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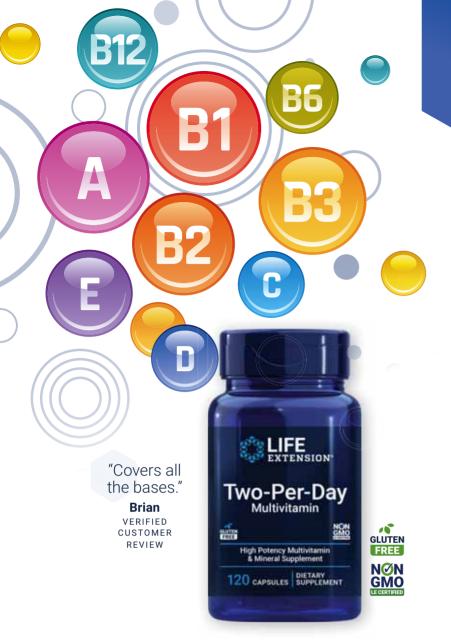
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November 2025

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When **Harvard** scientist **Kilmer McCully** identified elevated **homocysteine** as a **cardiovascular** risk factor, his findings were rejected for many years.

Upon Dr. McCully's passing, the **New York Times** ran a headline vindicating Dr. McCully's pioneering research, as we do in this editorial.

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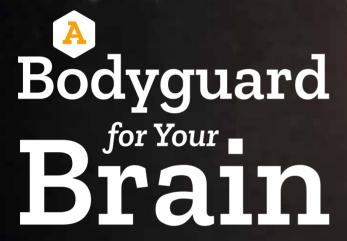
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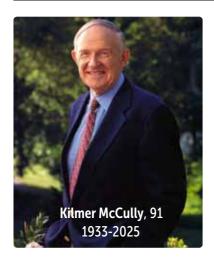




# Tribute to A Life-Saving Pioneer



WILLIAM FALOON



The **New York Times** headline read:1

"Kilmer McCully, 91, Dies, Pathologist Vindicated on Heart Disease Theory"

"His studies showed that a B vitamin deficiency could cause hardened arteries. It took the medical profession more than a decade to catch up."

Dr. McCully was a pathologist at *Harvard Medical School* who became famous, then infamous, and finally vindicated for his discovery that elevated **homocysteine** is a risk factor for **cardiovascular** diseases.<sup>1</sup>

For relentlessly advocating for <u>lower</u> homocysteine levels, his colleagues banished him to the basement, burying his theory for many years.<sup>1</sup>

Not accepting Dr. McCully's theory may have cost countless lives. Simple solutions can lower homocysteine and help reduce cardiovascular risks. Still, most physicians today debate the value of homocysteine **blood** testing.

Kilmer McCully passed away on February 21, 2025, at the age of **91** from metastatic **prostate** cancer.<sup>1</sup>

The irony of this is that both homocysteine and PSA (prostate specific antigen) can be tested in blood and offer a chance to take corrective actions before serious diseases manifest.

We published an article about the science supporting Dr. McCully's homocysteine hypothesis in **1981** and suggested our readers initiate steps to <u>lower</u> this atherogenic compound if elevated.<sup>2</sup>

This editorial is a tribute to Dr. McCully's pioneering research and describes strategies to reduce homocysteine, including a surprising method to optimize even stubbornly high homocysteine blood levels.



#### What is Homocysteine?

Homocysteine is an amino acid formed in the body from intake of another amino acid called **methionine**, which is high in certain meats and dairy products.<sup>3</sup>

High levels of homocysteine are associated with a range of diseases including Alzheimer's, 4,5 migraines, hearing loss, 7 cerebrovascular, and cardiovascular diseases. 9,10

Data going back many decades indicated a value in testing homocysteine levels as part of a comprehensive cardiovascular risk assessment.

Yet despite published evidence, most doctors still ignore this marker—potentially leaving some of their patients vulnerable to preventable cardiovascular disorders, including **ischemic stroke**.

Multiple B vitamins play a role in breaking down homocysteine. <sup>11-13</sup> Deficiency in these vitamins can result in elevated homocysteine levels. <sup>14</sup>

#### Dr. McCully's Discoveries

Homocystinuria (very high **urine** and **plasma** homocysteine levels) is a rare genetic disorder that results in early-age onset vascular disease.<sup>15</sup> In a case-series study of homocystinuria, a nine-year-old girl died from a stroke just like her uncle did at the age of eight.<sup>1</sup>

Hearing about this in the late 1960's, McCully tracked down the autopsy reports from these children which revealed hardened arteries but <u>no</u> cholesterol or fat in the plaque buildup.<sup>1</sup>

McCully ran experiments in rabbits which showed that injecting high doses of **homocysteine** led to moderate thickening in <u>all</u> their aortas. Upon further research he found that **vitamins B6** and **B12** helped lower homocysteine levels. When presenting his findings to the medical establishment, however, they were not motivated to take any action.<sup>1</sup>

McCully's theory on homocysteine was ignored until the **1990s** when large-scale studies led by other researchers produced results that supported his theories.

The famous *Framingham Heart Study* found that hardening of the arteries connected to the brain was associated with <u>elevated</u> homocysteine levels.<sup>16</sup>

Another study by authors that included researchers from the *Harvard School of Public Health* found that men with the *highest* levels of homocysteine had a <u>three-fold</u> greater risk of suffering a **heart attack** than men with lower levels.<sup>17</sup>



Regarding McCully's theory, an epidemiologist who helped lead the study that found men with high homocysteine levels faced **triple the heart attack** risk said:

"At the end of the day, he was right in the sense that homocysteine is a marker for higher risk for cardiovascular disease and he gets the credit for developing this theory and helping to provide the evidence for it."

## Who is Most At Risk of High Homocysteine?

In **1998**, the United States and Canada made it mandatory to fortify foods like cereal, flour, and bread with folate primarily to reduce the risk of neural tube defects, but it has also helped bring homocysteine down to healthy levels in many people.<sup>18,19</sup>

An interesting study compared the changes in **stroke mortality** during and after folate fortification in the U.S. and Canada to England and Wales (countries without folate fortification). From 1990 to 2002, all populations experienced a decline in stroke mortality. However, when the U.S. and Canada fortified their food with **folate** the **stroke** death decline accelerated **faster** compared to England and Wales.<sup>20</sup>

Post fortification, between 1999-2002, the mean levels of homocysteine amongst Americans declined to around **8-9 µmol/L**.<sup>21,22</sup> This was also the last time the average homocysteine level in the American population was evaluated that we could find.

We at *Life Extension*® recommend keeping homocysteine levels <u>below</u> 12  $\mu$ mol/L, with <u>under</u> 8  $\mu$ mol/L as the **optimal target**.

For those whose homocysteine levels are now in safe ranges because of fortification and increased use of folate-containing supplements, there is little to be concerned about.

Certain individuals, however, remain challenged with stubbornly **high** homocysteine levels.

Homocysteine is generally higher in men than women, with age, and in association with certain diseases such as chronic kidney disease, heart failure, dementia, and diabetes. Those hospitalized with these conditions frequently present with <u>elevated</u> homocysteine blood levels.<sup>23-25</sup>

Elevated homocysteine may also arise from mutations in genes that code for enzymes involved in the metabolism of methionine, including the MTHFR gene.<sup>26</sup>

These MTHFR genetic variants leave more folate in a <u>less</u> **bioactive** state due to inefficient methylation. Since the fortification of the food supply with folate, only about **12**% of those with the worst genetic variant of MTHFR have elevated homocysteine, compared to **33**% pre-fortification.<sup>27</sup>

The only way to know your homocysteine level is with blood testing, and if elevated it can easily be reduced to better support cardiovascular health.

A Norwegian study of about **5,000 adults** (ages 65–67), found that compared to those below **9 \mumol/L**, individuals with levels between **9–11.9 \mumol/L** had

a **30%** *higher* risk of cardiovascular death and **40%** *higher* risk of non-cardiovascular death. Those with levels between **12–14.9** µmol/L faced a **110%** and **90%** increased risk, respectively.<sup>28</sup>

#### Why Some Researchers Question The Benefits of Reducing Homocysteine

The cause of plaque build-up in the arteries will vary from individual to individual.

Including homocysteine testing in cardiovascular risk assessment could save many lives and much grief.

Some clinical trials fail to show a benefit from homocysteine reduction alone; we believe this is because they fail to consider all the <u>other</u> risk factors for cardiovascular disease.

There are **20 or more independent risk factors** for cardiovascular disease. Targeting one without the others will not accomplish ideal disease prevention.<sup>30,31</sup>

High plasma levels of homocysteine may further exacerbate damage to the inner lining of the blood vessels, called the **endothelium**, when combined with high LDL, glucose, and hypertension.<sup>9</sup>

#### Lower Homocysteine Connected To Mediterranean Diet's Benefits

A study published in *JAMA* in 2024 analyzed the biomarkers of about 25,000 women in connection with their adherence to a Mediterranean diet and health outcomes over the course of 25 years.<sup>29</sup>

Over the course of follow up, 3,879 deaths occurred. Those who had the greatest adherence to the Mediterranean diet had an 11% lower risk of mortality compared with those who had the lowest adherence after adjusting for lifestyle factors.

They also found that reduced homocysteine and inflammation explained some of the largest contributions to the lower mortality risk in people with the highest adherence to the Mediterranean diet.

Simply stated, reduced death risks were associated with lower homocysteine and other factors as you can see by the chart below:

## Reduced Death Risks Were Associated with:

- <u>Lower homocysteine, triglycerides</u> (other lipids)
- <u>Lower</u> C-reactive protein (other inflammatory markers)
- Lower creatinine (kidneys)
- Lower **insulin resistance** (diabetic markers)
- Lower body mass
- Higher alanine & citrate (mitochondria & protein synthesis)

#### How To Reduce Elevated Homocysteine

High homocysteine levels can be easily reversed by increasing intake of certain B vitamins such as vitamins B6, B12 (methylcobalamin) and folate (5-methyltetrahydrofolate) and reducing intake of methionine.<sup>32,33</sup>

One overlooked approach to lowering homocysteine further is with high doses (around **1,800 mg/day**) of **N-acetyl-cysteine** (NAC), which may help detoxify homocysteine *via* another mechanism.

It is believed that NAC's supplying of abundant **cysteine** into the bloodstream causes displacement of homocysteine from its binding to albumin in plasma, freeing it to then be cleared by the kidneys. <sup>34</sup>

#### Summary

We at Life Extension® have alerted the public about the potential dangers of excess homocysteine since 1981, echoing Dr. McCully's work.

Unfortunately, most blood test panels that screen for cardiovascular disease still omit homocysteine when convincing evidence suggests that **homocysteine testing** and treatment may save lives.

As we honor Dr. McCully, let us not repeat the mistakes of the past. Let's ensure that **homocysteine** is **no longer overlooked** in the prevention of cardiovascular diseases.

