

The Science of a Healthier Life®

LifeExtension.com

February 2022

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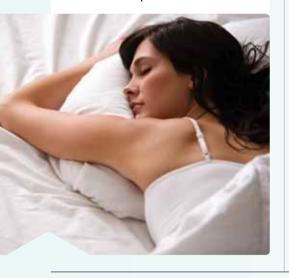
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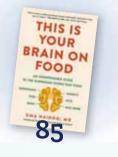
Cardiovascular deaths were *reduced* by 50% in older adults taking selenium and CoQ10 supplements.

#### **DEPARTMENTS**



#### IN THE NEWS

Vitamins C and E reduce dementia risk; fast-food availability linked to risk of diabetes; resveratrol helps control diabetes; NAD+ may improve cognitive function.



#### **AUTHOR INTERVIEW**

Psychiatrist, chef, and author of This is Your Brain on Food, Uma Naidoo, MD, explains what to eat to improve cognitive function, mood, energy, concentration, and libido, and highlights key supplements.



#### **SUPER FOODS**

Apples contain high levels of phytochemicals such as quercetin, flavonoids, and carotenoids, and are tied to a reduced risk of cardiovascular disease, cancer, asthma, and all-cause mortality.



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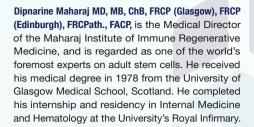
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## Sleep Loss and Weight Gain



WILLIAM FALOON

Two **trends** are simultaneously **worsening**.

As **sleep deprivation** rates surge **higher**, so do the numbers of overweight and obese people.

Human research links sleep loss with weight gain. 1,2

Published reports associated sleep loss with a 15% decrease in life expectancy.3-5

What's stumped everyone are effective solutions for chronic sleep disorders.

Over the past three years, four studies have been published that reveal a partial solution in the form of a low-cost supplement.6-9

Differing doses of the herb **ashwagandha** have been used by Americans for decades. Its ability to improve sleep was recently validated.

A 2019 placebo-controlled study showed that a lower potency ashwagandha extract taken twice a day reduced stress and anxiety, and demonstrated "significant improvement in sleep quality."6

A more impressive 2020 placebo-controlled study used a new ashwagandha that is more concentrated and taken only once at bedtime.8

The results found improvements as high as 72% across a wide spectrum of sleep measures.8

Those challenged with getting enough quality sleep should consider novel approaches being uncovered in the published scientific literature.

The ability to reduce one's calorie intake and disease risk in response to better sleep makes achieving restorative nocturnal rest a New Year's priority.

This might happen with the proper use of ashwagandha and other approaches that yield ancillary health benefits.



#### Impact of Sleep on Hunger

Most of us who suffer a night of **non-restorative sleep** tend to **eat** more the next day.

Epidemiologic evidence links sleep loss with obesity.<sup>10</sup>

An underlying cause involves changes in **brain activity** that increase our desire for high-calorie foods that cause weight gain.

Other factors linking weight gain to sleep deprivation are <u>increases</u> in hormones like ghrelin that stimulate hunger, and <u>decreases</u> in leptin that suppress appetite.<sup>11</sup>

One epidemiological study found that older adults **sleeping** less than five hours per night are at approximately **40**% *greater* risk of becoming **obese** compared to those sleeping seven to eight hours per night.<sup>12</sup>

#### **Sleep-Deprived People Age Faster**

Age-related disorders accelerate in response to insufficient sleep.

Harvard University Medical School published a report revealing the many health problems associated with sleep loss including:<sup>4</sup>

- Hypertension
- Immune impairment
- Cardiovascular disease
- Type II diabetes
- Common colds
- Obesity

The **Harvard** report referred to a study showing those who slept **less than seven hours** a night are nearly **three times** more likely to develop **cold symptoms** compared to those who slept **eight or more hours**.

Those with good sleep "quality" were the <u>least</u> likely to contract a **common cold**. 4,13

This **Harvard** report described <u>three</u> separate studies suggesting that insufficient sleep may <u>increase</u> mortality (death) risk by **15**%.<sup>3,4</sup>

#### The Whitehall II Sleep Study

The world woke up to the importance of **sleep** with the publication of a huge, **multi-decade** study conducted in Britain.

The study found that as people aged and their **sleep** duration shortened, risk of cardiovascular death more than doubled.<sup>5</sup>

The **Whitehall II** study has been referred to in numerous articles as demonstrating the **lethal** dangers of **sleep deprivation**. Newly published research supports many of its findings.

## Impact of Sleep on Cardiovascular Risks

A recent study published online in the *Journal of Preventive Cardiology* analyzed data from the National Health and Nutrition Examination Survey (NHANES).<sup>14</sup>

A total of **17,635** eligible participants were followed for a median of **7.5 years** to determine if they died from a **heart attack**, **heart failure** or **stroke**–in other words, to determine their cardiovascular mortality.







Researchers divided participants into three groups depending on their average sleep as follows:

- 1) Less than six hours,
- 2) Six to seven hours, and
- More than seven hours.

These people were tracked to ascertain how many in each group died from cardiovascular causes.

Those who slept less than six hours a night had a 45% increased risk of cardiovascular death compared to those who slept six to seven hours each night.

What confused people about this study is that it showed that those who slept more than seven hours each night also had an increased death risk.

We at **Life Extension** received calls about this and explained that this study measured sleep duration (number of hours) and not sleep quality.

We opined that people with underlying degenerative illnesses tend to require longer sleep periods, often because their "sleep quality" is impaired.

#### Measuring "Quality" Sleep

**Restorative sleep** is a critical aspect of the overall sleep experience yet many people are challenged to obtain restful sleep.

Early research focused on **number of hours** slept and not as much on the "quality" of sleep architecture.

Sleep quality can now be assessed with monitors as small as wristwatches.

This enables scientists to conduct clinical trials that precisely measure a variety of sleep parameters.

#### **Highly Standardized Ashwagandha**

Non-restorative sleep is an indicator of poor sleep "quality" that goes beyond mere number of hours slept.

Studies published in 2019, 2020, and 2021 describe the ability of ashwagandha extracts to improve the overall sleep experience. 6-9

The results from these studies provide consistent data about ashwagandha's ability to enable a better night's rest.

A new highly concentrated ashwagandha extract may have demonstrated more comprehensive enhancements to both sleep quantity and quality.

In a randomized, double-blind, placebo-controlled trial published in 2020, 150 people scoring high on nonrestorative sleep measures were given a new highly standardized ashwagandha extract at bedtime.8

Using a validated monitor worn on the wrist like a wristwatch, the following six sleep measures were assessed:

- Onset of sleep (how long it took to fall asleep)
- Sleep efficiency (percentage of time asleep while in bed)
- Total sleep time (number of hours slept)
- Average number of awakenings during the night
- Average times waking after sleep onset
- Total bedtime



At the end of the six-week study, the **ashwagandha group** showed a significant *increase* in **total sleep time** compared to **placebo**.<sup>8</sup>

Compared to placebo, the time to fall asleep and waking after sleep onset in the ashwagandha group were significantly reduced.

**Sleep efficiency** significantly **improved** in the ashwagandha arm of the **2020** published study. This means more time was spent asleep while in bed.<sup>8</sup>

Overall **improvement** in **restorative sleep** was **72**% in the **ashwagandha** arm of this study, indicating a meaningful enhancement of nightly rest.<sup>8</sup>

#### **Quality-of-Life Benefits**

The improvements demonstrated by the **wrist monitors** were clinically significant in the 2020 **ashwagandha** sleep study.

A second measure of perceived benefits also yielded intriguing findings.8

Questionnaires to evaluate **quality of life** were used at baseline, and six weeks later in both the **placebo** and **ashwagandha extract** groups.

Compared to baseline, the **ashwagandha** group showed **quality-of-life** <u>improvements</u>, which is expected in response to <u>enhanced</u> **sleep quality** and quantity.

#### Comparing Ashwagandha Sleep Studies

Consistent findings from **human** trials support a role for **standardized ashwagandha** in enabling more restful sleep.

The primary <u>active</u> constituents of ashwagandha are **withanolides**.

Three of the recent sleep studies used  $\underline{two}$  daily ashwagandha doses providing up to **30 mg** of withanolides. <sup>6,7,9</sup>

The fourth study used a *higher* concentration **ashwagandha extract** that provided **42 mg** of **withanolides** in <u>one</u> nighttime dose.<sup>8</sup>

What jumped to my attention is that the new *higher* concentrated **ashwagandha** (**42 mg**) yielded robust results with <u>once</u> nightly dosing, rather than having to take it <u>twice</u> daily like in other studies.

**Wrist-monitor** data from the *higher* concentrated **ashwagandha** (**42 mg** of **withanolides**) taken <u>once</u> nightly indicated better **sleep** improvements.

#### In This Month's Issue...

Many of you are determined to **shed body fat** to reduce your risk of degenerative illnesses. This might be impossible if you also suffer chronic **sleep deprivation**.

The article on page 34 of this issue describes how highly standardized ashwagandha + melatonin can enable more restorative sleep and an improved sense of wellbeing.

While there are no miraculous weight loss pills, a novel formulation described on page 44 enabled 5% weight loss to occur in obese individuals over a two-month period.

Combining standardized ashwagandha + melatonin at bedtime with more sensible eating, regular physical activity, and 5% weight loss can improve healthy longevity.

I want to thank readers of Life Extension Magazine® for their generous support in 2021.

As we aim to reverse human aging processes, improved sleep and reduced body fat are side benefits we plan to assess in upcoming clinical trials.

For longer life,

William Faloon, Co-Founder Life Extension Buyers Club

### Associations between Inadequate Sleep and Obesity in United States Adults 1977–2009

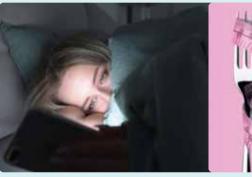
A startling **73%** of the U.S. population are defined medically as being overweight or obese.15

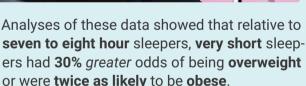
This means the **excess pounds** they carry increase their risk of degenerative disorders.

A 2014 published study looked at sleeping habits and obesity incidences starting in 1977. At the time, Americans did not have 24/7 television and computers and digital entertainment and electronic information. Time spent in front of display screens, especially late at night, was dramatically less back then than it is now.16

When the study period (1977 to 2009) ended, the following figures were observed in the **United States:** 

	1977	2009
Prevalence of <b>Obesity</b>	10.2%	27.7%
Prevalence of <b>Overweight</b>	31.2%	36.9%
Prevalence of Very Short Sleep (<5 hours)	1.7%	2.4%
Prevalence of <b>Short Sleep</b> (5-6 hours)	19.7%	26.7%
Prevalence of Long Sleep	11.6%	7.8%





Likewise, **short sleepers** had **20%** *greater* odds of being overweight or 57% greater odds of being obese. (Long sleepers had 20% greater odds of being obese, but no greater odds of being overweight.)

These findings are not surprising. Prevalence of very short and short sleep has gradually increased in recent decades. The authors of this study concluded:

"Inadequate sleep was associated with overweight and obesity for each available year."

