ chromium stabilized with Capros [®] amla extract (fruit), PrimaVie [®] Shilajit]	200 mcg
Molybdenum (amino acid chelate)	100 mcg
Inositol	50 mg
Alpha lipoic acid	25 mg
Bio-Quercetin[®] Proprietary Blend providing 35% quercetin (5 mg) [from Japanese sophora concentrate (flower bud)], 30% galactomannans (4 mg) [from fenugreek (seed)]	14 mg
Marigold extract [std. to 5 mg <i>trans</i> -lutein, 155 mcg <i>trans</i> -zeaxanthin]	11.12 mg
Apigenin	5 mg
Boron (boron amino acid chelate)	3 mg
Lycopene [Lycobeads [®] natural tomato extract (fruit)]	1 mg
Selenium [as sodium selenite, SelenoExcell [®] high selenium yeast, Se-methyl L-selenocysteine]	200 mcg

[^] RAE (retinol activity equivalents). [°] DFE (dietary folate equivalents). • NE (niacin equivalents).

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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. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.

† Ratings based on results of the 2024 ConsumerLab.com Survey of Supplement Users. More information at www.consumerlab.com/survey.

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- Mood swings
- Sleep disturbances
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- Joint discomfort
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Link Between Glucosamine and Reduced Mortality

BY RACHEL MORTON



Glucosamine and Joint Health

Glucosamine is a compound that acts as a precursor or building block for **cartilage**, the tissue that protects and cushions the ends of bones at the joints.⁹

It is commonly taken to maintain joint health and prevent or reduce the severity of **osteoarthritis**.⁹

Clinical trials have confirmed glucosamine's effectiveness in arthritis, whether taken alone or with **chondroitin**, another nutrient often used for joint health.¹⁰ For example, a systematic review of studies found that taking **glucosamine** long-term significantly **reduced pain** in those with knee osteoarthritis compared to a placebo.¹¹

Reduced All-Cause Mortality

Though glucosamine is usually taken for joint health, scientists conducting large observational studies made a striking discovery: Its use is associated with a **reduced risk of overall mortality**.

One population study following 77,510 individuals (ages 50-76) in Washington State over five to eight years found that **regular users** of **glucosamine**, with or without chondroitin, had an **18% lower risk of death from any cause** than those who did not use glucosamine.¹²

More than **five million** people in the U.S. take **glucosamine** annually, largely to support **joint** health and ease **arthritis** pain.¹

Recent findings indicate this low-cost compound may provide a stunning range of additional benefits.

In two large observational studies, scientists have found a link between **glucosamine** use and **reduced risk of death from any cause**.^{2,3}

These same studies also found that people taking **glucosamine** had lower rates of several age-related chronic diseases including:

- Cardiovascular disease,^{4,5}
- Alzheimer's and other forms of dementia,^{6,7}
- Type 2 diabetes,⁸ and
- Certain types of cancers.⁵

In addition, glucosamine use was linked to lower **risk of death** from major causes such as heart disease, cancer, respiratory, and digestive disorders.³

In another large study, analysis of data from the U.S. National Health and Nutrition Examination Survey (NHANES) found that those taking **glucosamine** and **chondroitin** had a remarkable **27%** lower risk of all-cause mortality, after controlling for multiple other factors that could affect risk of death.²

A large observational study evaluating the effect of glucosamine on mortality was conducted using data from the **UK Biobank** and followed approximately **495,077** individuals for an average of about **9** years. The analysis revealed a **15%** reduction in the risk of all-cause mortality among **glucosamine users** compared to non-users.³

Lower Disease Risk

Studies have also found that **glucosamine** use was associated with a lower risk of many specific disorders and causes of death.

For example, in the Washington state study, those taking glucosamine had a **13%** lower risk of death from cancer and a **41%** lower risk of death from **respiratory diseases**.¹²

In **2025**, another analysis of **glucosamine supplementation** data was published, this one also from the UK Biobank. Over 52,500 glucosamine users were compared to the same number of non-users and followed for nearly **14 years**. Regular glucosamine use was associated with an **8-27%** **lower risk** of seven different **age-related** chronic diseases.⁵

In the National Health and Nutrition Examination Survey (NHANES) study, regular glucosamine users were **58%** less likely to die of **cardiovascular** causes compared to non-users.²

These findings align with other large observational studies. The UK Biobank study and related analyses have shown that regular glucosamine use is linked to lower mortality and a reduced risk of several chronic diseases:

- **18-22%** lower risk of cardiovascular mortality,³⁻⁵
- **26%** lower risk of respiratory disease and mortality,³
- **26%** lower risk of digestive system disease mortality,³
- **18%** lower risk of coronary artery disease,⁴
- **17%** lower risk of developing type 2 diabetes,⁸
- **16%** lower risk of developing any type of dementia, including **16%** lower risk of Alzheimer's and **26%** lower risk of vascular dementia,^{6,7,13}
- **9%** lower risk of stroke,⁴ and
- **6%** lower risk of cancer mortality.³

How Glucosamine Works

Glucosamine's role in building cartilage has been well understood for years. But the link to reduced mortality and disease risk in observational studies led researchers to evaluate its other effects in the body.