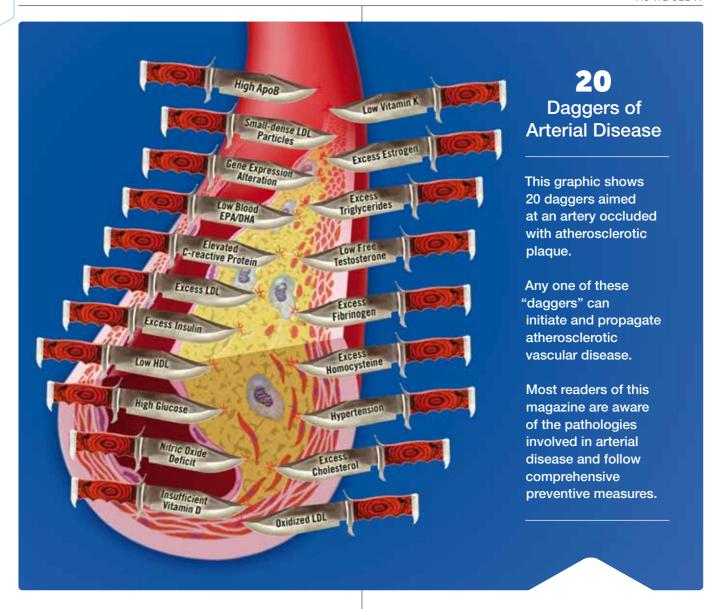
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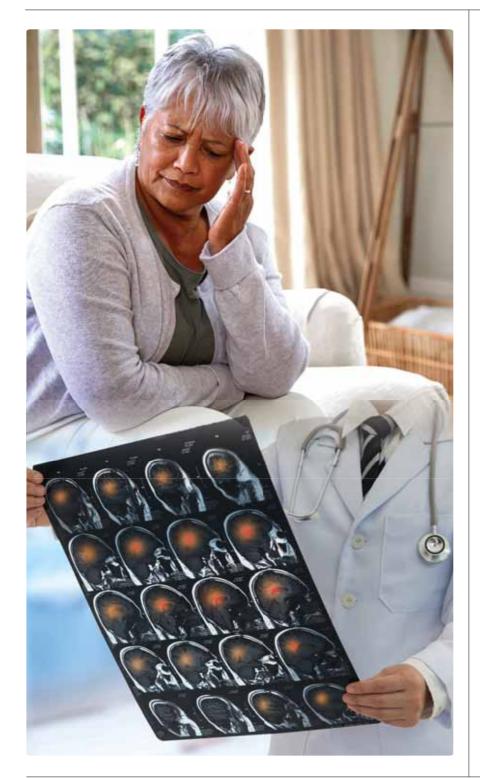
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## In the News



#### Folic Acid and Vitamin B12 **Could Help Protect Against Intracranial Aneurysms**

Researchers conducted a meta-analysis that included four studies with a total of 11,377 participants, to analyze the connection between serum levels of folate, vitamin B12, and homocysteine, and the formation of intracranial aneurysms.\*

An intracranial aneurysm is a weakness in a blood vessel in the brain that can leak or rupture. This can lead to subarachnoid hemorrhage, which is bleeding that occurs between the brain and the tissues that cover it and can cause permanent brain damage or death.

Research has indicated that high homocysteine levels (which are often accompanied by low levels of serum folate and vitamin B12) could be a risk factor.

Results of the meta-analysis showed an association between elevated homocysteine levels and the formation of intracranial aneurysms. There were also indications that folic acid and vitamin B12 could have a protective effect against intracranial aneurisms.

Editor's Note: The protective effect of folic acid and vitamin B12 against intracranial aneurysms is possibly due to the ability of these vitamins to break down homocysteine in the

\* J Clin Neurosci. 2025 May:135:111190.

## Vitamin D Helps Control Glucose in People with Type 2 Diabetes

Vitamin D supplementation could improve glucose control in people with **type 2 diabetes**, according to a recent systematic review and meta-analysis of 39 randomized, controlled trials involving 2,982 participants.\*

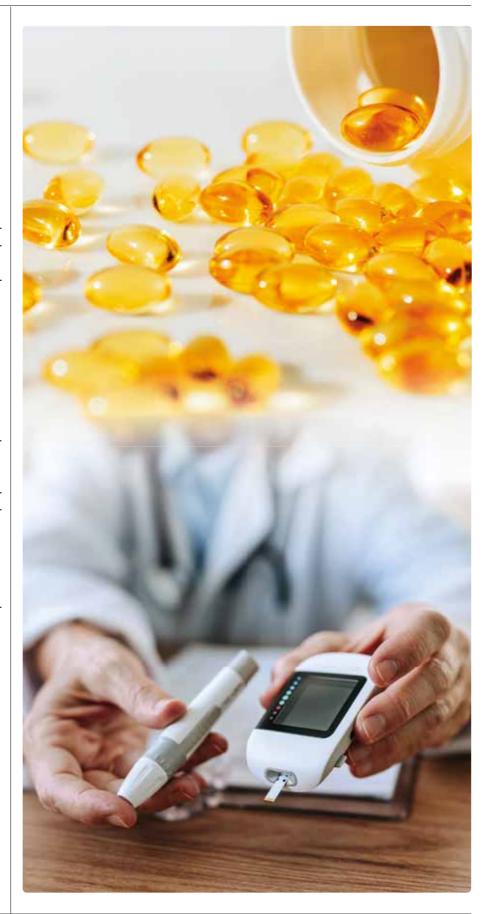
Thirteen of the studies evaluated vitamin D at less than **2,000 IU** daily and 26 evaluated vitamin D at greater than **2,000 IU** daily.

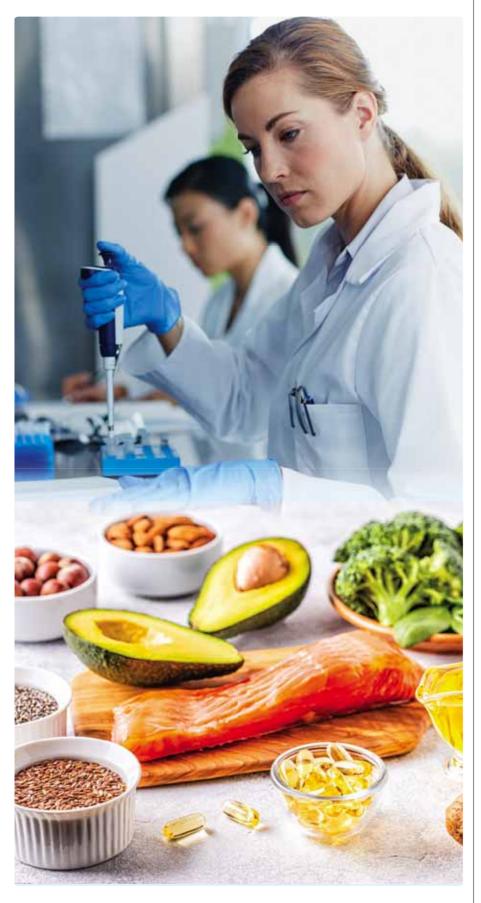
Researchers found that, compared to placebo, vitamin D supplementation resulted in an **8 mg/dL** reduction in fasting blood glucose. It also led to modest, but impressive, reductions in A1c (a measure of long-term glucose control), fasting insulin, and HOMA-IR (a measure of insulin resistance).

The effects were most prominent in patients who were overweight, vitamin D deficient, or had an A1c of 8% or greater at the start of the study.

**Editor's note:** "Our study suggests that vitamin D supplements can be recommended as complementary treatment for [type 2 diabetes] patients," the researchers concluded.

\* *Diabetes Obes Metab.* 2024 Dec;26(12): 5713-5726. Epub 2024 Oct 2.





#### Omega-3's **Anti-Inflammatory Effects Against** Chronic Inflammation

Omega-3 fatty acids and their derivatives (called specialized proresolving mediators, or SPMs) have anti-inflammatory effects.\*

Pre-clinical research has shown that they help resolve chronic inflammation. To determine the impact of specialized pro-resolving mediators on humans, researchers measured the following levels in 21 adults aged 53 to 73 who had low-grade inflammation:

- 1. Plasma phospholipid omega-3 content (a marker of dietary intake)
- 2. Specialized pro-resolving mediators (SPMs)
- 3. Anti-inflammatory markers

The results showed that as the omega-3 fatty acid levels increased, various markers of inflammation decreased. This suggests that higher dietary intake of omega-3 fatty acids reduces inflammation.

Similarly, as levels of specialized proresolving mediators (SPMs) derived from omega-3s increased, markers of inflammation decreased.

Editor's note: The results of this study support the anti-inflammatory properties of omega-3 fatty acids and their derivatives in subjects with chronic inflammation.

Prostaglandins Other Lipid Mediat. 2025 Jan:176:106948.

#### **Billions of People** on Earth Have **Inadequate Intake of** 7 Key Micronutrients

Of the estimated 8.2 billion people in the world, more than half are not consuming enough of seven important micronutrients, according to a study in Lancet Global Health.\*

For this study, researchers estimated the intakes of 15 essential micronutrients using data collected from the Global Dietary Database.

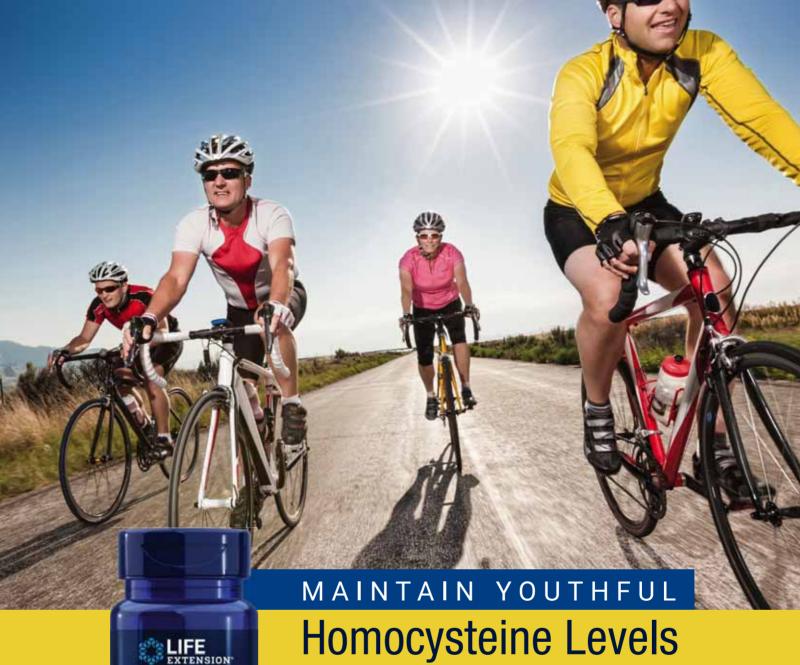
Based on nutrient intake from food alone (excluding fortification and supplementation), the scientists found that more than five billion people don't consume enough iodine, vitamin E, and calcium.

Additionally, more than four billion people don't get enough iron, riboflavin, folate, and vitamin C.

Editor's note: "Deficiencies in these and other micronutrients collectively contribute to a large burden of morbidity and mortality," the authors stated. They asserted that the study's results can be used by public health practitioners to target populations in need of intervention.

\* Lancet Glob Health. 2024 Oct;12(10): e1590-e1599. Epub 2024 Aug 29.