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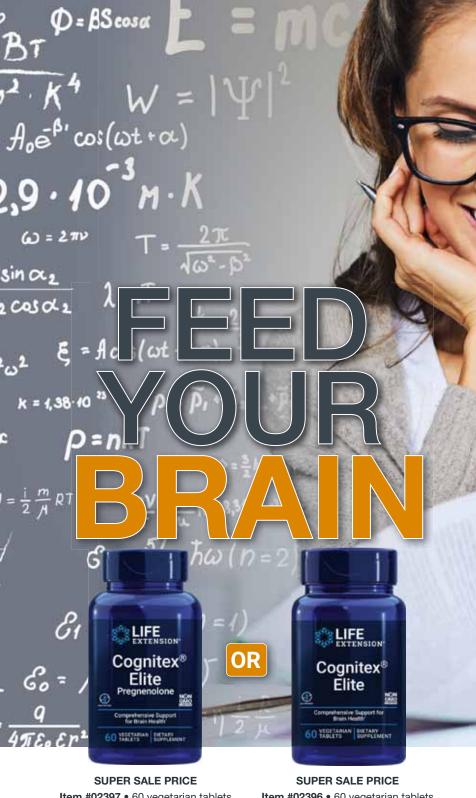


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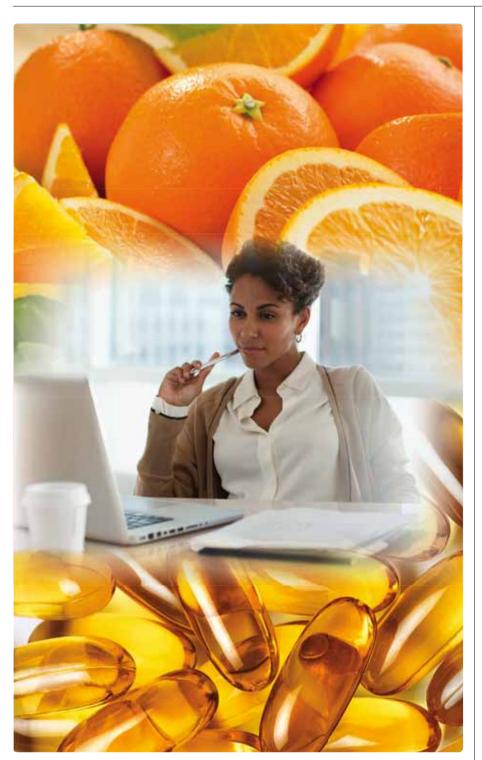
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## In the News



#### Vitamin C and E **Supplementation Lowers Risk of Cognitive Decline**

Supplementation with vitamins C and E may lower the risk of cognitive decline in people 65 and over, according to a study published in The Annals of Pharmacotherapy.\*

Researchers analyzed 5,269 men and women who were free of dementia at the start of the study, and followed them for 11 years.

Compared to non-supplementers, those who supplemented with vitamin C and/or vitamin E had a 38% lower adjusted risk of all-cause dementia and a 40% lower risk of Alzheimer's disease.

They also had a 23% lower risk of developing cognitive impairment without dementia.

Editor's Note: The study authors concluded, "This study supports a protective role of vitamin E and C supplements in the risk for Alzheimer's disease and all-cause dementia. In addition, these supplements may contribute to a reduced risk of CIND [cognitive impairment, not dementia]. Overall, these findings indicate additional support for the use of antioxidants as a preventive strategy against cognitive decline."

\* Ann Pharmacother. 2017 Feb;51(2):118-124.

#### **Fast-food Restaurant Availability Linked to** Type II Diabetes

A nationwide study found that living in a neighborhood with a higher availability of fast-food restaurants could increase the risk of developing type II diabetes.\*

Researchers analyzed data from more than four million veterans seen at 1,200 health facilities around the country who were followed for an average of 5.5 years.

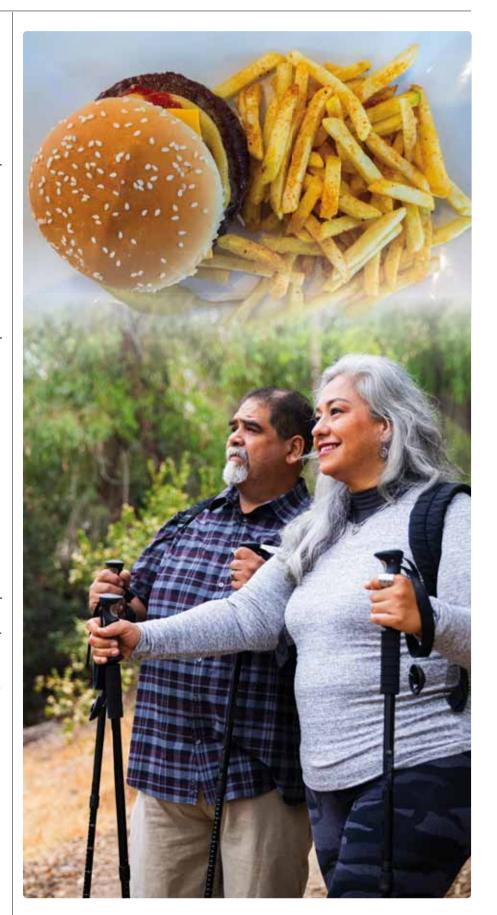
They examined the relationship between the "built food environment" and its connection to chronic disease. The built food environment indicates the physical buildings in a community in which people can make decisions about food, such as fast-food restaurants, grocery stores, and other food options.

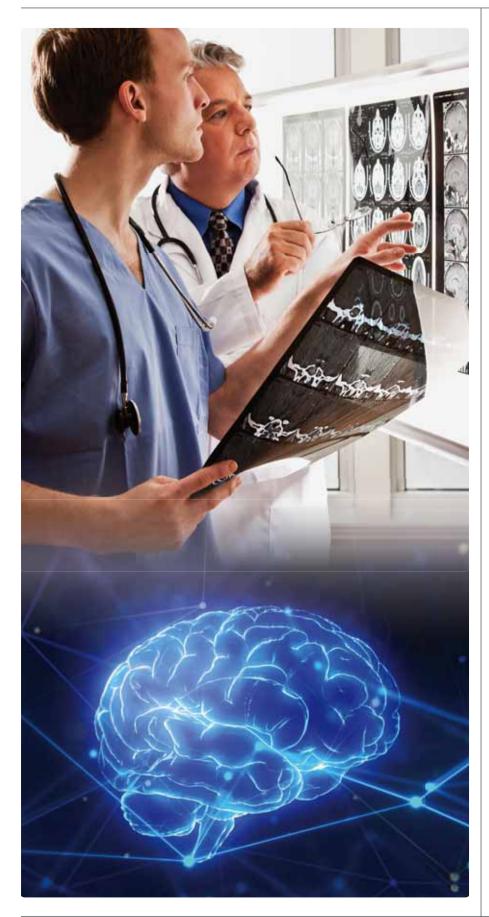
The researchers found that there was a link between the built food environment and the likelihood of developing chronic diseases like heart disease, type II diabetes, and certain types of cancers.

This association has been examined previously on a small scale. This was the first nationwide study using data from people living in 98% of the US census tracts across the country-to confirm the connection.

Editor's Note: The researchers concluded, "The more we learn about the relationship between the food environment and chronic diseases like type II diabetes, the more policymakers can act by improving the mix of healthy food options sold in restaurants and food outlets, or by creating better zoning laws that promote optimal food options for residents."

\* JAMA Network Open, 2021; 4(10): e2130789.





#### **NAD<sup>+</sup> Boosts Cognitive Function** in Animal Study

The Journal of Neuroinflammation reported that nicotinamide adenine dinucleotide (NAD+) improved cognitive function and inhibited neuroinflammation in an animal model of chronic cerebral hypoperfusion, an underlying cause of vascular dementia.\*

In this study, rats with reduced circulation to their brains were given daily injections of NAD+ for eight weeks. Researchers found that the NAD+ improved cognitive function and inhibited neuroinflammation.

The relevance of this study is that normal aged humans suffer significant cerebral circulatory deficits.

Maintaining more youthful NAD+ levels might circumvent some of the pathologies associated with deficient brain blood flow (hypoperfusion).

Editor's Note: NAD+ treatment alleviated CCH-induced neuronal death, microglial activation, and pro-inflammatory factor expressions in the cerebral cortex and hippocampus, the authors stated.

\* J Neuroinflammation. 2021 Sept 16; 18(1):207.

#### **Resveratrol Helps Modulate Glycemic Control** in Diabetics

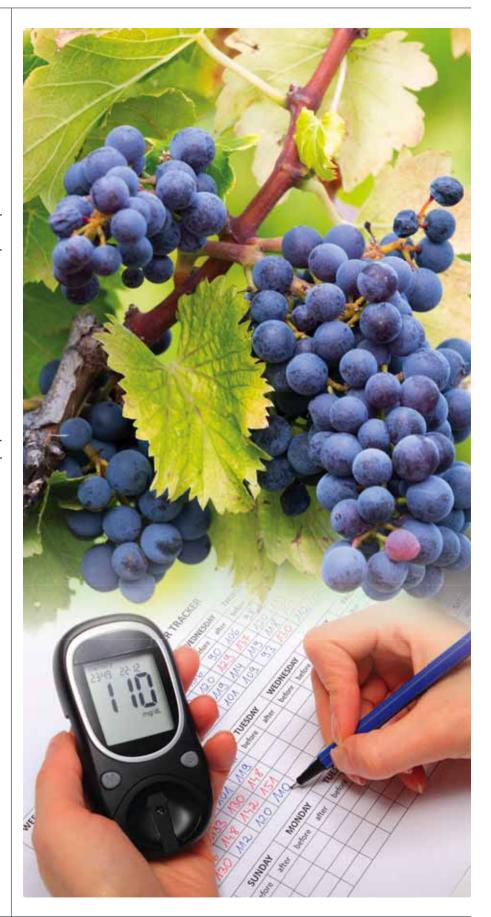
Supplementing with resveratrol was found to be associated with improvements in diabetics' glycemic control, according to findings from a meta-analysis of clinical trials published in Medicina Clinica (Barcelona).\*

The trials compared resveratrol to a placebo with or without concurrent antidiabetic medications or other drug treatment.

Resveratrol doses of 500 mg or more were associated with lower fasting blood glucose, fasting serum insulin, insulin resistance, total cholesterol, LDL cholesterol, and diastolic blood pressure, compared to a placebo.

Editor's Note: Resveratrol was associated with a greater reduction in hemoglobin A1c (a marker of long-term glucose control) compared to a placebo in trials of three months duration.

\* Med Clin (Barc). 2021 Oct 16;S0025-7753(21)00472-3.





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#### **Increasing Curcumin Bioavailability**

Curcumin is the main active ingredient in the spice turmeric.

It has potential benefits in combating a range of conditions such as diabetes, arthritis, cancer, and cardiovascular disorders.7,8

But curcumin itself has poor bioavailability. Only a small fraction of the amount consumed is absorbed into the bloodstream. And most of it is metabolized in the body into other compounds or eliminated from the body.9-11

Curcumin's use for **brain** disorders is also hindered by its limited ability to cross the **blood-brain barrier**.

Scientists have discovered a way around these

They found that supplementation with curcumin combined with galactomannans from the herb fenugreek resulted in levels of free curcuminoids in the blood up to 45.5 times greater compared to standard curcumin alone.6

This **curcumin-galactomannan** complex is able to easily cross the blood-brain barrier to deliver more curcuminoids than unformulated curcumin. 6,12

A 2021 animal study shows that this curcumingalactomannan complex delivered more curcuminoids to the brain's hippocampus than unformulated curcumin.12

The **hippocampus** is a region of the brain that has a major role in learning and memory.