Animal studies found that glucosamine may work in a number of ways to exert anti-aging effects, including:^{14,15}

- **Activating AMPK.** AMP-activated protein kinase (AMPK) is an enzyme that acts as a master regulator of cellular metabolism. In preclinical studies,

glucosamine has been shown to help activate AMPK and increase mitochondrial biogenesis—a pathway associated with improved metabolic health and longevity.^{15,16}

- **Improving blood glucose levels.** Elevated blood sugar can lead to type 2 diabetes and other metabolic diseases and contribute to accelerated aging. In aging mice, glucosamine intake has been shown to *lower* blood glucose levels, which may reduce metabolic diseases associated with aging.¹⁵
- **Mimicking a restricted calorie diet.** Restricting calorie intake activates pathways in our metabolism that have anti-aging effects. In animal models, glucosamine intake mimics some of the effects of calorie restriction, which has been linked to longer lifespan in rodents.^{14,15}
- **Enhancing mitochondrial health.** The mitochondria are the powerhouses that supply the energy each cell needs to function optimally. Declining mitochondrial function is a major hallmark of aging. In animal models, glucosamine helps *boost* mitochondrial function.^{15,16}
- **Improving protein balance.** Animal studies indicate that glucosamine helps cells maintain an optimal, healthy balance between protein synthesis and breakdown.^{15,17}

In both worms and mice, adding glucosamine or its related nutrient acetylglucosamine to the diet has been shown to **slow aging** and **extend lifespan**.^{15,17}

A **2025** study found **20%** associated reduced risk of sudden **cardiac arrest** in **glucosamine** supplement users in the United Kingdom.¹⁹

Approximately **19.1%** of the participants in a 2020 UK Biobank study reported regular use of glucosamine supplements.⁸

This large data set indicates that nearly one in five individuals in the United Kingdom regularly uses glucosamine.

In a clinical setting, a 28-day randomized controlled trial found that **1,500 mg** per day of glucosamine along with **1,200 mg** per day of chondroitin lowered levels of the inflammatory marker **C-reactive protein** (CRP) by **23%** in healthy overweight adults.¹⁸

These studies support the idea that glucosamine may provide benefits beyond joint health. Population studies suggest it could have broader, body-wide effects, but clinical trials are needed to confirm its impact on mortality and disease risk.

Summary

Glucosamine is commonly used to help support joint and cartilage health. Clinical trials have found long-term use may help reduce pain in those suffering from **osteoarthritis**.

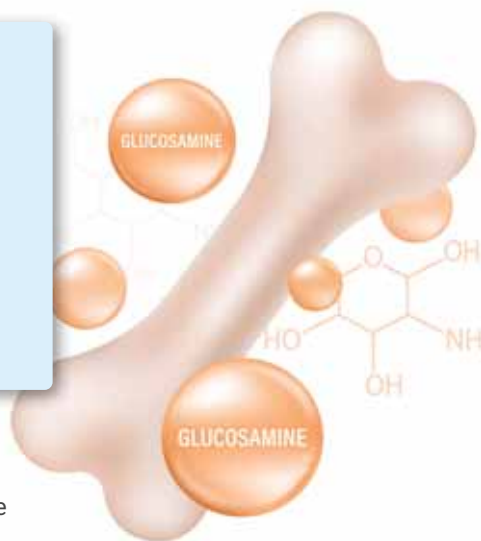
Scientists have also found an association between **glucosamine** use and a **lower risk of death** in large observational studies.

Several different observational studies have also shown that people taking glucosamine have a **reduced** risk of death due to **specific illnesses** like cardiovascular disease, cancer, and respiratory diseases, along with a lower risk of developing coronary heart disease, dementia, type 2 diabetes, and other diseases. •

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

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VERIFIED CUSTOMER
REVIEW

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JUST TWO CAPSULES A DAY PROVIDE:

Glucosamine sulfate 2KCl (derived from corn)	1,500 mg
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"Terrific."

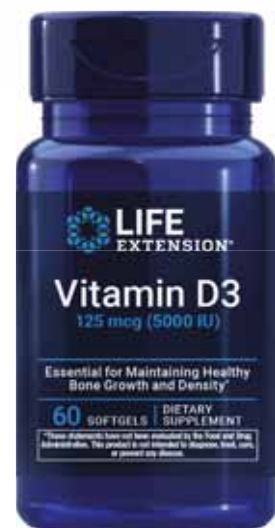
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VERIFIED CUSTOMER
REVIEW

Defend Your Health

Vitamin D3 Systemic support for immune function, bone health, and whole-body health.

CAUTION: Individuals consuming more than 50 mcg (2,000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10,000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.



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Item #01713

125 mcg (5000 IU) • 60 softgels

1 bottle **\$6.75**

4 bottles \$5.85 each



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ZINC UP YOUR IMMUNE HEALTH

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

Tina

VERIFIED CUSTOMER REVIEW



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Item #01813

50 mg • 90 vegetarian capsules

1 bottle **\$6.08**

4 bottles \$5.40 each



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

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

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

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

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

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Linked to Healthy Aging

Selenium promotes the body's production of **glutathione**, a powerful cellular antioxidant. It also encourages healthy cell division, thyroid health, and immune function.

Super Selenium Complex combines three complementary forms of selenium with vitamin E for additional antioxidant protection.

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100 vegetarian capsules
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lasts more than three months.



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GLUCOSAMINE

BEYOND JOINT HEALTH

"Good stuff!"

Kimberley

VERIFIED CUSTOMER
REVIEW

Glucosamine has been used for decades to support **joint function** and **protect cartilage**.

Recent studies reveal it may also support cellular **autophagy**.

Large cohort studies suggest that people who take **glucosamine** regularly are more likely to live longer, healthier lives.¹⁻⁴

Each capsule of this formula provides **750 mg of glucosamine**.

HIGH DOSE + LOW COST Glucosamine Sulfate

SUPER SALE PRICE

Item #02420 | 750 mg, 60 capsules
1 bottle **\$10.80** | 4 bottles \$9.45 each

References

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Item #01945 | 60 vegetarian capsules
1 bottle **\$8.10** | 4 bottles \$7.20 each



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

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

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

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73 **GLUCOSAMINE AND MORTALITY RISK**

Two large observational studies found that **glucosamine**, used to support joint and cartilage health, was associated with a *reduced* risk of **mortality** from *any cause*.

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