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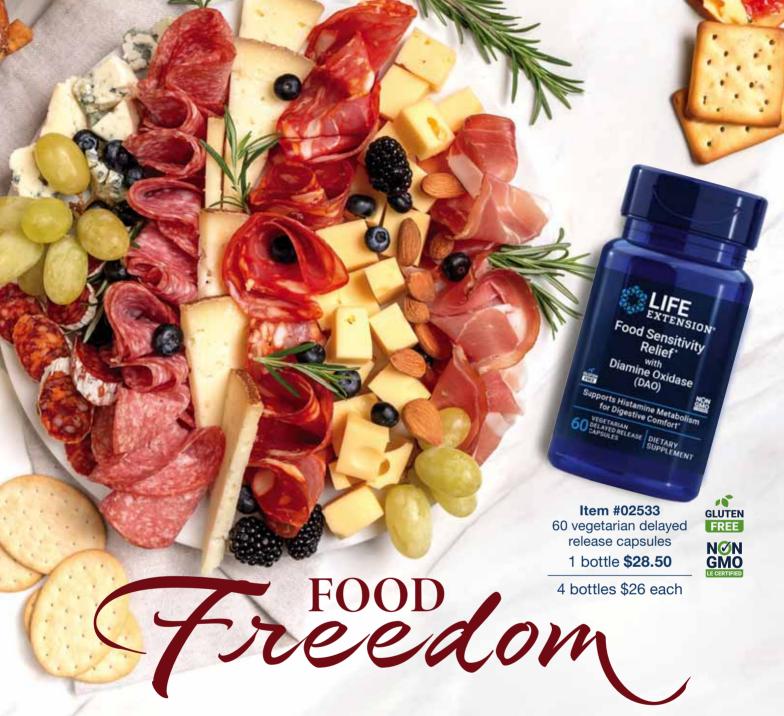
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Food Sensitivity Relief provides plant-based diamine oxidase.

Human studies showed that supplementation with diamine oxidase before meals may help provide occasional digestive relief due to histamine food sensitivity.<sup>2-4</sup>

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CAUTION: This product breaks down histamine but won't prevent severe allergic or gluten-related (celiac) reactions. Do not knowingly ingest food you are allergic to.

1. Biomolecules. 2020 Aug 14;10(8):1181. 2. Clin Nutr. 2019 Feb;38(1):152-8. 3. Food Sci Biotechnol. 2019 Dec;28(6):1779-84. 4. J Clin Med. 2023;12(20).



- helping to ease occasional bloating and gas,<sup>1,2</sup>
- promoting regularity, 1,2,3
- maintaining healthy stool consistency and comfort.1,2

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1. Gut Microbes. 2024 Jan-Dec;16(1):2338322. 2. Int J Food Sci Nutr. 2014 Dec;65(8):994-1002. 3. Lett Appl Microbiol. 2011 Jun;52(6):596-602.





## Reclaim Your VITALITY



**East Indian** alobe thistle (Sphaeranthus indicus)

BY MARSHA MCCULLOCH, MS, RD

A 2025 systematic review and meta-analysis found that around 43% of older adults experience low energy levels and 58% report a high degree of perceived physical and mental fatigability.1

In other words, diminished vitality.

Vitality is what keeps a person feeling energetic and ready to embrace life each day.2

Several lifestyle factors promote vitality, including good sleep, healthy nutrition, and regular physical activity, which helps maintain muscle strength.2-4

Scientists searched the plant world for a way to enhance traditional methods of supporting energy and physical function.

After a rigorous investigation, they combined two plant extracts to promote muscle strength and vitality.5

In a clinical trial of aging men and women, those taking this **extract blend**, compared to placebo, had 4.5 times greater improvement in **hand grip** strength, boosted walking distance by 86%, and improved feelings of vitality twice as much as exercise alone.5

#### **Understanding Vitality**

**Vitality**, feeling energetic and full of life, is crucial for healthy aging and longevity.<sup>3</sup> It makes it easier to maintain **independence** and enjoy daily activities as we **age**.<sup>2,3</sup>

Vitality is reflected in our **energy levels**, **muscle strength**, and **immune responses**, among other factors.<sup>3</sup>

**Resistance training,** a crucial component to improved **vitality**,<sup>6</sup> is one of the best ways to support muscle mass and strength as we age. Exercising the **legs** is particularly key since they are essential for maintaining mobility, balance, and walking patterns.<sup>7,8</sup>

Another vitality factor, particularly for men, is promoting youthful levels of testosterone, a hormone that helps maintain muscle mass and function.<sup>9,10</sup>

Scientists suspected the plant world could help with these and other aspects of vitality.

#### **Rediscovering Ancient Rejuvenating Herbs**

Ayurveda botanical medicine is known for its rejuvenating effects<sup>11</sup> and is associated with youthfulness, a strong body, and long life.<sup>12</sup>

Ayurvedic therapies commonly target factors that drive the aging process, including **inflammation**, declining **immune** function, and **mitochondrial** dysfunction.<sup>12</sup>

To support youthful aging, scientists screened many Ayurvedic botanicals to formulate a vitality blend.



First, they selected **East Indian globe thistle** (*Sphaeranthus indicus*), traditionally used for its rejuvenating properties. 13,14

Globe thistle flower is rich in compounds shown in preclinical research to have anti-inflammatory and immune-supportive properties.<sup>15,16</sup>

Next, after an extensive search, they formulated an extract from the bark of the mango tree (Mangifera indica).

Mango tree bark is rich in mangiferin, a compound shown in preclinical research to support cellular energy production and the creation of mitochondria. <sup>17,18</sup> Mitochondria generate energy needed for bodily processes including muscle contraction. <sup>19,20</sup>

Mangiferin is also a potent anti-inflammatory and immune-supportive compound.<sup>21</sup>

#### **Improving Vitality**

Scientists tested an East Indian globe thistle flower + mango tree bark extract blend in 92 healthy, physically active adults aged 55 to 70 years.<sup>5</sup>

Subjects took either **650 mg** of the **extract blend** or a **placebo** every morning after breakfast.

All participants completed a home **strength training** program using resistance bands three days a week throughout the study.

This trial assessed aspects of **vitality** including perceptions of vitality and energy as well as physical components of **vitality** such as muscle strength and endurance.

A standard **quality-of-life** questionnaire was used to assess perceptions of vitality. Overall, the **dual-extract** supplemented group had <u>twice</u> the **improvement in** perceived **vitality** and **energy** compared to the **placebo** arm.<sup>5</sup>

In addition, change from baseline in total **testosterone** levels was **2.6** times *greater* in **men** (but not in women) treated with the extract blend compared to the placebo group. **Free testosterone** (the active form) increased **4.3** times <u>more</u> from baseline in the treatment group than in the placebo group.<sup>5</sup>

Testosterone plays a crucial role in maintaining **muscle mass** and sexual function in men.<sup>22-24</sup> Men typically experience a reduction in testosterone levels starting around age 35.<sup>25</sup>

Testosterone levels did <u>not</u> change in female subjects in the study, which means hormone-related side effects were not an issue in women.



#### **Boosting Strength and Endurance**

Within just **four weeks**, measures of muscle **endurance** and **muscle** and **handgrip strength** significantly improved in the extract group compared to placebo.<sup>5</sup>

After 12 weeks, compared to **placebo**, those taking the **extract blend** had:<sup>5</sup>

- 51% greater resistance to muscle fatigue,
- 86% greater improvement in walking speed,
- 4.2 times greater improvement in leg strength, and
- 4.5 times greater improvement in handgrip strength.

**Handgrip strength** is a good indicator of overall **muscle strength** and quality of life in older adults.<sup>26,27</sup> It is one of several tests that are used to measure **biological age**.<sup>28</sup>

Overall tolerance of the extract blend was good and without side effects.<sup>5</sup>

This blend can safely help maintain vigor and vitality in older age.

- Vitality, or feeling lively and energetic, declines with age. That can erode independence and quality of life.
- Maintaining muscle strength and endurance is key to preserving vitality.
   Regular exercise, including resistance training, can help, but may not be enough on its own.
- To promote vitality, scientists searched for and developed a combination of extracts from East Indian globe thistle flower and mango tree bark.
- In a clinical trial, oral intake of the extract blend plus resistance exercise resulted in **4.2 times** more **leg strength** and **twice** the improvement in feelings of energy and **vitality** compared to exercise alone.
- The extract blend also improved functional fitness, boosting walking speed by 86% compared to placebo, which could facilitate the completion of everyday tasks and activities.

#### Summary

Vitality or zest for life can dwindle as we age.

Researchers combined **East Indian globe thistle flower** and **mango tree bark** extracts to help restore vitality.

In a clinical trial, daily oral intake of the extract blend significantly improved feelings of **vitality** and **energy, muscle strength**, **endurance**, and **walking speed** in aging adults.

The extracts worked quickly, producing improvements in strength and endurance within **four weeks**. ■

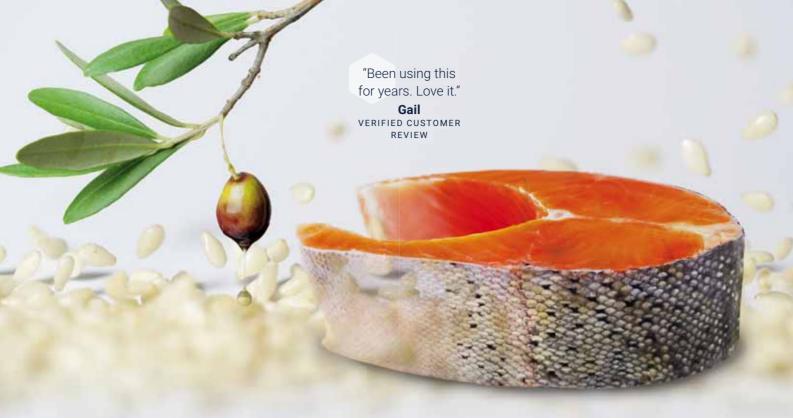
If you have any questions on the scientific content of this article, please call a **Life Extension**Wellness Specialist at 1-866-864-3027.

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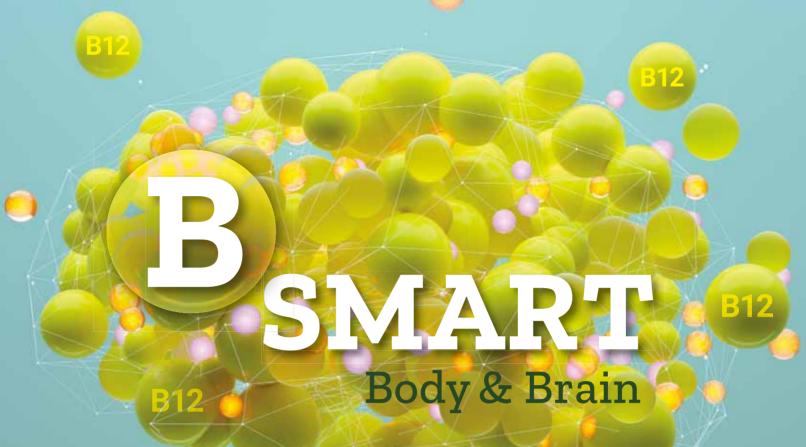
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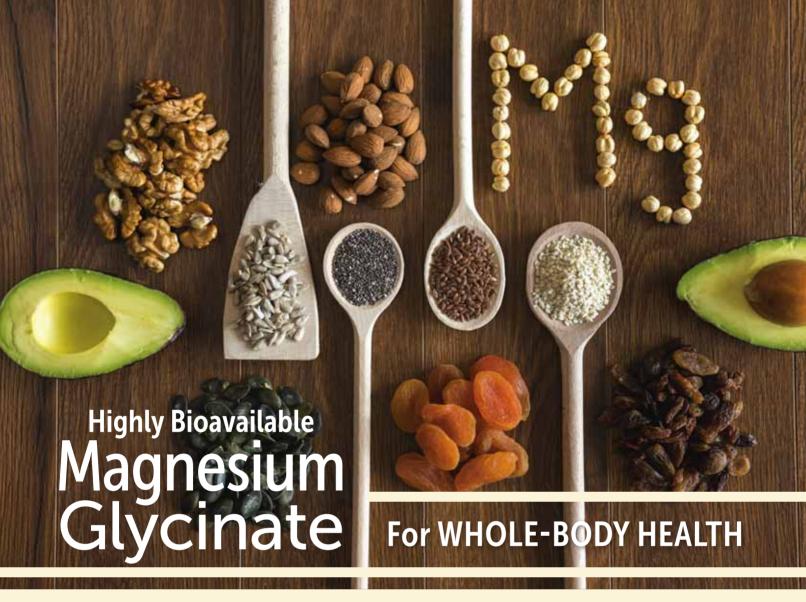