Two **human** studies confirm the brain benefits of this novel curcumin-galactomannan complex.

In one, this formulation was effective at reducing stress, anxiety, and fatigue.13

In a 2020 human study, oral intake of 500 mg of the curcumin-galactomannan complex twice daily resulted in positive changes in brain activity levels and improved performance in audio-visual and memory tests.4

Electroencephalogram (EEG) results verified the curcumin-fenugreek complex's penetration of the blood-brain barrier, providing brain benefits previously unavailable.

#### **Preventing Cognitive Decline**

Neurodegeneration is characterized by the progressive damage and loss of function of neurons that occurs with aging and neurodegenerative diseases.

Some of the common mechanisms underlying these diseases include:

- Chronic inflammation, which can damage brain cells.14
- Oxidative stress, which leads to cell damage and death, 15,16 and
- Accumulation of misfolded proteins, which are toxic to neurons.16

Curcumin targets all these problems.

Preclinical research shows that curcumin can reduce neuroinflammation 2,3

Other work in preclinical models shows that curcumin could protect the brain against oxidative stress by activating the protein Nrf2,17,18 which is involved in increasing antioxidant levels in the brain.19

Curcumin also activates antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase<sup>17</sup> and directly neutralizes free radicals.<sup>20</sup>

Studies in rats show that curcumin can reverse memory loss caused by aging. 12,21

Besides its antioxidant and anti-inflammatory effects, curcumin spurs the formation of new neurons in a brain region called the hippocampus.5

A population-level study of elderly Asian individuals showed that regular curcumin intake in the form of curried food was associated with protection against cognitive decline.22



- Curcumin is an active compound in turmeric, the spice. It has potent antiinflammatory, antioxidant, and anticancer properties.
- By reducing inflammation, oxidative stress, and the buildup of toxic proteins, curcumin may prevent cognitive decline.
- Lab and animal research shows this compound may also reduce damage from strokes, prevent Parkinson's disease, relieve symptoms of multiple sclerosis, and ease diabetic neuropathy.
- Combining curcumin with a fiber called galactomannans makes it up to 45.5 times more bioavailable than standard curcumin. It can also more easily pass through the blood-brain barrier, enabling it to exert its neuroprotective effects.

#### **Fighting Parkinson's Disease**

Parkinson's disease is a common neurodegenerative disorder that leads to tremors, muscular rigidity, slowness of movement, and difficulty maintaining balance.<sup>23</sup>

These symptoms are caused by the loss of dopamine neurons in a brain region called the substantia nigra, which plays an important role in movement and motivated behaviors.24

While the underlying cause of Parkinson's disease is not clearly understood, both mitochondrial dysfunction and oxidative stress have emerged as major contributors to the neurodegeneration seen in Parkinson's disease.25

Curcumin alleviates both oxidative stress and mitochondrial damage in animal models of Parkinson's.<sup>26,27</sup>

In human patients with Parkinson's disease, low levels of the antioxidant glutathione are observed in dopamine neurons from the substantia nigra. Curcumin activates antioxidant enzymes to prevent the depletion of glutathione.28

Parkinson's also involves the formation of clumps of the misfolded protein alpha-synuclein.29 These protein aggregates have toxic effects on dopamine neurons.

Preclinical studies show that curcumin can inhibit the accumulation of alpha-synuclein and prevent the death of dopamine neurons. 30,31 This may help slow the development of Parkinson's disease.

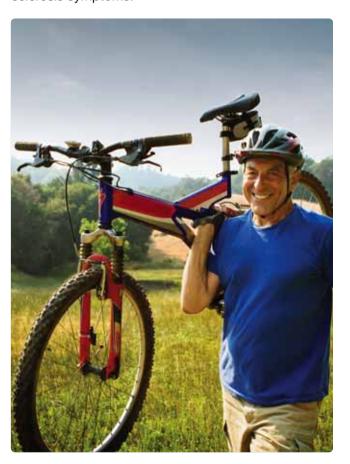
#### **Relieving Multiple Sclerosis Symptoms**

Multiple sclerosis is an autoimmune disorder that afflicts over 2.5 million people worldwide.32 Severe cases can lead to vision loss, paralysis, and impaired brain function.

Multiple sclerosis occurs when the immune system causes neuroinflammation in the central nervous system and interruption of the blood-brain barrier.33

This inflammation damages the protective myelin sheath that covers nerve fibers. The resulting harm to neurons hinders their ability to communicate.

Curcumin has been shown, in animal models, to lower levels of pro-inflammatory proteins and aid in myelin repair. This reduced the severity of multiple sclerosis symptoms.33-35



#### **Easing Diabetic Nerve Pain**

Neuropathic pain is caused by damage to the nerves that relay pain signals from the muscles and skin to the spinal cord and brain. It often affects patients with diabetes.36

Studies in mice show that curcumin can reduce diabetes-related hyperalgesia (increased sensitivity to pain).37,38

Various inflammatory cytokines, such as nuclear factor-kappa B (NF-kB) and TNF-alpha, are responsible for the pain associated with diabetic neuropathy.<sup>39</sup> Curcumin reduces levels of these pro-inflammatory cytokines to relieve hyperalgesia.38

In a rat model of diabetic neuropathy, curcumin reduced the oxidative stress that contributes to the dysfunction of neurons.40

#### **Reducing Damage from Strokes**

There are two major types of **strokes**: **ischemic** and hemorrhagic.

Ischemic strokes account for almost 90% of all strokes. They are caused by a blood clot or obstruction in an artery. The disruption in blood flow to the brain leads to oxygen deprivation, brain cell death, and damage to the blood-brain barrier.41

Animal studies show that curcumin reduces the size of the ischemic injury and prevents behavioral impairment. Curcumin exerts these neuroprotective effects by:

- Preventing damage to the blood-brain barrier,42
- Inhibiting cell death,<sup>43</sup>
- Counteracting oxidative stress,44 and
- Reducing the inflammatory response.<sup>45</sup>

The other main kind of stroke is caused by intracerebral hemorrhage, in which there is a bursting or leaking of a blood vessel. One of its major complications is a cerebral edema, when fluid builds up around the brain. The increased pressure and lower cerebral blood flow can damage brain cells.

Curcumin alleviates edema and reduces behavioral impairments in animal models of intracerebral hemorrhage. It does this by modulating the expression of proteins called aquaporins that reduce brain water content.46



Traumatic brain injuries caused by external mechanical force also result in inflammation, cerebral edema. blood-brain barrier damage, and oxidative stress. 47,48 Rodent models show that curcumin can reduce the brain damage caused by trauma by countering these adverse effects.49-51

#### **Summary**

Most neurodegenerative diseases share common features, including the accumulation of toxic proteins, inflammation, and oxidative stress.

**Curcumin** helps reduce or prevent all of these. Studies have shown that it may help reduce or slow the development of a wide variety of brain disorders.

A curcumin-galactomannan complex is highly absorbable and easily crosses the blood-brain barrier.

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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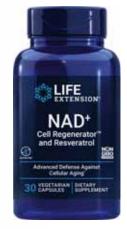
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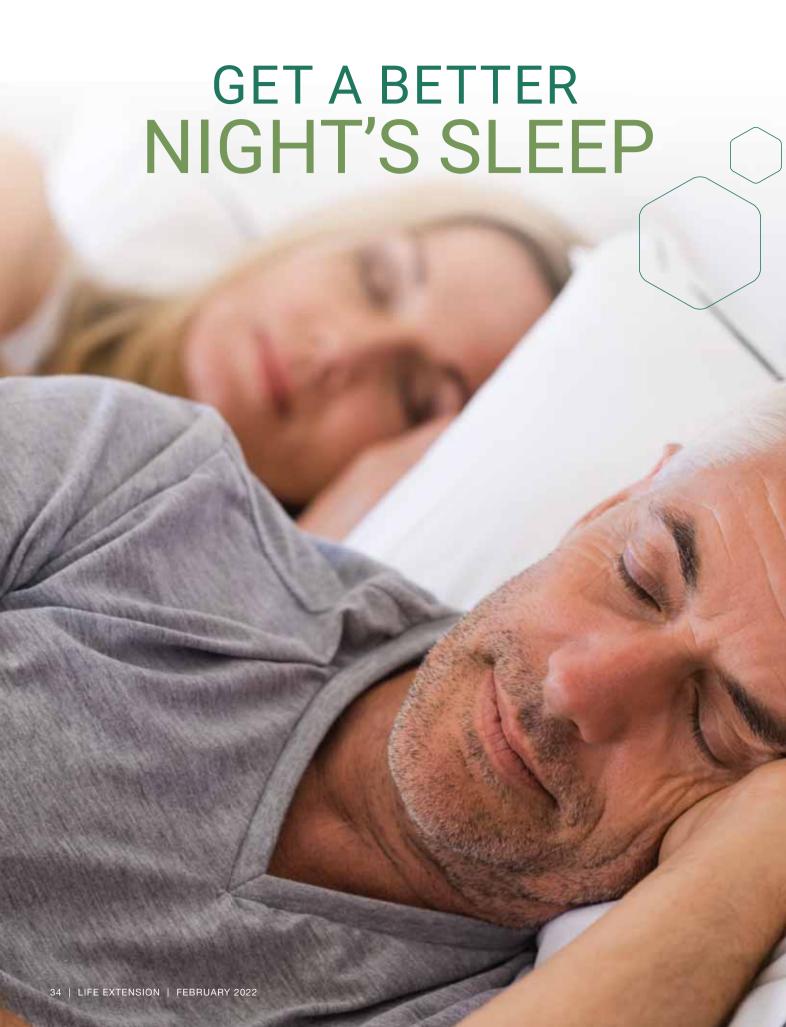
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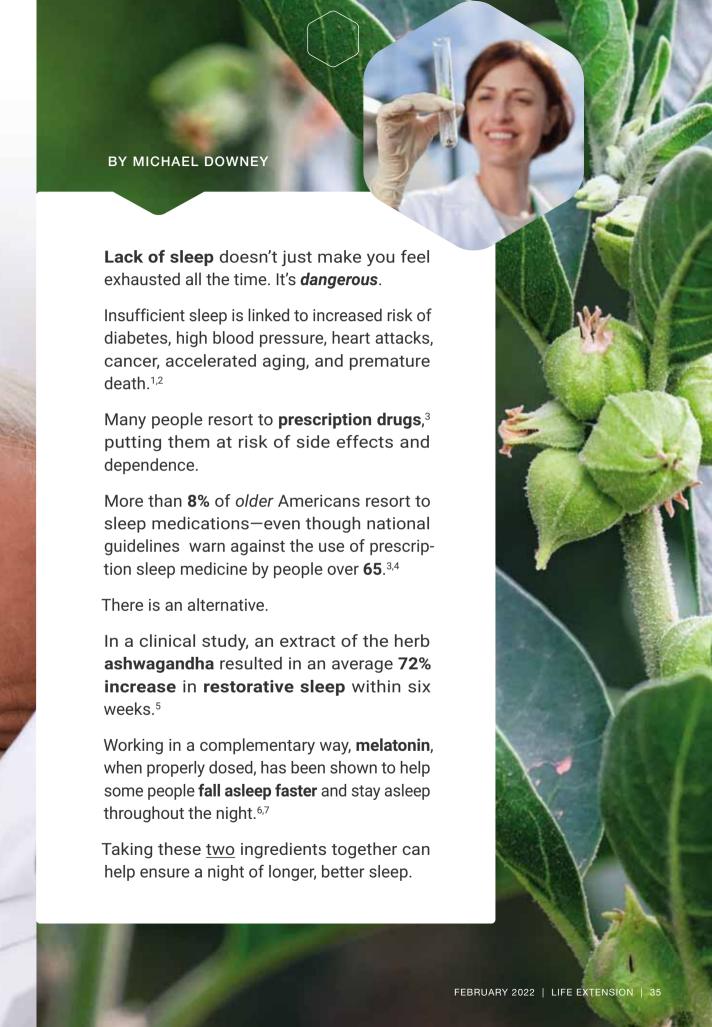
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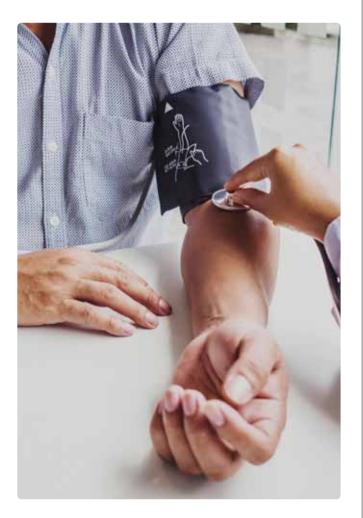
### **Health Risks of Inadequate Sleep**