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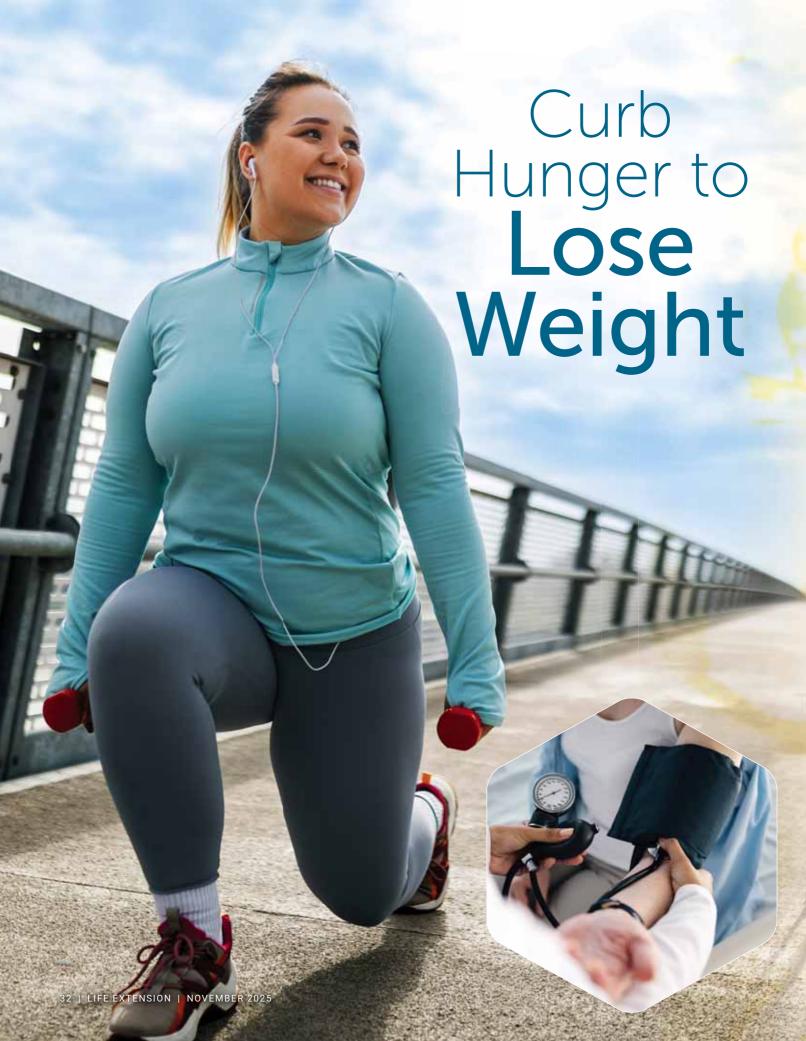
30 VEGETARIAN DIETARY SUPPLEMENT

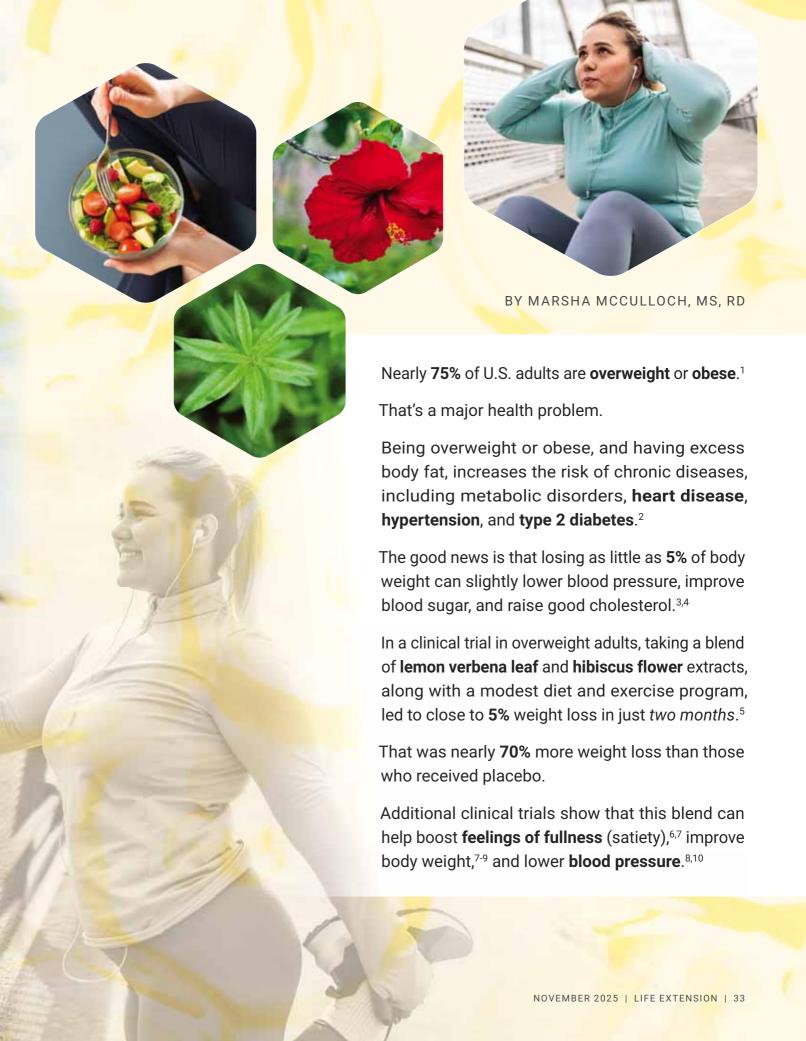
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For full product description and to order Active Vitality & Strength, call 1-800-544-4440 or visit www.LifeExtension.com

STRENGTHERA™ is a trademark of PLT Health Solutions-Laila Nutraceuticals LLC.

\* Kumar JP. A randomized, double-blind, placebo-controlled study to evaluate the benefit of L112542F6 supplementation in conjunction with an exercise program to enhance muscle strength in healthy aging subjects. Internal Study Report. 2023.





#### The Problem with Weight Loss

A nagging appetite can make it difficult to lose weight.<sup>11</sup>

People who go on diets frequently gain the weight back.<sup>12</sup>

When calories are restricted, metabolism and the hormones that control hunger are altered. These changes can make it harder to lose more weight and keep it off.<sup>13,14</sup>

After weight loss, the body makes more **ghrelin**, a hormone that increases hunger. It may also produce less **GLP-1**, a hormone that helps you feel full.<sup>14</sup>

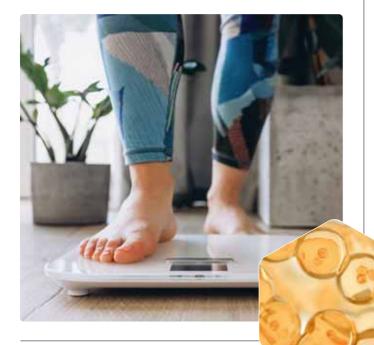
Fortunately, extracts of two plants, **hibiscus** and **lemon verbena**, are effective **non-drug** options for appetite control and weight loss.

#### **Help Shedding Pounds**

In a **clinical trial**, 46 overweight or obese women were given either a standardized **500 mg** blend of **lemon verbena leaf** and **hibiscus flower extracts** or a **placebo** 20-30 minutes before breakfast daily for 60 days.<sup>8</sup>

They were also encouraged to follow a moderate **2,200**-calorie diet and walk 30 minutes per day.

The extract group showed enhanced satiety and lost over **8-10 pounds**, over **5%** of their weight, in just **two months**. This was roughly **twice** the weight loss of the placebo group.<sup>8</sup>



#### **Curbing Appetite**

In an earlier clinical trial, overweight and obese adult women took 500 mg of the lemon verbenahibiscus extract blend or a placebo daily before breakfast. Participants were advised to consume 2,200 calories and walk at least half an hour daily during the two-month study.<sup>5</sup>

Compared to placebo, the **extract group** showed *higher* levels of the appetite-suppressing **GLP-1** hormone.

**Ghrelin** levels <u>increased</u> in the **placebo** group but remained stable in the **extract-supplemented** group. These <u>two</u> hormonal changes were associated with greater satiety and **reduced hunger**, as measured by validated scales throughout the intervention.<sup>5</sup>

In another randomized, double-blind, placebo-controlled crossover trial, similar results were observed. Participants who took the extract reported greater fullness and consumed about **9**% fewer calories during an unrestricted meal.<sup>6</sup>

This lower-calorie intake coincided with a **12%** increase in satiety-promoting **GLP-1** after breakfast and a **22%** increase in **GLP-1** after lunch.<sup>6</sup>

In a randomized controlled trial published in 2024, 61 healthy overweight adults took a **lemon verbena-hibiscus extract blend** or a placebo 30 minutes before breakfast for three months.<sup>7</sup>

By the end of the study, the extract group reported 12% improvement in hunger satisfaction one hour after breakfast. Satiety did not improve in the placebo group.<sup>7</sup>

Researchers attributed the weight loss to the extract blend's ability to improve **appetite regulation**.<sup>5,6</sup>

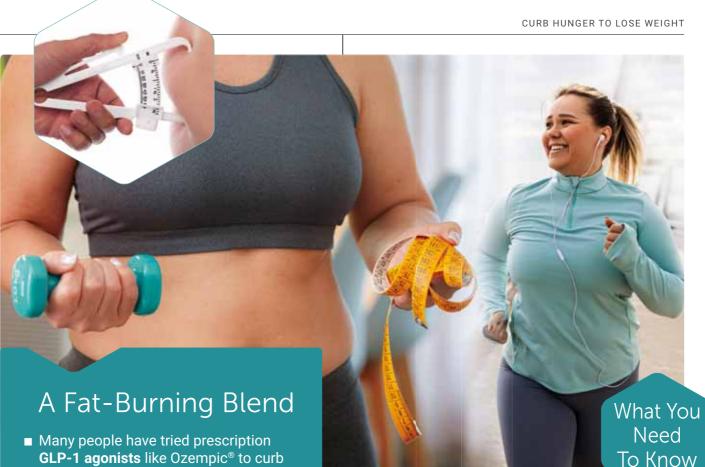
#### **Better Body Composition**

There's a common problem with weight reduction: it can result in the loss of both fat and lean tissue, including **muscle**. <sup>15</sup> This is a potential concern with **GLP-1 agonist** drugs. <sup>16</sup>

In a 12-week trial, healthy but sedentary overweight adults took **500 mg** of the combined **lemon verbena-hibiscus extracts** or a **placebo** daily while maintaining

their usual eating and lifestyle habits.9,17

The extract group achieved a **6.9**% decrease in **body fat** compared to the baseline, while *maintaining their muscle mass*. The placebo group had little change.