The Centers for Disease Control and Prevention (CDC) and others recommend that adults get seven or more hours of sleep a night.8,9

More than **one in three adults** get suboptimal sleep on a regular basis.1 Studies show that frequently getting too little sleep may increase the risk of:10-13

- Obesity,
- Depression,
- Dementia.
- · Heart disease.
- Type II diabetes,
- · Some cancers, and
- · Other chronic health issues.

For every one-hour reduction in sleep per night, there is about a 6% increase in the risk of death from any cause.2



Sleep problems worsen with age. 14 Changes in hormones as we grow older have been linked to insomnia and poor sleep quality. 15-17 Some medications prescribed to older adults can also disrupt sleep.<sup>18</sup>

About **nine million** people in the U.S. rely on sleep medications. 19 But they come with side effects like memory problems and dizziness, potential for physical dependence, a "hangover effect" that leads to poor mental performance the day after use, and other risks. 20-24

Both the U.S. Food and Drug Administration (FDA) and drug manufacturers themselves advise that these medications are for short-term use only. It should also be noted that the risks of sleep medications are greater for older adults.4

### **Balancing and Regulating Sleep Patterns**

Scientists have been investigating safer ways to help people fall asleep more quickly and improve their sleep quality.

Two hormones that regulate and balance the cycles of wakefulness and sleep are cortisol and melatonin.

Cortisol is often thought of as the stress hormone. known for driving the body's fight-or-flight response. It also helps to control the wake-sleep cycle.

Normally, cortisol levels rise as we approach the end of our sleep cycle, reaching their highest point around **9 AM** to enhance wakefulness. Then, to pave the way for sleep, cortisol levels decline during the day, bottoming out around **midnight**.<sup>25</sup>

In a world of chronic stress, this cortisol rhythm is often thrown out of balance and can interfere with sleep. Poor sleep can result in even higher cortisol levels, setting up a vicious circle.25

Melatonin is known as the sleep hormone. It activates receptors in the brain that regulate sleep and the body's circadian (daily) rhythm.<sup>26</sup>

Melatonin production declines with age, contributing to some of the sleep problems seen with advanced age.27,28

Cortisol and melatonin both work to regulate sleep and wakefulness.

Scientists have identified ashwagandha and melatonin as two ingredients that can regulate and balance hormones to promote more restful sleep.



### **Ashwagandha Promotes Calm**

Ashwagandha is an herb that has been used in traditional Indian medicine for thousands of years.<sup>29</sup> Extracts of its roots and leaves contain a mix of beneficial compounds, including withanolide glycosides.<sup>30</sup>

Ashwagandha root powder has been shown to lower cortisol levels. It also reduces the anxiety and stress that increase cortisol production.31

Researchers have documented these anxietyreducing properties.<sup>29,32</sup>

In one study of adults with self-reported high stress, an extract of ashwagandha (standardized to 35% withanolide glycosides) led to a significant reduction in scores on stress-assessment scales. The use of this extract was also associated with reduced levels of cortisol in the morning.33

Another way that ashwagandha reduces stress is by activating nerve-cell receptors for a calming neurotransmitter called GABA.34

### Fall Asleep Faster, Stay Asleep Longer

- Lack of sleep is a serious health threat, increasing the risk of many chronic illnesses and premature death.
- About nine million Americans take prescription drugs to get to sleep. They come with potentially dangerous side effects and can lead to dependency.
- An extract of the herb ashwagandha standardized to 35% withanolide glycosides helps lower anxiety and stress and reduces levels of the stress hormone cortisol. In a clinical trial, it led to a 72% increase in restorative sleep.
- Maintaining higher nighttime levels of the "sleep hormone" melatonin promotes faster sleep onset and higher-quality sleep. Combining immediate-release and extended-release forms can allow people to stay asleep all night.
- A blend of ashwagandha and melatonin can rebalance nighttime cortisol and melatonin levels, providing a longer, more restorative sleep.

### **Clinically Validated Results**

To validate ashwagandha's effects on sleep, scientists tested a standardized 35% withanolide glycoside extract.

Every evening for six weeks, 75 volunteers were given a placebo and 75 were given 120 mg of ashwagandha extract.

Those in the ashwagandha group had significantly improved quality of sleep, including a:5

- 72% increase in restorative sleep, measured by a standard, weekly sleep questionnaire,
- Significant improvement in sleep efficiency (total sleeping time as a percentage of total time spent in bed),
- 27% decrease in sleep onset latency (time needed to fall asleep), and
- 15% decrease in wake after sleep onset (time spent awake after first falling asleep).

No adverse effects related to ashwagandha were reported.

### **Maintaining All-Night** Melatonin Levels

Melatonin is produced by the pineal gland in response to darkness, and it helps control the body's sleep-wake cycles.35

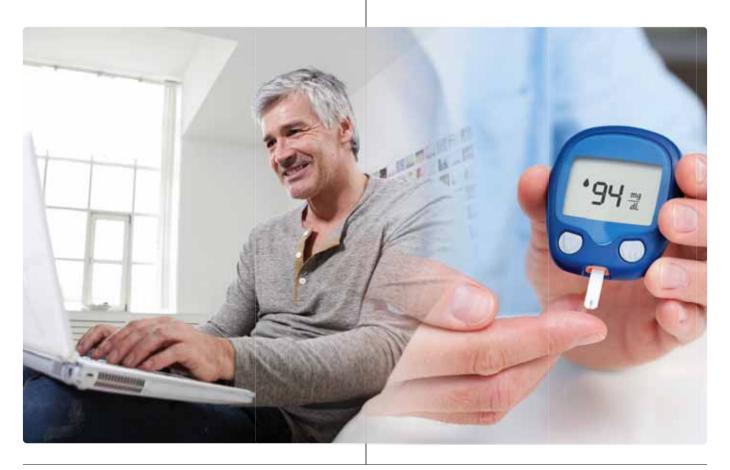
Levels of melatonin fall with age. This can result in impaired sleep and contributes to some of the consequences of disordered sleep, such as accelerated cognitive decline, cardiovascular disease, and metabolic disorders.<sup>27</sup>

Many of these effects are believed to be related to melatonin's impact on specific brain cells and regions of the brain involved in controlling our daynight cycles.27,36

Chronic conditions, such as elevated blood sugar, can also suppress normal melatonin production, which may account for poor sleep among diabetics.37

Boosting melatonin has been shown to help normalize sleep-wake patterns and enhance high-quality sleep.38,39

Human studies have shown that raising melatonin levels via supplementation can improve sleep patterns, quality, and duration.<sup>6,7</sup>





Increasing melatonin levels results in significant improvements in:6,7,40

- Sleep efficiency (total sleeping time as a percentage of total time spent in bed),
- Sleep onset latency (time needed to fall asleep), and
- Awake after sleep onset (time spent awake after first falling asleep).

### Maintaining Melatonin All Night Long

Many people take melatonin before bedtime.

Researchers have now developed a way to maintain melatonin levels all night long to enable a longer and more restorative sleep.

Scientists developed a dual-action form of melatonin containing:

- 0.5 mg of *immediate-release* melatonin, and
- 1.0 mg of extended-release melatonin.

This melatonin combination allows an initial elevation in melatonin levels and then delivers melatonin throughout a period of approximately seven hours.

The immediate-release melatonin can help people get to sleep faster and experience more restful and regenerative sleep. The extended-release melatonin can support a full night of uninterrupted sleep.

A placebo-controlled study of elderly subjects who complained of insomnia confirmed that taking an extended-release form of melatonin improved sleep quality.6

Taking this dual-action **melatonin** along with an extract of ashwagandha standardized to 35% withanolide glycosides in the evening can support a longer, more **restorative sleep** that promotes overall health.

### **Summary**

Sleep problems often worsen with age.

Ashwagandha helps reduce elevated cortisol levels that can impair sleep and has been shown in a clinical trial to result in an average 72% increase in restorative

Melatonin helps reset the body's sleep-wake cycles and promotes more effective, restful sleep. A dualaction formulation that combines immediate-release and extended-release melatonin can help people get to sleep faster and stay asleep throughout the night.

Taking ashwagandha extract standardized to 35% withanolide glycosides and dual-action melatonin 30 to 60 minutes before bedtime promotes the hormonal balance that allows more restorative, more refreshing sleep. •

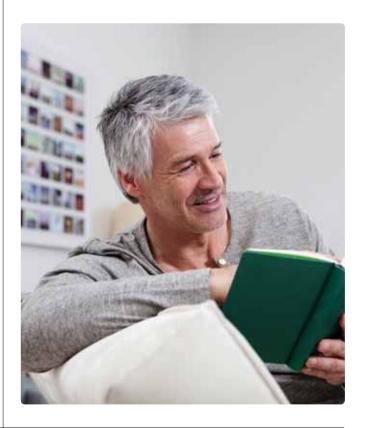
If you have any questions on the scientific content of this article, please call a **Life Extension** Wellness Specialist at 1-866-864-3027.

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# **CURB** Hunger and **Burn More Fat**

BY MARSHA MCCULLOCH, MS, RD

Many people want to lose weight to look and feel better.1,2

Shedding extra pounds also supports healthier aging.

Excess body weight is associated with an increased risk of heart disease, type II diabetes, and several types of cancer.

Sleep apnea, osteoarthritis, and high **blood pressure** are directly related to surplus body mass.3,4

Research shows that losing as little as 5% of body weight can provide health henefits 5

The wrong kind of **dieting** causes biological changes that can make it challenging to lose weight, including an increase in hunger hormones.<sup>6</sup>

But it doesn't have to be so difficult.

Researchers have identified a blend of extracts from lemon verbena leaf and hibiscus flower that can reduce hunger signals and promote satiety (a feeling of fullness).7-10

Two clinical trials have shown that these extracts can almost double the amount of weight loss compared to a placebo, when used in conjunction with a healthy diet and exercise.7,8

To improve compliance and support healthy weight loss, a lifestyle app has been developed that further facilitates losing weight with these extracts. Over 85% of the app users taking the supplement reduced their body weight, losing an average of 12.6 pounds in three months.11

### Why Weight Loss Is So Hard

Shedding pounds is rarely easy.

**Dieting** causes changes in metabolism and appetiterelated hormones that can make it harder to lose weight and keep it off.<sup>6</sup>

For example, weight loss leads to a rise in circulating **ghrelin**, a hunger hormone that *increases* **appetite**. 12

Weight loss also causes the body to secrete *less* **glucagon-like peptide-1** (**GLP-1**), a hormone that increases satiety.

Furthermore, a decrease in body weight reduces resting energy expenditure, or what we commonly refer to as metabolic rate.<sup>6</sup>

### Lemon Verbena and Hibiscus

**Hibiscus** is known for a bright red herbal tea made from its flower.

**Lemon verbena** is an herb beloved for its lemony aroma and flavor.

Both plants are rich in **polyphenols** that can help promote weight loss—without the unwanted side effects of drugs.<sup>7,13,14</sup>

In a preclinical cell study, **hibiscus extract** was shown to significantly *inhibit* the creation of new **fat** cells. It also reduced the accumulation of **triglycerides** in fat cells.<sup>15</sup>

When excess triglycerides build up in fat cells, it leads to **oxidative stress**. That can trigger the **inflammation** that promotes diseases associated with **obesity**. 16

In the cell study, **hibiscus** extract led to a **30%** reduction in the generation of damaging **reactive oxygen species**. <sup>15</sup>

Preclinical research has shown that **lemon verbena** extract can decrease **triglyceride** accumulation in fat cells.<sup>17</sup>

**Triglycerides** are the most common type of **fat** in your body. They come from foods like butter, oils, other fats and glucose-boosting foods (starches) and sugary beverages.

Triglycerides not needed for energy production circulate in the blood and are **stored** in our cells as **fat**.

### **Curbing Appetite**

A blend of **lemon verbena leaf** and **hibiscus flower** extracts was tested in a rigorous, placebo-controlled trial of 47 overweight and obese women.<sup>7</sup>



All subjects were advised to ingest approximately 2,200-calories a day. They were also encouraged to walk at least half an hour daily during the two-month

Roughly half the participants took 500 mg of the plant extracts 20 to 30 minutes before breakfast every day. The other half were given a placebo.

Those taking the lemon verbena-hibiscus combination had a 56.4% decrease in feelings of hunger, on average. They also experienced a significant increase in the satiety-promoting hormone GLP-1, accompanied by an increase in food intake-related satisfaction.

Decreased appetite may have been one factor that led to greater weight loss. In two months, the treatment group lost 7.7 pounds, while the placebo group lost only 4.6 pounds.

If this does not sound like much weight, it represents the real-world challenges people face when attempting to shed excess body weight.

### **Controlling Calorie Intake**

In another trial, scientists gave 33 overweight and obese men and women 500 mg of lemon verbena-hibiscus extract or a placebo daily before breakfast.9

After 60 days, both groups returned to the lab and were fed a standardized breakfast. A few hours later, they were served a buffet-style lunch.

The group taking the extracts ate almost 10% fewer calories at lunch than the placebo group did and reported a significant improvement in satiety.

After taking the **lemon verbena-hibiscus** extract, the men and women had a 12% increase in GLP-1 after breakfast and a 22% increase after lunch, promoting a feeling of fullness.

### **Trimmer Waistlines**

Shedding pounds promotes metabolic health.<sup>18</sup> In a placebo-controlled clinical trial of overweight or obese women, scientists tested whether 500 mg of lemon verbena-hibiscus extract could increase weight loss.8

All the women were instructed to walk at least 30 minutes daily and encouraged to consume 2,200 calories a day.



### Herbal Appetite Control for Weight Loss

- Losing as little as 5% of body weight can reduce the risk of many chronic diseases, including heart disease and type II diabetes.
- Difficulty controlling appetite is a major obstacle for people trying to lose weight.
- Extracts from a blend of lemon verbena leaf and hibiscus flower can increase satiety hormones to help curb appetite.
- Clinical trials of a combination of lemon verbena and hibiscus extracts have shown that it can reduce body weight by 5% within two months and trim the waistline by more than 2.5 inches.
- These extracts work best when combined with a healthy diet and regular exercise. Studies have shown that a digital app can help keep weight loss efforts on track and promote a healthier lifestyle.

After two months of taking the plant extracts,8 overweight participants with an average body mass index (BMI) of 27 kg/m<sup>2</sup>:

- Lost over **eight pounds**, or **5.4%** of their starting weight,
- Decreased their body mass index (BMI) by 1.5 points,
- Trimmed their waistline by **2.7 inches**,
- Reduced their percentage of body fat by 1.3%,
- · Lowered their systolic blood pressure (top number) by 20.6 mmHg, and
- Decreased their resting heart rate by 8.5 beats per minute.

These changes were all significantly better than the changes in subjects given a placebo.

Most notably, the extract group lost about twice as much weight and almost four times as many inches from their waistline as the placebo group.

Obese participants (average BMI of 34 kg/m²) taking the extracts lost over 10 pounds, or 5.3% of their body weight.

They also lowered their heart rate by eight beats per minute and reduced systolic blood pressure by 18.4 mmHg.

A reduction in heart rate is significant because an elevated resting heart rate is one of the predictors of both cardiovascular and all-cause mortality.



Life Extension has long recommended the Mediterranean diet for maintaining healthy weight, heart health and longevity. (See Life Extension Magazine® December 2021).

In addition, the American Heart Association recommends moderate, regular exercise.<sup>21</sup> This should include, 150-300 minutes a week of heart-pumping exercise, muscle strengthening two days a week, and reduced sitting.



### **Summary**

A combination of lemon verbena and hibiscus extracts has been shown to promote fat burning and shift appetite hormones in ways that make it easier to eat less and lose weight.

Controlled clinical trials of overweight adults have found that taking 500 mg of combined lemon verbena-hibiscus extracts for two months can produce an average of 5% reduction in body weight.

Modest, sustainable weight loss like this can go a long way toward reducing the risk of common cardiovascular and metabolic 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.

### Boost Motivation with a Mobile App



As our phones become increasingly integrated into our lives, many people are relying on mobile apps to improve their health. There are apps with exercise programs, sleep-tracking programs, and now an app that was especially designed to improve weight loss in conjunction with the lemon verbena-hibiscus extract

Mobile apps can support a more comprehensive approach to weight loss, which could help with managing weight over the long term. 19,20

In a 90-day real-world study, 397 volunteers took 500 mg of a lemon verbena-hibiscus extract blend daily, administered in a yogurt drink.11

They also used a custom app designed to help them develop a healthier lifestyle.

The interactive app:11

- Gradually introduced healthy behavior changes,
- Provided reminders to take the extract blend,
- Encouraged water, vegetable, and fruit intake.
- · Tracked exercise, food, and water intake,
- · Helped track weight changes, and
- · Provided motivational messages and incentives.

In those completing the study, the app boosted adherence to the extracts by more than **five times** compared with typical dietary supplements.11

The participants' lifestyle improved, too. They doubled their water intake and fruit and vegetable consumption. And they increased their exercise by 33% over baseline.

These changes paid off.

Over **85%** of the users reduced their body weight, losing an average of 12.6 pounds in three months.11

(A similar app is available at no charge to lemon verbena-hibiscus extract users.)

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**SUPER K** is the best-selling **vitamin K** formula for bone and heart health. It costs only **23 cents** a day and provides in one softgel:

Vitamin K1 1,500 mcg (converts to K2 in some people)

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**Super K Elite** provides 2 <u>additional</u> forms of vitamin K and even *higher* potencies of K1, MK4, and MK7. **Super K Elite** costs **54 cents** a day and provides in one softgel:

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Vitamin K2 (MK-4) 1,500 mcg (for bone & vascular health)

Vitamin K2 (MK-7) 181 mcg (long-acting protection)

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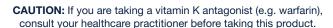
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- > Saffron has been shown to help support vision as demonstrated by doctors' eye exams.1
- > Alpha-carotene further helps support macular density.1



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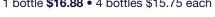
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# AMPK to Better Manage Body Weight

Most people today consume excess calories.

This results in **mTOR** constantly running at high gear, which is a factor in unwanted **fat storage**.

Studies show that <u>increasing</u> **AMPK** activity turns down excess **mTOR**.<sup>1</sup>

### Reduce Cell Fat Storage

Scientific studies show that <u>increasing</u> **AMPK** activity can encourage cells to store less fat and burn it as energy.<sup>2,3</sup>

AMPK Metabolic Activator was formulated based on data showing <u>reduced</u> belly fat in response to just one of its ingredients (*Gynostemma pentaphyllum*).<sup>3</sup>

This **Gynostemma pentaphyllumn + hesperidin** formula is designed to support healthy **AMPK** cellular activation.

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## Eat Right, Choose Wisely and Sleep Well

When it comes to losing weight, we tend to think of eating salads, skipping dessert, or going for a run. While those are great, we're forgetting something important—sleep.

As it turns out, not getting enough sleep can put a damper on your weight loss plans.

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Human studies show that **lemon verbena** leaf and **hibiscus flower** extracts promote satiety and encourage **weight loss**...in just 8 weeks.<sup>†</sup>

In one clinical trial, participants taking this plant extract duo reduced their body weight by an average of **5.4**%—while losing **2.7 inches** from their waistlines.<sup>1</sup>

Another clinical trial resulted in an average **50.4**% *increase* in feelings of satiety.<sup>2</sup>

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

Metabolaid® is a registered trademark of MONTELOEDER, S.L.

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Take one capsule 30-60 minutes before bedtime.

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30 VEGETARIAN DIETARY SUPPLEMENT





# **Boost Testosterone** Levels without Drugs

### BY CARL RITTER

**Testosterone** levels drop as men get older. This begins *much* earlier than most realize.

As early as age 30, testosterone levels start falling at a rate of about 1% per year. 1,2

Decreased libido and erectile dysfunction are well-known symptoms associated with low testosterone levels.3 But this hormone deficit affects more than the reproductive system.

Low levels of testosterone are also associated with depression, obesity, diabetes, heart disease, osteoporosis, muscle wasting, and more.4-8

Studies also show that *low* testosterone levels in aging men are associated with an increased risk of death from any cause.9

Three plant-based nutrients have been identified that support the body's ability to produce testosterone, significantly raising levels

In one clinical study, a proprietary blend of pomegranate and cacao extracts was shown to increase **free testosterone** by as much as 48% in aging males.10

In cell and animal studies, luteolin, a flavonoid found in fruit and vegetables, has been shown to *inhibit* the **aromatase** enzyme. 11,12 This enzyme converts testosterone into estrogen.

These nutrients can help support more youthful testosterone balance in aging men.