- **GLP-1 agonists** like Ozempic<sup>®</sup> to curb hunger. But these drugs can come with gastrointestinal and other side effects.
- A blend of lemon verbena leaf and hibiscus flower extracts works in a similar way, with evidence that it may boost levels of the appetite-suppressant hormone **GLP-1** without side effects. These extracts also promote **fat burning**.
- In clinical trials, this extract blend reduced body weight by about 5% within two months (70%-100% more weight loss than placebo), trimmed belly size by 2.3-2.5 inches, and reduced blood pressure.

The extract group also had a decrease in abdominal fat.9 This kind of fat, also called visceral fat, is closely associated with a higher risk of cardiovascular and metabolic disease.18

In the 2024 study, those taking the extracts had a 5.7% reduction in body fat over three months and an 8.2% reduction in abdominal fat. Again, no significant muscle loss occurred.7

# **Burning Fat**

The boost in fat loss by the lemon verbena-hibiscus blend may be explained, in part, by its ability to activate an enzyme called AMPK (activated monophosphate protein kinase).6,19

AMPK signals cells to burn fat for energy and store less fat. 19 With age, AMPK activity drops significantly.20,21

Other preclinical research suggests polyphenols in the extracts support the growth of beneficial gut bacteria in ways that may promote AMPK activity and weight control.<sup>22</sup>

# **Lower Blood Pressure**

The benefits of the **lemon verbena leaf-hibiscus** flower blend extend to metabolic health.

As discussed above, in one randomized controlled trial, overweight or obese women took 500 mg of the extracts or a placebo before breakfast for two months, while following a 2200 calorie diet and walking 30 minutes daily.8

While the placebo group experienced little change, the extract blend-supplemented groups experienced the following:

- In overweight women, a drop of 16% (over 20 mmHg) in systolic blood pressure (top number) from baseline, while obese women saw their systolic blood pressure go down by more than 14% (over 18 mmHg).8
- Reduction in abdominal circumference (belly size) on average of about 2.5 inches in the overweight group, and over 2.33 inches in the obese group.8
- Decrease in **resting heart rate** of over **8.5** beats per minute in the overweight group, and eight beats per minute in the obese group.8 An elevated resting heart rate is a key predictor of mortality.23

The extract was well-tolerated with no side effects.8 This weight loss and improved metabolic health can support overall healthy aging.

# Summary

A blend of extracts of lemon verbena leaf and hibiscus flower has demonstrated weight loss and metabolic benefits.

The blend has been clinically shown to result in an amount of weight loss known to reduce chronic disease risk in just two months when supported by moderate dietary changes and light physical activity.

The extract blend helps with weight loss by promoting fat burning and a feeling of fullness.

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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# Item #02500

30 vegetarian capsules

1 bottle **\$42.75** 

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









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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.

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> Caution: Temporary flushing, itching, rash, or gastric disturbances may occur. \* Br J Pharmacol. 2004 Mar;141(5):825-30.

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Little-Known Nutrient for Healthier Aging

BY MARSHA MCCULLOCH, MS, RD

Many people know about the health benefits of mushrooms.

But few are aware of the compound that scientists believe is largely responsible for those benefits: L-ergothioneine.

A growing number of studies are linking L-ergothioneine to improved health and youthful aging.1

The problem is that **L-ergothioneine** levels in the body naturally decline with age, especially after age 60.2

Fortunately, oral L-ergothioneine, made using a specialized fermentation method, has been shown to boost levels in the body.3

L-ergothioneine is a powerful **anti-inflammatory**.<sup>4,5</sup> In preclinical studies it has been shown to protect cells against **DNA damage**.<sup>6,7</sup>

Human observational studies and clinical trials suggest it could improve cognitive function, 3,8 promote younger-looking skin,9 support cardiometabolic health,10 improve sleep,11 and reduce the risk of allcause mortality.12

# **Understanding L-Ergothioneine**

L-ergothioneine is an amino acid, but not one the body can produce.6

The only organisms known to make L-ergothioneine are certain mushrooms and a few microbes. 6,13 Most people in the U.S. get only small amounts of L-ergothionine in their diet.4

Once consumed, a special transporter in the body shuttles L-ergothioneine into cells.1,4

L-ergothioneine is a powerful antioxidant. 13 lt concentrates in the mitochondria of cells and tissues, including those that are frequently exposed to harmful oxidative stress, such as the brain, eyes, heart and **blood vessels**, and **skin**. 14,15 Preclinical studies have shown its potential to protect cells against damage to DNA, proteins, and lipids. 16,17

Interest in L-ergothioneine exploded when a study found that people in Italy (who consume 4.6 mg of L-ergothioneine a day) had a significantly *longer* life expectancy than Americans (who average only 1.1 mg of L-ergothioneine daily).4

When scientists administered L-ergothioneine to mice orally, their average **lifespan** increased by a stunning 21% compared to untreated animals.18

# **Preserving Telomeres to Slow Aging**

A key driver of biological aging and age-related disease is the shortening of telomeres.19

Telomeres are **protective caps** at the ends of chromosomes. Chromosomes are threadlike structures inside the nucleus of a cell, made up of DNA, proteins, and other material, that carry the genetic information for the whole organism and for each cell.20 Every time cells divide, telomeres shorten.21

When telomeres get too short for the cell to divide, the cell may become senescent.19 Senescent cells can be dysfunctional and promote chronic inflammation.<sup>22</sup>

The accumulation of senescent cells can promote visible signs of aging, such as wrinkles,23 and increase risk of age-related health conditions, 24,25 including cognitive decline. 24,26,27

Preclinical research suggests L-ergothioneine reduces telomere shortening, which may slow the aging process. 5,21,28

When scientists used L-ergothioneine to treat cultured human cells for eight weeks and compared them to untreated cells, they found the amino acid:21

- · Boosted the median telomere length, and
- Reduced the <u>percentage</u> of short telomeres.

These benefits were especially strong when cells were exposed to oxidative stress.

# **Protecting Cognition**

In a study of 470 older adults attending memory clinics, those with lower blood levels of L-ergothioneine had worse brain function, including poorer memory.<sup>29</sup>

> Over the next five years, those with lower L-ergothioneine levels had significantly faster rates of **decline** in overall cognitive function.<sup>29</sup>

> Another study found that Alzheimer's disease patients with lower L-ergothioneine levels had a 12% faster rate of disease progression over two years.30

To test whether taking oral L-ergothioneine could improve brain function and delay cognitive decline, scientists in Singapore enrolled 19 adults aged

60 and older who had mild cognitive impairment. They were randomized to receive 25 mg of L-ergothioneine or a placebo three times a week for one year.8



The treatment group had significant improvements in memory and learning ability compared to the placebo.

The L-ergothioneine group also experienced stabilization of **neurofilament light chain** levels, a marker of brain injury and neurodegenerative disease,<sup>31</sup> while the measure worsened in the placebo group.8

In a larger study, 140 healthy older adults with subjective memory concerns3 were given either 25 mg of L-ergothioneine, 10 mg of L-ergothioneine, or a placebo daily for 16 weeks.

While the 10 mg dose boosted L-ergothioneine blood levels six-fold, the 25 mg dose boosted L-ergothioneine levels **16-fold** in the same period.

Both L-ergothioneine groups had significant improvements in brain function, including:

- Executive function, the ability to plan and execute goals,
- Complex attention, focusing on multiple things at once.
- Cognitive flexibility, the ability to adapt to new or changing information, and
- Verbal memory.

But only the 25 mg L-ergothioneine group had significant improvements in prospective memory, remembering to perform actions in the future, and in the ability to fall asleep.3

# Support Healthy Aging with L-Ergothioneine

What You Need To Know

- L-ergothioneine is an amino acid found in mushrooms and a few other foods that helps promote youthful aging. Few people get enough from their diet, and the body can't make the compound.
- Higher dietary intake of L-ergothioneine is associated with longer life expectancy, lower rates of heart disease and cardiovascular mortality, and better brain function.
- Preclinical studies show that L-ergothioneine helps protect **telomeres**, potentially slowing biological aging.
- In a clinical trial, daily oral intake of **25 mg** of L-ergothioneine helped improve cognitive function and promoted quality sleep.



# **Other Health Benefits**

Many other potential health benefits of L-ergothioneine have been uncovered, including:

Cardiometabolic wellness. In a population study that followed 3,236 adults for 20 years, higher blood levels of L-ergothioneine were associated with a 15% lower risk of heart disease, a 21% lower risk of cardiovascular mortality, and a 14% lower risk of death from any cause.<sup>10</sup>

**Improved sleep.** When poor sleepers (ages 40 to 75) took **20 mg** of L-ergothioneine daily for four weeks, **sleep problems** <u>decreased</u> and **sleep quality** <u>improved</u>, compared to placebo.<sup>11</sup>

These and other benefits may add up to better health and more youthful aging.

# **Summary**

**L-ergothioneine**, an amino acid found in mushrooms, could be a game changer for youthful aging.

Preclinical research has shown it protects the **telomeres** of cells, helping to slow the aging process.

In human studies, L-ergothioneine has improved cognitive ability and ability to fall asleep.

Standardized **L-ergothioneine** produced by a specialized fermentation process has been shown to help boost body levels of this amino acid and shows promise to promote **healthy aging**.

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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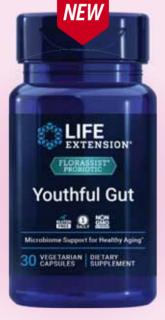








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# Reduce Nighttime Bathroom Visits

BY LAURIE MATHENA



As men get older, it is common to experience an increase in **lower urinary tract** symptoms such as urgency, incontinence, dribbling, and weak urine stream.<sup>1</sup>

One of the most *common* and bothersome of these symptoms is **nocturia**, which is waking to urinate one or more times during the **night**.<sup>1,2</sup> This disrupts **sleep**, while increasing the risk of falls and other serious health problems.<sup>3</sup>

Fortunately, nocturia does <u>not</u> have to be a normal part of life.

A novel combination of five compounds has been shown to help markedly **reduce** nocturia symptoms in men.<sup>4</sup>



Five Ways to Support Urinary Health

2017–2020 NHANES data show that about 40% of U.S. men aged 40 and older are affected.<sup>5</sup> After age 70, up to 60% of men need to urinate at least **twice** per night.<sup>6</sup>

These nighttime bathroom trips contribute to increased risk of falls, sleep disturbance, depression, reduced daytime activity and work productivity, and elevated morbidity and mortality.<sup>3</sup>

Two of the underlying causes of **nocturia** include **enlargement** of the **prostate** gland (benign prostatic hyperplasia, or BPH) and **overactive bladder**.<sup>1</sup>

The following five compounds have been shown to address men's urinary health from a variety of angles.