### **Importance of Testosterone**

**Testosterone** is a hormone produced primarily in the testes of men and in the ovaries of women. A small amount is also made in the adrenal glands of men and women. 13-15

This sex hormone is critical to the development of the male reproductive system. But testosterone levels also impact metabolism, energy, muscle strength and mass, inflammation, cognition, mood, and more.16

Low levels of testosterone become increasingly common and more severe as men age. 17-20

Not only does this rob men of energy, virility, and the youthful feeling of general well-being, but it is also associated with age-related chronic conditions, including heart disease and diabetes. 9

In one meta-analysis, low testosterone levels were associated with an increased risk of death due to cardiovascular disease or any cause.9

### "Free" and "Bound" Testosterone

Testosterone circulates in the blood bound to circulating plasma proteins, most importantly sex hormone binding globulin (SHBG) and albumin. 13,21

Only about 2% of circulating testosterone is non-protein bound, or free .22 This free testosterone is the biologically active form.

For testosterone to exert its effects, free testosterone must bind to receptors in target tissues.

Total testosterone is the measure of all circulating testosterone, including that which is bound to carrier proteins like sex hormone binding globulin (SHBG). In this "bound" form, testosterone is not available for the body to use.

Both total testosterone and free testosterone drop significantly with advancing age.

What's more, being **overweight** or **obese** has been associated with increases in the levels of an enzyme called aromatase. This enzyme converts testosterone into estrogen, one of the primary sex hormones in women.23,24

As a result, overweight men, especially those with a high amount of **abdominal fat**, are at *higher* risk for low testosterone levels.

### **Pomegranate and Cacao Raise Testosterone**

Scientists have been searching for ways to safely elevate testosterone levels without drugs.

In one study, researchers found that in healthy adult men and women, intake of pomegranate fruit juice for just two weeks increased salivary testosterone levels by 23%-27%. Measures of mood and well-being were also improved.25

These findings inspired scientists to screen hundreds of other plant extracts and nutrients for the ability to raise testosterone levels.

In a study using testes cells from mice, they confirmed that pomegranate extract raised testosterone production. They also discovered that cacao seed extract-from the same beans used to make cocoa





and chocolate-significantly increased testosterone production.26

When combined, the pomegranate and cacao seed extracts had an impressive impact on testosterone production in an animal model.

In a study on rats, this pomegranate-cacao combination boosted total testosterone levels by over 72% after just six weeks.27

### **Results from Human Studies**

In a clinical trial, the **pomegranate** and **cacao** extracts were tested in men ranging from 36 to 55 years of age.<sup>10</sup> They were randomized to receive either a combination of both extracts or a placebo.

After eight weeks, free testosterone levels were elevated by over 48% compared to baseline in men receiving 400 mg of the pomegranate-cacao blend.

Notably, **free testosterone** increased by a *greater* percentage than total testosterone.

That wasn't all. In those taking pomegranate and cacao extract, overall well-being improved. Measures of stress dropped by 26%. Hand grip strength increased by almost 25%, compared to baseline.

- terone drop steadily after around age 30.
- Low testosterone is associated with erectile dysfunction, loss of virility, and serious chronic health issues including heart disease, obesity, depression, and more.
- Scientists have found that a proprietary blend of pomegranate and cacao extracts stimulate production and increase blood levels of testosterone.
- In a clinical trial, this combination increased biologically active free testosterone by as much as 48% and led to reduced stress, increased hand grip strength, and other health improvements.
- Luteolin, a flavonoid found in several fruits and vegetables, was shown in cell and animal studies to support testosterone production and reduce its conversion into estrogen.



The study also measured what's known as the **Aging Males' Symptoms** scale, which includes:<sup>28</sup>

- · Joint pain and muscle aches,
- Excessive sweating,
- Sleep problems and exhaustion,
- Anxiety and irritability,
- Depression and feeling burned out, and
- Decrease in libido and other sexual problems.

Measures of these symptoms were reduced by 19% in those who took the **pomegranate-cacao** combination.

A similar study was performed in healthy **younger** men, aged 21 to 35.<sup>29</sup> Even in this age group, pomegranate and cacao increased **free testosterone** by **25%**. Hand grip strength and the circumference of the upper arm increased as well.

### Luteolin Supports Testosterone Production

**Luteolin** is a flavonoid found in several herbs, fruits, and vegetables, including celery, broccoli, parsley, and thyme.

Preclinical studies have shown that luteolin may support healthy **testosterone** levels by at least two different ways:

- Increasing StAR protein: The steroidogenic acute regulatory (StAR) protein is an enzyme that is required for testosterone production to occur.<sup>30</sup>
- Inhibition of aromatase: Luteolin has also been found to inhibit aromatase—the enzyme that converts testosterone into estrogen—in cell culture and animal models.<sup>11,12</sup>

Scientists combined **luteolin** with **pomegranate** and **cacao** extracts to help support healthy **free testosterone** levels.

### **Summary**

**Testosterone** is the primary male sex hormone. It plays important roles in reproductive function and impacts many other aspects of health.

Beginning around age **30**, levels of testosterone in men begin to *decline*.

**Low testosterone** is associated with loss of energy, erectile dysfunction, and increased risk for heart disease, obesity, diabetes, osteoporosis, muscle wasting, and other health conditions.

Scientists have discovered that a proprietary blend of **pomegranate** and **cacao seed** extracts can raise blood levels of free testosterone in men. <sup>10,29</sup>

In one study free testosterone was increased by as much as 48% in aging males taking this proprietary blend.10

The increases in free testosterone also correlated with improvements in levels of stress, strength, mood, and more.

Evidence from cell and animal studies suggests that luteolin may also support testosterone levels by increasing production and preventing its breakdown to estrogen.

The combination pomegranate/cacao with added luteolin may offer a solution to the age-related decreases in testosterone levels seen in men. •

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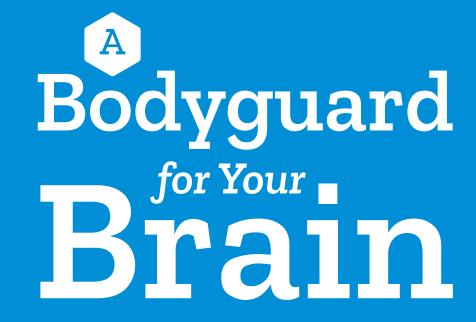
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\*European Journal of Nutrition. 2011;50(5):387-389

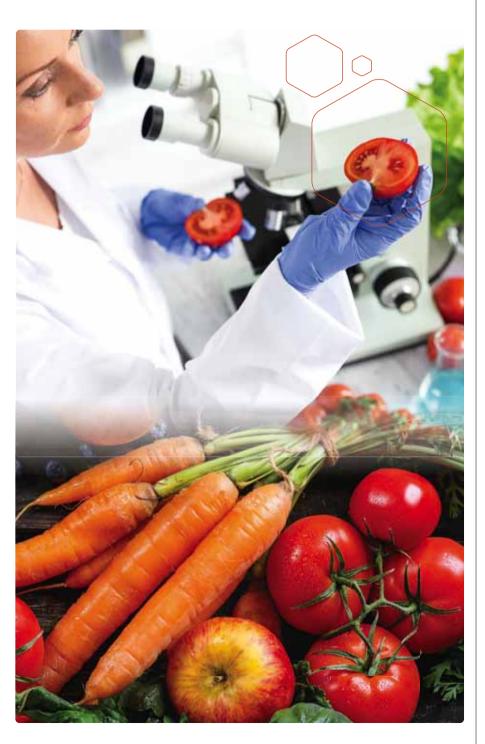




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### **New Studies Corroborate** LYCOPENE BENEFITS

BY LAURIE MATHENA



If you've ever wondered what makes a tomato red or a grapefruit pink, the answer is a carotenoid called lycopene.

In the body lycopene promotes blood vessel function, supports normal insulin sensitivity, and helps maintain healthy blood pressure levels.

But lycopene is best known for its role in helping reduce the risk of prostate cancer.

Because of its multi-targeted health benefits, lycopene has been described as an important nutrient for longevity.1

In just the past year alone, new studies have added to lycopene's list of health benefits:

 Lycopene protects against obesity and diabetes.2 After evaluating about 200 articles, researchers concluded that lycopene exhibits antidiabetes and anti-obesity activities in multiple organs. They concluded that lycopene consumption could help lower the risk of obesity and diabetes.

- Lvcopene inhibits prostate cancer.3 A review summarized numerous original and review articles, evaluating the many ways that lycopene helped to prevent or suppress cancer. The authors concluded that lycopene suppressed the progression and proliferation of prostate cancer cells and induced apoptosis of these malignant cells in in-vivo and in-vitro conditions. It also modulated the signaling pathways and their proteins, potentially preventing and aiding in the treatment of prostate cancer.
- Lycopene intake reduces allcause mortality.<sup>4</sup> In a review of studies, researchers determined that dietary lycopene or serum lycopene was associated with reduced all-cause mortality, prostate cancer, stroke, cardiovascular disease, metabolic syndrome, and male infertility.

• Lycopene could help protect against peripheral neuropathy.<sup>5</sup> In an animal study, oral administration of lycopene helped ameliorate central and peripheral nerve injuries caused by a platinum-based chemotherapeutic drug called oxaliplatin.

One drawback is that it isn't easily available in adequate amounts through diet alone.

Fortunately, it's easy to supplement with lycopene to derive the myriad benefits detailed in studies published in 2020-2021 that corroborate findings dating back to the 1980s.

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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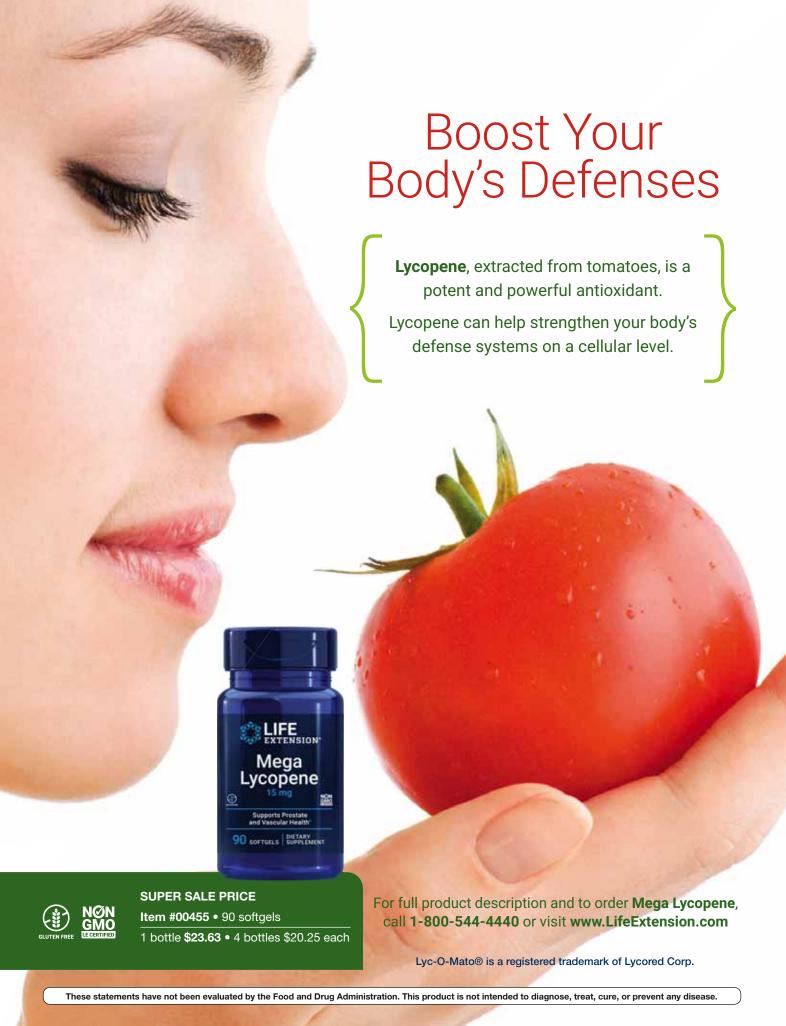
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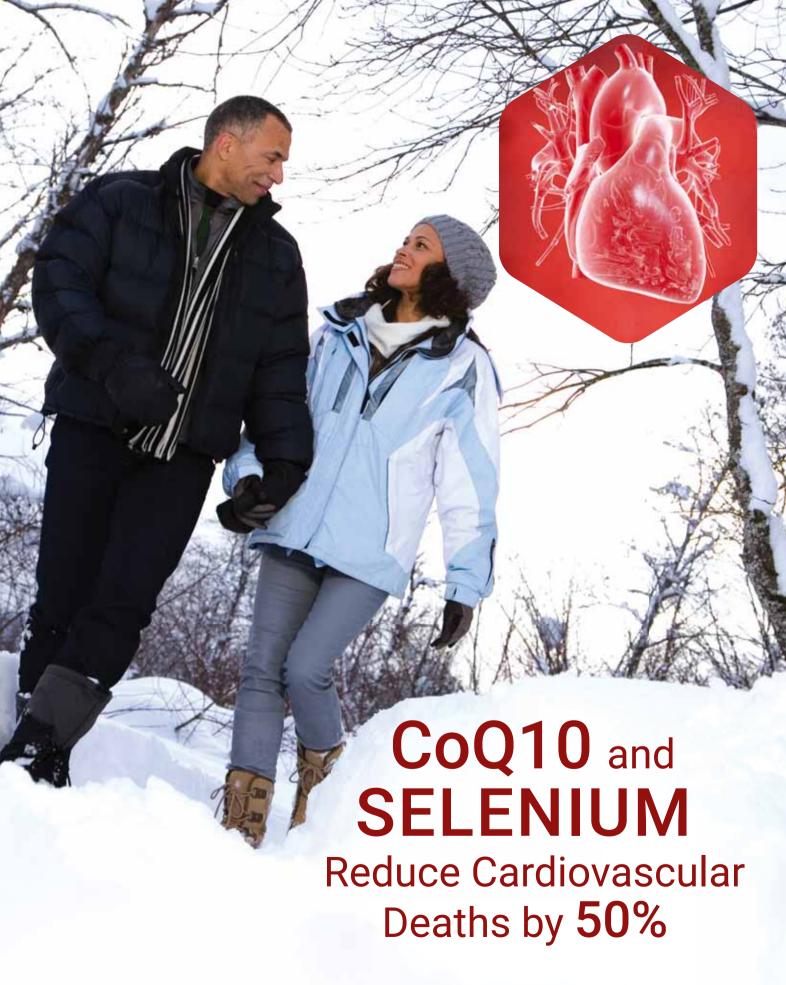
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#### Reductions in **Cardiovascular Death**

In the initial study, researchers from Sweden chose healthy adults between the ages of 70 and 88 years old. Subjects were randomized to receive either a combination of 200 mg of coenzyme Q10 and 200 mcg of selenium daily or a placebo for four years.

During the follow-up period of more than five years after the end of the nutrient intervention, 12.6% of those who had received the placebo suffered a cardiovascular death. But only 5.9% of those in the selenium + CoQ10 group did—less than half the mortality rate.1

Results from two subsequent additional follow-ups have been remarkable.

**Ten years** after the supplementation ended, the risk of death due to cardiovascular disease was still 49% lower in those who had received the nutrients.3 This result was true even for subjects who had existing heart disease.

After 12 years, the benefit continued; the risk of death was 41% lower in those who had received selenium and CoQ10.2

The benefits remained consistent when focusing only on subjects who had existing heart disease, diabetes, or high blood pressure.

#### **Improved Markers of Health**

Slashing the rate of cardiovascular mortality is impressive enough.

But in the last few years, several in-depth analyses of the original trial have determined that selenium and CoQ10 also improved several markers of cardiovascular and general health, including:

- Quality of life. In those given selenium and CoQ10, measures of mental and physical quality of life were maintained better than in those who took the placebo.12
- Hospitalization. Subjects who received the two nutrients spent a remarkable 246 fewer days, on average, in the hospital than placebo recipients.<sup>12</sup>
- Heart function. Those receiving the selenium and CoQ10 had significantly better cardiac function (measured by an echocardiogram) than placebo recipients.1
- **Fibrosis**. Fibrosis, the development of rigid, scarred tissue, is a common element of many chronic diseases, including in the heart. Those receiving the supplementation had a reduction in fibrosis for biomarkers compared to those taking a placebo.6





- Oxidative Stress and Inflammation. Oxidative stress and chronic inflammation are significant contributors to many forms of age-related disease. In this study, several markers of oxidative stress and chronic inflammation were decreased in those taking the nutrients.9-11,13
- Clot Formation. D-dimers are protein fragments produced by blood clots. Elevated levels in the blood correlate with cardiovascular disease. Taking selenium and CoQ10 was found to prevent an increase in D-dimers.7
- Glycation. Blood sugar can attach to proteins, lipids, or DNA and damage them. This process is known as glycation, and it is a contributor to most chronic diseases. Fructosamine, a compound found in blood that is a marker of glycation, is associated with risk of cardiovascular disease.14-19 Fructosamine was reduced in those receiving the combination of nutrients.5
- Cardiovascular and Pulmonary Risk. High levels of the protein NT-proBNP in the blood is a marker of heart failure. It can also be an indicator of coronary and valvular heart disease, pulmonary hypertension, pulmonary embolism, and stroke risk.<sup>20-22</sup> Selenium and CoQ10 intake was associated with reduction in NT-proBNP levels.1

These results clearly show that taking selenium and CoQ10 did more than reduce death from cardiovascular causes. It also improved many measures of heart and overall health.

#### A Combination that Cuts Cardiovascular Death

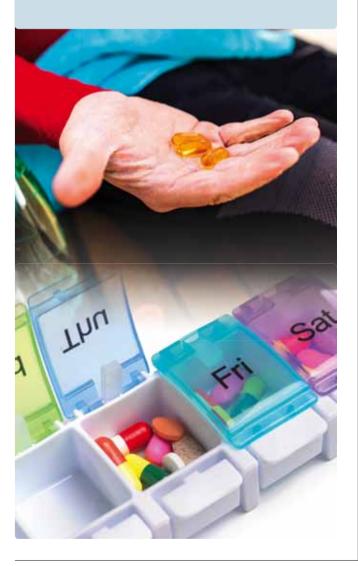
- Selenium and coenzyme Q10 (CoQ10) are nutrients that prevent damaging oxidative stress. Coenzyme Q10 plays a vital role in mitochondrial health to maintain cellular energy.
- A landmark study in Sweden showed that older individuals who took 200 mg of coenzyme Q10 and 200 mcg of selenium daily for four years had dramatically lower cardiovascularrelated deaths compared to those who received a placebo, by more than half!
- A follow-up showed that the group taking the nutrients still had lower rates of death 12 years after the supplement intervention ended.
- Several sub-studies have shown that the four-year combination of CoQ10 and selenium also improved quality of life, heart function, and biomarkers of heart and blood vessel health.

#### Statin Drugs Deplete CoQ10

Many people take statin drugs to lower cholesterol and reduce risk of cardiovascular disease

But that comes with a problem: Statin drugs can deplete coenzyme Q10 levels.29,30 That's because the enzyme that statins inhibit is the same enzyme that produces a compound required to make new CoQ10 in the body.

Since low CoQ10 production may raise the risk of heart disease, those taking statins should be particularly concerned with their blood levels of CoO10.



#### How Selenium and **CoQ10 Help the Heart**

On their own, selenium and coenzyme Q10 each helps protect the heart.

Several studies have shown that there is a link between cardiovascular disease and lower blood levels of both nutrients.23-27

Selenium and CoQ10 are involved in the body's defenses against oxidative stress, a major contributor to cardiovascular disease. And CoQ10 is crucial for the proper function of the cell's powerhouses, the mitochondria.28

Selenium is important for different enzymes, including glutathione peroxidase and thioredoxin reductase. These are both critical parts of the body's built-in antioxidant system that shields against oxidative damage.5

Selenium and CoQ10 may represent a powerful duo for the prevention of heart disease and reduction in cardiovascular deaths.

#### **Summary**

A clinical trial showed that a combination of sele**nium** and **coenzyme Q10**, taken for four years, reduced cardiovascular death in a group of older adults, even five years past the end of the intervention.

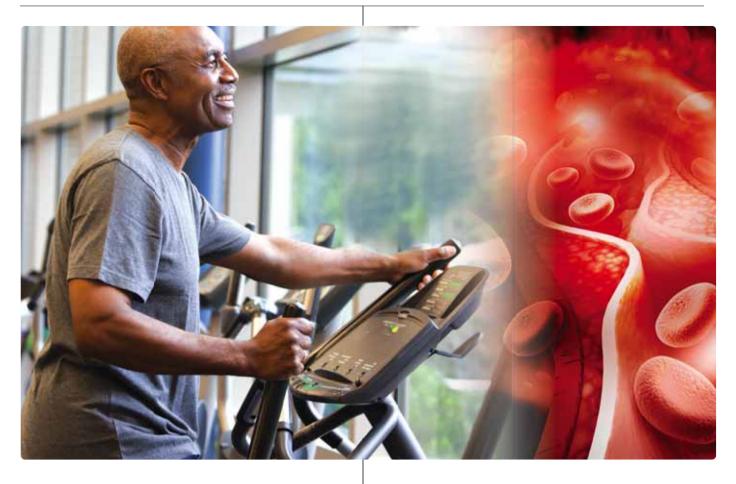
Beyond that, 12 years of follow-up have now demonstrated that the protection against cardiovascular death and disease continued for over a decade after the supplementation period ended.