Beta-sitosterol is a plant compound that can help mitigate underlying causes of LUTS (lower urinary tract symptoms) associated with prostate enlargement.<sup>7</sup> In a clinical study of men with enlarged prostates, beta-sitosterol reduced urinary symptom severity by 50%.<sup>8</sup>

Pygeum bark extracts have

been shown to help improve lower urinary tract symptoms and quality of life in men with BPH.9 One meta-analysis of clinical trials found that Pygeum

extracts reduced nocturia by 19%, reduced residual volume by 24%, and increased peak urine flow by 23% in men with BPH.10

- Lycopene is a carotenoid that was shown in a study to improve lower urinary tract symptoms, quality of life, and maximum urine flow rate in men with BPH 11
- Boron has been shown in preclinical studies to reduce markers of inflammation, 12,13 modulate sex-hormone production,13 and reduce the impact of growth factors that may contribute to prostate enlargement.14
- Melatonin, a hormone that helps some people sleep better,15 has been shown to reduce

nocturia. In elderly men, supplementation was associated with less frequent nighttime urination and improved quality of life.16

# **Better Together**

Based on the ability of these compounds to address numerous aspects of urinary health, Life Extension conducted a clinical trial to determine if they could work together to reduce the number of nighttime bathroom visits in men suffering from nocturia.4

For the trial, 30 healthy men from 45 to 75 years old with mild lower urinary tract symptoms took a blend of these five compounds every night before bed for 60 days.

They answered questions on the **International Prostate Symptom Score** (IPSS), a questionnaire that assesses the severity of lower urinary tract symptoms at the beginning and end of the study.4

After 60 days, there was a 16.3% decrease (improvement) in the overall IPSS scores from baseline. The impact on *nocturia* was especially notable.

At the beginning of the study, 87% of the men had some degree of nocturia. After 60 days, only 23% reported nocturia symptoms.

In the 37% of men with severe nocturia (waking two to three times per night to urinate), **none** of them reported waking more than once per night after treatment.

In fact, by the end of the study, not a single man reported waking more than once per night to urinate.

# Summary

Nocturia affects more than half of men over age 50. It is associated with an increased risk of falls and other serious health problems.

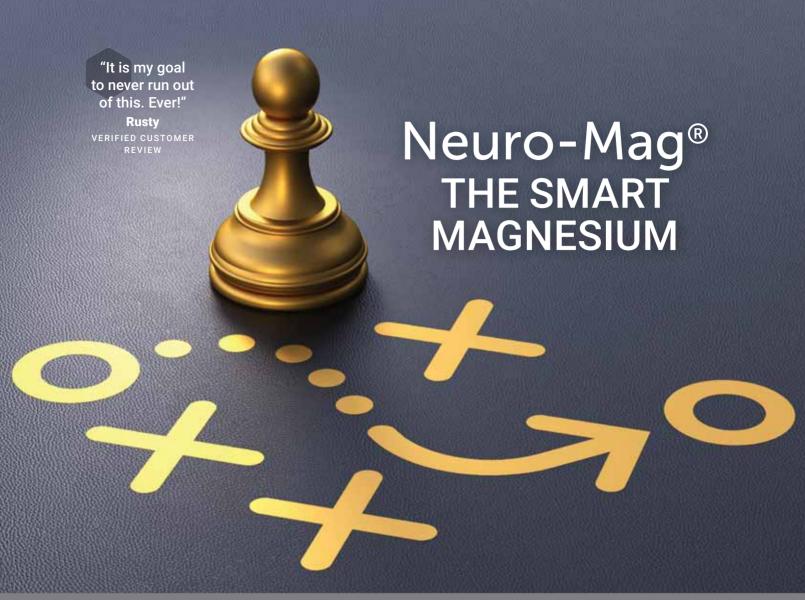
A novel combination of compounds can help reduce the frequency of nighttime urination while improving other lower urinary tract symptoms.

These compounds include betasitosterol, Pygeum bark extract, lycopene, boron, and melatonin.

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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Reduce MIGRAINE Symptoms

**Migraine** is the most common headache,<sup>1</sup> and a leading cause of disability in women under the age of 50 globally.<sup>2</sup>

They are frequently severe and debilitating, and can last for *days*.<sup>1</sup>

Researchers have identified several nutrients that can help **ease the suffering** in those with migraine episodes.

In separate **clinical trials**, daily intake of these nutrients helped reduce the frequency or severity of migraine attacks.<sup>2-6</sup>

Together, they may optimize **migraine relief**.

# What Causes Migraine?

A migraine can cause moderate to severe pain that may affect one or both sides of the head and often extends to the neck. It may also involve the face, which is why it is frequently mistaken for a "sinus headache." The pain can last for hours or even days.1

Migraines often make daily activities almost impossible, lead to missed work or other obligations, and reduce quality of life.

In addition to head pain, migraine symptoms include nausea, vomiting, sensitivity to light, sound, and/or smell, and for some, an aura (or sensory disturbance) such as visual changes or speech difficulties.1

Various changes in and around the brain contribute to these headaches.

**Inflammation** can trigger events that may include changes in blood vessels, nerves, and other tissues. For example, increased levels of a pro-inflammatory protein called calcitonin gene-related peptide has been tied to migraine.7

This inflammation may make nerves more sensitive to stimulation and contribute to headaches experienced during a migraine.<sup>7</sup>

# Six Nutrients That Help Fight Migraine

Scientists have long searched for ways to help those suffering from migraine headaches.

In the medical literature, several nutrients have shown promising results in clinical trials.

Life Extension collaborated with Sydney Scotia, an actor, director, and producer known for her role in the Netflix series Some Assembly Required. She suffered from migraine since age 12.

Sydney took inspiration from her medical challenge, the one billion people worldwide impacted by migraine, and her father, Dr. David Dodick, a prominent neurologist and migraine expert.

She founded the research company MINDED and assembled a world-class scientific advisory board with the goal of developing safe and effective ways to manage migraine headaches.

The following six nutrients were carefully screened for their benefits in managing migraine symptoms.

# **MAGNESIUM CITRATE**

Magnesium is a mineral known to support neurotransmission and cognitive function, reduce inflammation, and promote healthy blood vessel reactivity and nerve function.8

Inadequate magnesium intake is common and may contribute to migraines.8,9

In a clinical study, adults with a history of migraine received either 600 mg of magnesium citrate or a placebo daily for three months.4

> Those receiving magnesium had a 41.6% reduction in the **frequency** of migraine attacks, compared with a 15.8% reduction in the placebo group. The number of days with migraine and the need to use drugs to treat attacks also decreased significantly in the magnesium group.

The researchers concluded that magnesium citrate appears to be an effective way to prevent migraines.

# VITAMIN B2

Vitamin B2 (riboflavin) is vital for cellular energy production by mitochondria. 6,10 Scientists believe that deficits in this energy metabolism could be one underlying cause of migraine and that B2 intake might help prevent headaches.6



In a clinical trial, taking 400 mg of vitamin B2 daily for three months reduced the frequency of migraine attacks and the number of days with headaches. In those taking B2, 59% of subjects had their number of headache days cut at least in half. Only 15% of placebo recipients had a similar reduction.6

# **FOLATE (VITAMIN B9)**

Vitamin B9, also known as folate or folic acid, helps prevent overactivation of helper cells in the brain and regulates inflammatory processes in animal models.11 It also helps reduce homocysteine, which can damage blood vessels when levels are high, especially in individuals with low baseline folate levels. 12,13

In women with migraine, taking 2,000 mcg of folate daily for three months decreased the frequency of migraine attacks compared to placebo by about 31% from baseline.3

Folate intake also reduced MIDAS (Migraine Disability Assessment) scores, which evaluate the severity of migraine attacks and their impact on daily life.

Use of **rescue medications** (such as pain relievers) to treat migraine attacks also decreased by about 36% in those taking folate.

## **VITAMIN B12**

Vitamin B12 is vital for the optimal functioning of the nervous system. Deficiency can cause nerve damage and other neurological issues.14

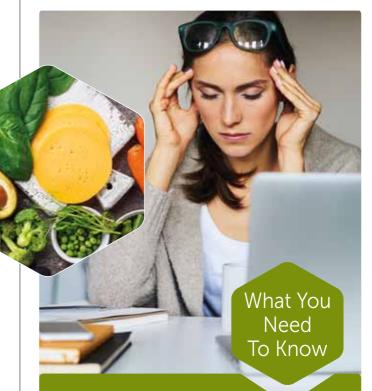
Preclinical studies indicate that B12 may help reduce nerve damage and inflammation in the nervous system.15

In the same study cited above that evaluated vitamin B9, a different group of female migraine sufferers received either 500 mcg of B12 or a placebo

> daily for three months. The B12 group had a 43% reduction in frequency

> > of migraine attacks, compared with a slight increase in the placebo group.3

> > B12 also reduced the need for rescue medications to treat migraines by 43%.3



# Relief for Migraine Sufferers

- Migraines are common and can last for days. Symptoms may include head pain (typically on one side), nausea, sensitivity to light and sound, visual changes, and other neurological symptoms.
- Six promising nutrients have demonstrated activity against migraine attacks: magnesium citrate, vitamins B2, B9 (folate), B12, and D3, and coenzyme Q10 (CoQ10).
- These ingredients have been shown in separate clinical trials to reduce frequency, duration, and severity of migraine headaches and to reduce the need for migraine medications.
- A **combination** of these nutrients may maximize relief for those suffering from migraine and other headaches.

# **COENZYME Q10 (COQ10)**

Coenzyme Q10 is essential for normal mitochondrial function and cellular energy production. It may help reduce migraines by lowering inflammation and regulating blood vessel tone, which plays a role in migraine. 16

In a placebo-controlled trial of adults with migraine, taking 300 mg of CoQ10 daily for three months reduced frequency of migraine attacks by 43% and significantly reduced the number of days with headache and nausea. About 48% of those taking CoQ10 reduced their migraine frequency by half or more.5

### VITAMIN D

Vitamin D has benefits throughout the body. Studies show that vitamin D deficiency is linked to a higher risk of various chronic conditions, including type 2 diabetes, cancer, infections, and cardiovascular, autoimmune, and neurological diseases. 17,18

In a clinical study, adults with migraine took 2000 IU (50 mcg) of vitamin D3 or a placebo daily. The impact of migraine in participants was measured by MIDAS score.19

After three months, taking vitamin D3 reduced:

- Frequency of migraine attacks by 35%,
- · Duration of headaches by 39%,
- Severity of migraine by 25%,
- MIDAS score by about 35%, and
- Need for rescue headache medication by **54%**.

As an additional measure, researchers tested for proinflammatory calcitonin gene-related peptide (CGRP), a protein that has been demonstrated to be a key trigger of migraine.2

> Those receiving vitamin D3 had 14% lower levels of the pro-inflam-

> > matory protein CGRP at the end of the study compared to the start. The scientists concluded that vitamin D's ability to help relieve migraines likely stems, in part, from reducing CGRP.

A combination of these six nutrients may optimize the

ability to ease symptoms of migraine and other headaches.

# Summary

Migraine headaches can make sufferers miserable. Six nutrients have been shown in clinical trials to help reduce the frequency and severity of attacks.

Together, these ingredients may significantly reduce the impact of migraine headaches, bringing relief to millions.

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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**Fast-Acting Liquid Melatonin** is a popular way to enhance the absorption of melatonin for sleep onset support.

The nice-tasting, citrus-vanilla flavor enables convenient "drop" dosing of *Fast-Acting Liquid Melatonin* for occasional sleeplessness.

Item #02234 • 3 mg per 20 drops, 2 fl. oz

1 bottle **\$9** • 4 bottles \$8.25 each



FOR OCCASIONAL SLEEPLESSNESS.



**Life Extension** also offers a full range of melatonin in solid forms and a variety of dosages.

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

**CAUTION:** Do not consume alcohol, drive or operate heavy machinery after taking this product.

# Fisetin The Healthy-Aging Flavonoid

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

Fisetin has low bioavailability due to its breakdown in the small intestines.

Bio-Fisetin® solves this problem by enclosing fisetin with fiber from the fenugreek herb.

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

1. *EBioMedicine*. 2018 Oct;36:18-28. 2. *J Nutr Sci*. 2022 Sep 9;11:e74.

Studied against powder fisetin (98% purity)

For full product description and to order Bio-Fisetin® call 1-800-544-4440 or visit www.LifeExtension.com Item #02414 30 vegetarian capsules 1 bottle \$11.25 4 bottles \$10 each







**Krill Healthy Joint Formula** promotes healthy joint comfort *and* range of motion through its **patented blend** of Deep-sea whole krill oil, hyaluronic acid, and astaxanthin.

**Human** studies showed that, taken daily, the formula in this product:

- Reduced joint discomfort by 55% in less than 3 months<sup>1</sup>
- Supported joint discomfort relief for 63% of participants in less than 3 months<sup>1</sup>
- Significantly improved physical function scores by the 6th and 12th week<sup>2,3</sup>

Take **Krill Healthy Joint Formula** alone or with other jointhealth supplements.

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1. Journal of Orthopedic Research and Therapy. 2023;8(1).

2. Nutrients. 2023 Aug 29;15(17):3769.

3. Nutrients. 2024;16(12):1961.

Item #01600 30 softgels 1 bottle \$24

Krill Healthy Joint

4 bottles \$21.75 each



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





#### Item #02544

Daily Supplement for Head Comfort'

Gluten Free | Non-GMO 60 vegetarian capsule DIETARY SUPPLEMENT

60 Vegetarian capsules 1 bottle **\$33** 4 bottles \$32 each

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

Migra-Health™, Powered by Life Extension®, is a product manufactured for MINDED

### **Daily Support** for Cranial Comfort

The Migra-Health™ formula contains six nutrients

that have been individually studied and shown to help relieve different aspects of occasional head discomfort, including frequency and duration:1-7

Magnesium<sup>1</sup> Riboflavin<sup>2,3</sup> Folate<sup>6</sup> CoQ10<sup>4,5</sup>

Vitamin B12<sup>6</sup> Vitamin D37

1. Cephalalgia. 1996;16(4):257-63. 2. Neurology. 1998;50(2):466-70. 3. Nutr Neurosci. 2022 Sep;25(9):1801-12. 4. Neurology. 2005;64(4):713-15. 5. BMJ Open. 2021 Jan 5;11(1):e039358. 6. Curr J Neurol. 2022;21(2):105-18. 7. Neurol Sci. 2020;41(5):1183-92.

# Need an Energy Boost?

# The Choice is Yours

CREATINE provides energy-boosting effects to cells throughout the body to support:\*

- Promotes cellular energy and muscle strength<sup>1-3</sup>
- Increased workout capacity and performance in various age groups<sup>1-3</sup>
- Enhanced lean muscle mass and healthy body composition<sup>1,3</sup>



## **Creatine Powder**

This premium-grade, pure *creatine monohydrate* is an unflavored powder that dissolves quickly in water or your beverage of choice. Contains no sugar. Every scoop provides **5 grams** of creatine monohydrate.

Item #02543 Net Wt. 300 g (0.66 lbs.) 60 servings 1 jar \$18 • 4 jars \$16.50 each



## **Creatine Capsules**

Each capsule supplies **500 mg** of premium-grade, pure *creatine monohydrate*. Take two capsules twice daily with water or your beverage of choice. Contains no sugar.

Item #01529 120 capsules 1 bottle \$13.50 4 bottles \$12 each



#### Creatine & Acetyl-L-Carnitine Energy Plus

Premium-grade, pure creatine monohydrate for muscle strength, exercise performance and cellular energy, combined with acetyl-L-carnitine for physical and mental energy and healthy cognitive function.<sup>1-3</sup>

Every scoop provides **5 grams** of creatine monohydrate and **2 grams** of acetyl-L-carnitine. This unflavored, fine powder dissolves easily and contains no sugar.

Item #02532 Net Wt. 233 g (0.51 lbs.) 1 jar \$24.75 • 4 jars \$22 each



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



1. J Int Soc Sports Nutr. 2017;14(1):18. 2. Open Access J Sports Med. 2017;8:213-26. 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.

# Improving Brain Aging with Senolytics



The **immune system** has a well-known role in protecting us from infections and cancer.<sup>1</sup>

In a major article published in the journal *Neuron* in 2025, scientists from the Department of Brain Sciences at Israel's Weizmann Institute of Science have proposed that **brain health** is more closely influenced by the **immune** system than had previously been known.<sup>2</sup>

In short, they explain that brain fitness depends on immune fitness.

This means **aging** of the **immune** system leads to **brain aging**, and that *rejuvenating* the immune system may help revitalize brain function.

One way researchers believe it might be possible to rejuvenate immune and brain health is with **senolytics**.

Preclinical studies indicate that these compounds may help <u>eliminate</u> dysfunctional **senescent cells**, which contribute to many problems associated with the aging immune system<sup>3,4</sup> and the **brain**.<sup>5,6</sup>

## How Senescence Harms the Brain

As cells age and accumulate damage, they can become **senescent**. These cells no longer function properly and fail to die off to make room for healthy new cells.<sup>7</sup>

Senescent cells can also produce a slew of **pro-inflammatory compounds** that circulate in the blood, potentially driving disease and harming brain health.<sup>7</sup>

Many of these pro-inflammatory compounds originate in immune cells. Elevated levels cause neuro-inflammation and rapid aging in the brain. They are associated with an increased risk of cognitive impairment and dementia.<sup>2</sup>

In addition, neurons, **microglia** (the brain's immune cells), and other cells in the brain can all become **senescent** themselves.<sup>2,6,8,9</sup> In mice, the accumulation of **senescent microglia** in the aged brain correlates with cognitive decline and neuroinflammation.<sup>6,9</sup>

## Restoring Immune and Brain Health

Studies in preclinical models show that restoring a more youthful immune system *improves brain function*.

In animal experiments, transfusing young healthy mice with the **blood of elderly mice** causes their brain function to deteriorate, leading to impairment in cognitive functions like learning and memory. 10-13

Conversely, transfusing young, healthy blood plasma into aged mice leads to <u>improvements</u> in **neurogenesis** (the production of new brain cells), **synaptic plasticity** (the ability of synapses to adapt to stimuli), and **cognitive function**.<sup>14</sup>

As bone marrow cells age, they secrete a protein called **cyclophilin A**, which contributes to cognitive decline. *Blocking* this protein in elderly mice increases vital synaptic proteins, supports brain cell growth, and improves cognitive function.<sup>15</sup>

In mouse models, **rejuvenating** the immune system by transplanting *young* **bone marrow** protects older animals against **cognitive decline** and neuroinflammation. <sup>16</sup> (We cannot do this safely in humans yet because of graft-versus-host risk.)

## How Senolytics Can Help

The Israeli scientists who published the **2025** article note that increasing **exercise** and improving **diet** can help boost immune function, reduce inflammation, and protect cognitive function.<sup>2</sup>

One promising additional intervention that is already in clinical trials is **senolytic therapy**.

#### **Plant-Derived Senolytics**

One of the first effective senolytic treatments used a plant-derived polyphenol called **quercetin**. 18

Even greater senolytic effects were found when combining quercetin with the cancer drug dasatinib.<sup>19</sup> Quercetin and dasatinib target different senolytic activating factors in senescent cells.<sup>20</sup> Dasatinib, however, can cause side effects.<sup>21</sup>

Recent research has identified the potential of **theaflavins**, polyphenols from black tea, to mitigate cellular senescence and delay the onset of age-related diseases.<sup>22-25</sup> In mouse models, theaflavins have been shown to inhibit cellular senescence.<sup>26</sup>

**Fisetin**, another plant polyphenol was found to be the most potent plant-derived senolytic in a study of 10 flavonoids.<sup>27</sup> It has been shown to be neuroprotective in animal models of Alzheimer's<sup>28</sup> and Parkinson's disease<sup>29,30</sup> and has increased lifespan<sup>27,31</sup> in animal models.

These senolytics may help eliminate senescent cells' burden.

**Apigenin**, a polyphenol found in plants like chamomile and parsley, has been found in preclinical models to reduce the pro-inflammatory compounds produced by senescent cells. 32,33

A <u>combination</u> of these four plant-derived compounds could help reduce senescent cells and the damage they do.



**Senolytics** help eliminate senescent cells, including in the brain and immune system.<sup>5</sup>

Studies have shown that reducing senescent cell numbers leads to improvements in brain function in preclinical models of brain aging and cognitive decline.<sup>6,9,17</sup>

For example, giving mice a combination of two senolytics, **querce-tin** (a plant-derived polyphenol) and **dasatinib** (a cancer drug), reduced the number of senescent microglial cells in the brain. This reduced the pro-inflammatory environment and *improved cognitive function*.<sup>6</sup>

In another study in mice, clearing senescent cells protected cognitive function from deterioration.<sup>3</sup>

Several **human trials** of senolytic therapy are currently underway in patients with Alzheimer's disease and mild cognitive impairment.<sup>2</sup>

#### **Summary**

A recent article in the scientific journal *Neuron* reports that an agerelated decline in **immune** function helps drive the development of cognitive decline and **dementia**.

Many of these changes are caused, in part, by **cellular senescence** in the immune system, bone marrow, and brain.

**Senolytic** compounds remove harmful senescent cells, including immune *and* brain cells, potentially decreasing neuroinflammation and protecting the brain from agerelated deterioration. •

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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Triple Strength ProstaPollen™

Ultra Prostate Formula

#### **KIDNEY & BLADDER SUPPORT MINERALS** 00862 Cran-Max® Cranberry Whole Fruit Concentrate 01661 Boron 01424 Optimized Cran-Max® 02107 Extend-Release Magnesium 01921 **Uric Acid Control** 01677 Iron Protein Plus 01209 Water-Soluble Pumpkin Seed Extract 02403 Lithium 01459 Magnesium Caps LIVER HEALTH & DETOXIFICATION 01682 Magnesium (Citrate) 01922 Advanced Milk Thistle • 60 softgels 02535 Magnesium Glycinate 01925 Advanced Milk Thistle • 120 softgels 01328 Only Trace Minerals 02240C Anti-Alcohol Complex 01504 Optimized Chromium with Crominex® 3+ 01651 Calcium D-Glucarate 02309 Potassium with Extend-Release Magnesium 01571 Chlorophyllin 01740 Sea-Iodine™ FLORASSIST® Liver Restore™ 02402 01879 Se-Methyl L-Selenocysteine 02521 Glutathione 01778 Super Selenium Complex Glutathione, Cysteine & C 01541 00213 Vanadyl Sulfate 01393 HepatoPro 01813 Zinc Caps 01608 Liver Efficiency Formula **MISCELLANEOUS** 01522 Milk Thistle • 60 veg capsules 01534 N-Acetyl-L-Cysteine 00577 Potassium Iodide 01884 Silymarin **MOOD & STRESS MANAGEMENT** 02361 SOD Booster 02519 Ashwagandha Plus **LONGEVITY & WELLNESS** 02434 Calm-Mag 00457 Alpha-Lipoic Acid 02312 Cortisol-Stress Balance 02414 Bio-Fisetin® 00987 **Enhanced Stress Relief** 01214 **Blueberry Extract** 02542 **GABA** 01438 Blueberry Extract and Pomegranate 01683 I -Theanine 02431 Essential Youth - L-Ergothioneine 02175 SAMe (S-Adenosyl-Methionine) 02119 GEROPROTECT® Ageless Cell™ 200 mg, 30 enteric coated vegetarian tablets 02415 GEROPROTECT® Autophagy Renew 02176 SAMe (S-Adenosyl-Methionine) 02401 GEROPROTECT® Stem Cell 400 mg, 30 enteric coated vegetarian tablets 02211 Grapeseed Extract 02174 SAMe (S-Adenosyl-Methionine) 02527 Healthy Aging Powder 400 mg, 60 enteric coated vegetarian tablets 00954 Mega Green Tea Extract (decaffeinated) 02429 Theanine XR™ Stress Relief 00953 Mega Green Tea Extract (lightly caffeinated) **MULTIVITAMINS** 02540 Mega L-Ergothioneine 02199 Children's Formula Life Extension Mix™ 01513 Optimized Fucoidan with Maritech® 926 Life Extension Mix™ Capsules 02354 02230 Optimized Reservatrol Elite™ 02364 Life Extension Mix<sup>™</sup> Capsules without Copper 01637 Pycnogenol® French Maritime Pine Bark Extract Life Extension Mix™ Powder 02356 02210 Resveratrol Elite™ Life Extension Mix™ Tablets 02355 02301 Senolytic Activator® 02357 Life Extension Mix™ Tablets with Extra Niacin 01208 Super R-Lipoic Acid 02365 Life Extension Mix<sup>™</sup> Tablets without Copper 01919 X-R Shield 02292 Once-Daily Health Booster • 30 softgels LUNG HEALTH 02291 Once-Daily Health Booster • 60 softgels 02512 Healthy Lungs 02313 One-Per-Day Tablets 02317 Two-Per-Day Capsules • 60 capsules **MEN'S HEALTH** 02314 Two-Per-Day Capsules • 120 capsules 02538 Hair Growth for Men 02316 Two-Per-Day Tablets • 60 tablets 02209 Male Vascular Sexual Support 02315 Two-Per-Day Tablets • 120 tablets 00455 Mega Lycopene Extract Whole Food Multivitamin 02428 02306 Men's Bladder Support **NERVE & COMFORT SUPPORT** 02515 Men's Vitality Packs 02202 ComfortMAX™ PalmettoGuard® Saw Palmetto and Beta-Sitosterol 01789 01790 PalmettoGuard® Saw Palmetto/Nettle Root 02303 Discomfort Relief 02544 MigraHealth Formula and Beta-Sitosterol Prelox® Enhanced Sex for Men 01373 **PERSONAL CARE** 01940 Super MiraForte with Standardized Lignans 02322 Hair, Skin & Nails Collagen Plus Formula 02500 Testosterone Elite

01278

00408

02252

Life Extension Toothpaste

Venotone

Youthful Legs

PEIC	CARE	01074	mositor Caps
01932	Cat Mix	02244	Liquid Vitamin D3 • 50 mcg (2000 IU)
01931	Dog Mix	02232	Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)
PROBIOTICS		01936	Low-Dose Vitamin K2
01622	Bifido GI Balance	00373 01939	No Flush Niacin
01825	FLORASSIST® Balance	01939	Optimized Folate (L-Methylfolate) Pyridoxal 5'-Phosphate Caps
02421	FLORASSIST® Daily Bowel Regularity	01400	Super Absorbable Tocotrienols
02125	FLORASSIST® GI with Phage Technology	02334	Super K
01821	FLORASSIST® Heart Health	01863	Super Vitamin E
02250	FLORASSIST® Mood Improve	02422	Vegan Vitamin D3
02208	FLORASSIST® Immune & Nasal Defense	02028	Vitamin B5 (Pantothenic Acid)
02120	FLORASSIST® Oral Hygiene	01535	Vitamin B6
02203	FLORASSIST® Prebiotic	00361	Vitamin B12 Methylcobalamin
02505	FLORASSIST® Probiotic Women's Health	01536	Vitamin B12 Methylcobalamin
02539	FLORASSIST® Probiotic Youthful Gut		1 mg, 60 veg lozenges
SKIN	CARE	01537	Vitamin B12 Methylcobalamin
02423	Daily Skin Defense		5 mg, 60 veg lozenges
01938	Shade Factor™	02228	Vitamin C and Bio-Quercetin®
02129	Skin Care Collection Anti-Aging Serum		60 veg tablets
02130	Skin Care Collection Day Cream	02227	Vitamin C and Bio-Quercetin®
02096	Skin Restoring Ceramides		250 veg tablets
02528	Vegan Pro Collagen	01753	Vitamin D3 • 25 mcg (1000 IU), 90 softgels
SLEE		01751	Vitamin D3 • 25 mcg (1000 IU), 250 softgels
		01713	Vitamin D3 • 125 mcg (5000 IU), 60 softgels
01512	Bioactive Milk Peptides	01718	Vitamin D3 • 175 mcg (7000 IU), 60 softgels
01511	Enhanced Sleep without Melatonin	01758	Vitamin D3 with Sea-Iodine™
02234	Fast-Acting Liquid Melatonin	02040	Vitamins D and K with Sea-Iodine™
01669	Glycine	WEIG	HT MANAGEMENT & BODY COMPOSITION
02308 01722	Herbal Sleep PM L-Tryptophan	02479	7-Keto® DHEA Metabolite
01722	Melatonin • 300 mcg, 100 veg capsules		100 mg, 60 veg capsules
01083	Melatonin • 500 mcg, 200 veg capsules	02207	AMPK Metabolic Activator
00329	Melatonin • 1 mg, 60 capsules	02504	Body Trim and Appetite Control
00329	Melatonin • 3 mg, 60 veg capsules	02478	DHEA Complete
00331	Melatonin • 10 mg, 60 veg capsules	02506C	Mediterranean Weight Management
00332	Melatonin • 3 mg, 60 veg lozenges	01432	Optimized Saffron
02201	Melatonin IR/XR	02511	Thermo Weight Control
01787	Melatonin 6 Hour Timed Release	02509	Waistline Control™
	300 mcg, 100 veg tablets	WOMI	EN'S HEALTH
01788	Melatonin 6 Hour Timed Release	01942	Breast Health Formula
	750 mcg, 60 veg tablets	02537	Daily PMS Relief
01786	Melatonin 6 Hour Timed Release	02534	Estrogen Balance Elite
	3 mg, 60 veg tabs	01894	Estrogen for Women
01721	Optimized Tryptophan Plus	02541	Hair Growth for Women
01445	Quiet Sleep Melatonin • 5 mg, 60 veg capsules	02204	Menopause Relief
02502	Rest & Renew	02319	Prenatal Advantage
02526	Serene Sleep	02536	Sexual Health for Her
VITAMINS		01649	Soy Isoflavones
01533	Ascorbyl Palmitate	02513	Women's Bladder Support
00920	Benfotiamine with Thiamine		
01945	BioActive Complete B-Complex		
00102	Biotin		

00084

02229

02075

02070

Buffered Vitamin C Powder

Fast-C® and Bio-Quercetin®

Sesame Lignans

01913 High Potency Optimized Folate

Gamma E Mixed Tocopherol Enhanced with

Gamma E Mixed Tocopherol & Tocotrienols

## Comprehensive Senolytic Support

The Senolytic Activator®

formula provides the following nutrients:

- THEAFLAVINS
   (polyphenols from black tea)
- BIO-QUERCETIN® (ultra-absorbable form)
- APIGENIN
  (a natural flavonoid)
- BIO-FISETIN®
   (up to 25 times greater bioavailability)\*

With age, our body accumulates senescent cells that affect the day-to-day function of the healthy cells around them.

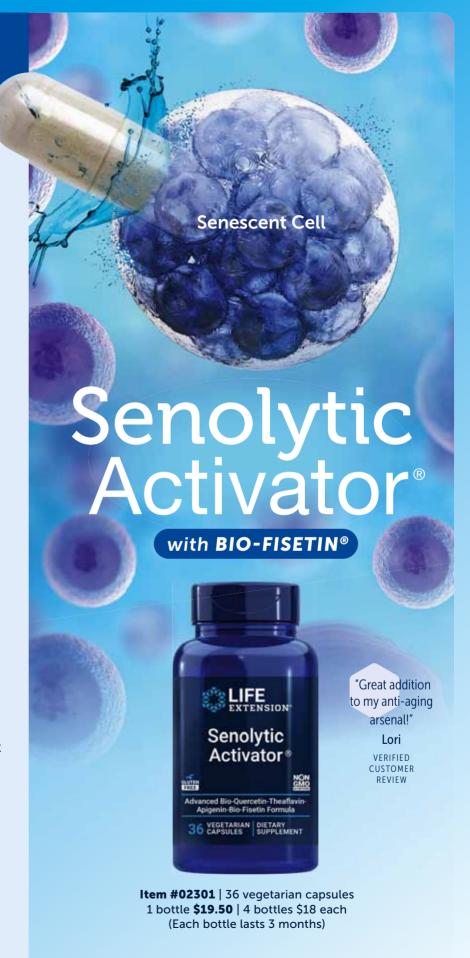
Senolytics are compounds that promote the body's natural processes for clearing senescent cells.

The **Senolytic Activator**<sup>®</sup> supplement provides four ingredients, including a bioavailable form of the Bio-Fisetin<sup>®</sup> supplement to support healthy aging.

The suggested dose of the **Senolytic Activator**® supplement is **3 capsules** once a week. Each bottle lasts 3 months and costs very little.

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

\* Studied against powder fisetin (98% purity)





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

Item #02407 500 mg 60 vegetarian capsules

1 bottle **\$24.75** 4 bottles \$22.75 each Patented technology combining turmeric and fenugreek fiber results in up to 45 times greater bioavailability of free curcuminoids.

<sup>‡</sup>Studied against powder turmeric extract standardized to 95% curcuminoids



#### The Science of a Healthier Life®

PO BOX 407198 FORT LAUDERDALE, FLORIDA 33340-7198

#### IN THIS EDITION OF LIFE EXTENSION MAGAZINE®





#### 7 TRIBUTE TO A LIFE-SAVING PIONEER

Harvard scientist Kilmer McCully identified **homocysteine** as a **cardiovascular** risk factor, but his theory was rejected for many years. The **New York Times** ran an obituary vindicating Dr. McCully's pioneering research.



A **clinical trial** of aging men and women found two **plant extracts** significantly *boosted* **vitality** and **muscle strength**.





#### 32 CURB HUNGER TO LOSE WEIGHT

In a clinical trial of **overweight** adults, a blend of **plant extracts**, along with a modest diet and exercise program, led to close to **5% weight loss** in just *two months*.



**L-ergothioneine**, an amino acid, found in **mushrooms**, protected **telomeres** in preclinical studies. In **human** trials, **L-ergothioneine** *improved* **cognitive ability** and **cardio-metabolic function**.



In a clinical trial, **five compounds** helped *reduce* **nocturia symptoms** in men. After 60 days, not a *single* subject woke more than once a night to urinate.



Six **nutrients**, in separate clinical trials, *decreased* frequency, duration, and severity of **migraine** headaches and reduced the need for migraine medications.