Analyses show that selenium and CoQ10 not only reduced mortality, but also reduced hospitalizations for heart disease, improved quality of life, boosted heart function, decreased inflammation, and improved other markers of cardiovascular and general 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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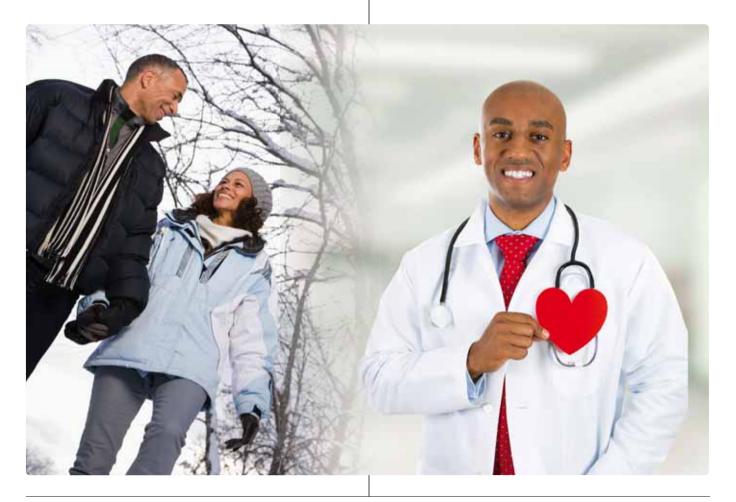


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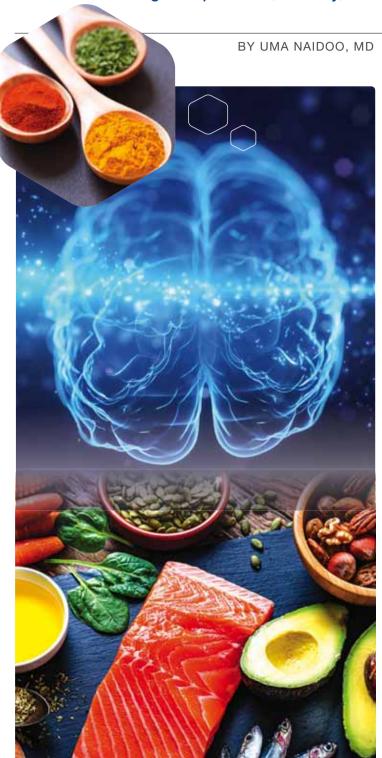
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#### This is Your Brain on Food

An Indispensable Guide to the Surprising Foods that Fight Depression, Anxiety, PTSD, OCD, ADHD, and More



Food has a profound effect on **mental health**. It impacts your risk of depression, brain fog, and Alzheimer's, and plays a role in libido, sleep, OCD, and much more.

In *This is Your Brian on Food*, board-certified psychiatrist, nutrition specialist, and professionally trained chef Uma Naidoo reveals cutting-edge research on the direct connection between the gut and the brain.

Naidoo says that because many doctors overlook this connection, they are missing a key component to successful treatment and recovery.

"Until we solve nutritional problems, no amount of medication and psychotherapy is going to be able to stem the tide of mental issues in our society," said Naidoo.

In this book, Naidoo explains how you can use diet to achieve well-being in every aspect of your mental health. She offers practical advice on what to eat (and what not to eat) to improve your cognitive function, mood, energy, concentration, libido, and more.

She also highlights key nutrients and supplements that help build the foundation of healthy brain function.

In this interview with *Life Extension* Dr. Naidoo explains the critical gut/brain connection, and offers practical tips to help with depression, memory, sleep problems, and more.

-LAURIE MATHENA

LE: How does food influence your hrain?

Dr. Naidoo: Food influences your brain directly and indirectly. When food is broken down by the microbiota into fermented and digested materials, its components directly influence neurotransmitters such as serotonin, dopamine, and GABA, which travel to the brain and change the way you think and feel.

When food is broken down, its constituent parts can also pass through the gut wall into the bloodstream, and certain metabolites can act on the brain that way as well.

Food's most profound effect on the brain is through its impact on your gut bacteria. Some foods promote the growth of helpful bacteria, while others inhibit this growth.

Because of that effect, food is some of the most potent mental health medicine available, with dietary interventions sometimes achieving similar results to specifically engineered pharmaceuticals, at a fraction of the price and with few, if any, side effects.

On the other hand, food can also made you sad-certain food groups and eating patterns can have a negative effect on your gut microbiome and your mental health.

The idea of using food as medicine for mental health is central to nutritional psychiatry, and in my opinion, it's crucial to finding meaningful, lasting solutions to mental health problems.

Until we solve nutritional problems, no amount of medication and psychotherapy is going to be able to stem the tide of mental issues in our society.

LE: How can something as basic and natural as eating be as potent as a drug that cost millions of dollars to develop and test?

**Dr. Naidoo:** The primary reason gut bacteria have such a profound effect on mental health is that they are responsible for making many of the brain chemicals.

If normal gut bacteria are not present, production of neurotransmitters such as dopamine, serotonin. glutamate, and gamma-aminobutyric acid (GABA)-all critically important for the regulation of mood, memory, and attention-is impacted.

Many psychiatric disorders are rooted in deficits and imbalances of these chemicals, and many psychiatric drugs are tasked with manipulating their levels.

Therefore, if your gut bacteria are intimately involved with producing these vital chemicals, it stands to reason that when your gut bacteria are altered, you risk doing damage to this complex web of body and brain function.

That's a lot of responsibility for a group of microscopic organisms!

LE: Does this mean that your diet can impact your risk of depression?

Dr. Naidoo: When discussing depression and the gut with my patients, I often use the phrase "blue bowel," a lighthearted name for the very serious relationship between depression and your gut.

Food changes the types of bacteria present in your gut microbiome. Your gut bacteria may become less diverse as a result of your diet, which may cause the bad bacteria to outgrow the good bacteria, triggering a cascade of negative health effects.

Studies in humans appear to confirm this hypothesis. In 2019, psychiatrist Stephanie Cheung and her colleagues summarized findings from six studies that looked at gut health in patients with depression.

They reported that patients with major depressive disorder had at least 50 types of bacterial species in their gut microbiome that were different from those of control subjects without major depressive disorder.





Recent research suggests that bacterial species associated with higher quality-of-life indicators are depleted in depressed subjects, while bacteria that cause inflammation are often found in higher numbers in people suffering from depression.

This tells us that inflammation and depression are closely linked.

LE: If you're suffering from gutinduced depression, how do you reset your gut microbiome to help achieve a healthy mental state?

**Dr. Naidoo:** The key is to increase probiotics and prebiotics in your diet. Probiotics are live bacteria that convey health benefits when eaten. Probiotic-rich foods contain beneficial bacteria that help your body and brain.

In 2010, Michael Messaoudi and his colleagues studied 55 healthy men and women who were randomly assigned to receive either a daily probiotic formula or a placebo for 30 days.

Compared to the placebo group, those in the probiotic group reported less depression, and urinary levels of cortisol (the body's main stress hormone) were lower, indicating that their brains were less depressed and less stressed.

Why was this the case? Certain species of gut bacteria have the ability to boost levels of brain chemicals such as gamma-aminobutyric acid, which may speed relief from depression and other mental health conditions.

Magnesium is also important for proper brain function. Countless studies have suggested that depression is related to magnesium deficiency. Several case studies, in which patients were treated with 125-300 mg of magnesium, have demonstrated rapid recovery from major depression, often in less than a week.

LE: Another issue people struggle with as they get older is memory. Why is the typical Western diet so bad for memory?

Dr. Naidoo: High-fat and highglycemic-index (high-GI) foods can alter brain pathways necessary for learning and memory, with neurons in the hippocampus and prefrontal cortex especially affected.

The hippocampus is the part of the brain most involved in forming relational memories.

High-fat and high-GI diets can affect the hippocampus in a variety of ways. First, the Western diet can hamper the expression of critical growth factors like brain-derived neurotrophic factor and other hormones that promote healthy function in the hippocampus.

Second, poor diets can affect insulin signaling and insulin sensitivity in the body's tissues. It's unclear exactly what insulin's role is in the

hippocampus, but studies have indicated that it likely impacts memory.

One recent study showed that high saturated fat intake in male rats interfered with insulin signaling in the hippocampus, which led to interference with hippocampal function and corresponding relational memory abilities.

Third, a diet high in saturated fat and refined sugar in male rats showed increased oxidative stress, which damages brain cells and reduces the efficacy of cell-to-cell communication in the hippocampus.

Dietary components such as saturated fat may also exacerbate inflammation in the brain, which has been linked to cognitive decline in aging and risk of developing Alzheimer's disease.

Inflammation disrupts many of the chemical pathways instrumental in memory formation, such as those that rely on dopamine and glutamate. The nerves themselves become sluggish and information travels far more slowly.

LE: Besides cutting out high-fat and high-GI foods, what nutrients can someone take to improve memory?

Dr. Naidoo: Curcumin has antioxidant, anti-inflammatory, and neurotrophic activities. In fact, one recent review of 32 animal and laboratory studies showed that it can reverse some brain damage caused by Alzheimer's.

A 2019 review of curcumin studies also showed improvement in attention, overall cognition, and memory.

Another is saffron. In 2010, Shahin Akhondzadeh and his colleagues tested whether saffron could impact cognition. They administered either 15 mg capsules of saffron or a placebo twice daily to people with mild to moderate Alzheimer's disease.

After 16 weeks, saffron produced a significantly better outcome on cognitive function than placebo.

**LE:** Many of our readers struggle with getting adequate sleep. How can you eat for better sleep?

**Dr. Naidoo:** The best recipe for sleep often lines up with a healthy diet. For example, in 2014, Ryoko Katagiri and her colleagues reported that women who ate more noodles and sweets and less vegetables and fish had worse sleep than those with healthier diets.

Broadly speaking, I recommend you follow a healthy, whole-foods diet like the Mediterranean eating pattern, and make sure to include or exclude certain foods based on how they affect your sleep.

**LE:** What is one specific nutrient that's been proven to help improve sleep?

**Dr. Naidoo:** You can add improved sleep to the long list of benefits of omega-3 polyunsaturated fatty acids. A number of studies in animals demonstrate that omega-3s decrease inflammation and normalize sleep, and that they protect the brain from memory impairment in sleep-deprived mice.

There are also an increasing number of studies that demonstrate the beneficial effects of omega-3s on human sleep.

For instance, in 2018 Leila Jahangard and her colleagues conducted a study on 50 depressed patients. Compared to those on a placebo, the participants who received omega-3s improved their depression, anxiety, and emotional control, and over time they improved their sleep as well.

**LE:** What are some ways to help clear up brain fog?

**Dr. Naidoo:** "Brain fog" occurs when you cannot think clearly, when you cannot concentrate or multitask, or when you lose short-term and long-term memory.

In 2015, Theoharis Theoharides and his colleagues showed that luteolin, a type of flavonoid, has numerous neuroprotective properties that decrease brain fog. As an antioxidant and anti-inflammatory agent, this substance prevents toxic destruction of nerve cells in the brain.

In 2018, Lucy Harper and her colleague Justine Bold showed that gluten can cause brain fog. After consuming gluten, some people find themselves thinking less clearly and wanting to sleep all day. If you are suffering from brain fog, cut out gluten to see if you improve. It may turn out that you have celiac disease or non-celiac gluten sensitivity.

Phosphatidylserine (PS) is required for healthy nerve cell membranes and coverings, and its protective effects can prevent brain fog. In 2010, Akito Kato-Kataoka explained that six months of soybean-derived PS improved memory function in elderly Japanese adults.

**LE:** What are your thoughts on taking drugs to treat mental health issues?

**Dr. Naidoo:** Modern mental health medications can be a godsend to patients who struggle with a variety of disorders, and I don't want to downplay their importance as a therapy in many circumstances.

But what sometimes gets lost in discussions about mental health is a simple truth: the food you eat can have just as profound an effect on your brain as the drugs you take.

It's important to work with a mental health professional to develop the right mix of psychotherapy and anti-depressant medication when necessary. But no matter what, the food you eat will be an important part of the puzzle.

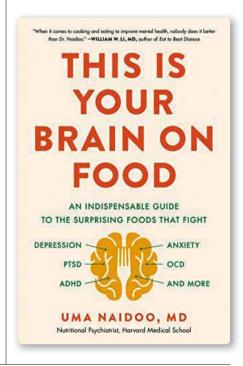
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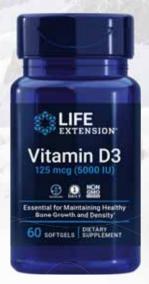
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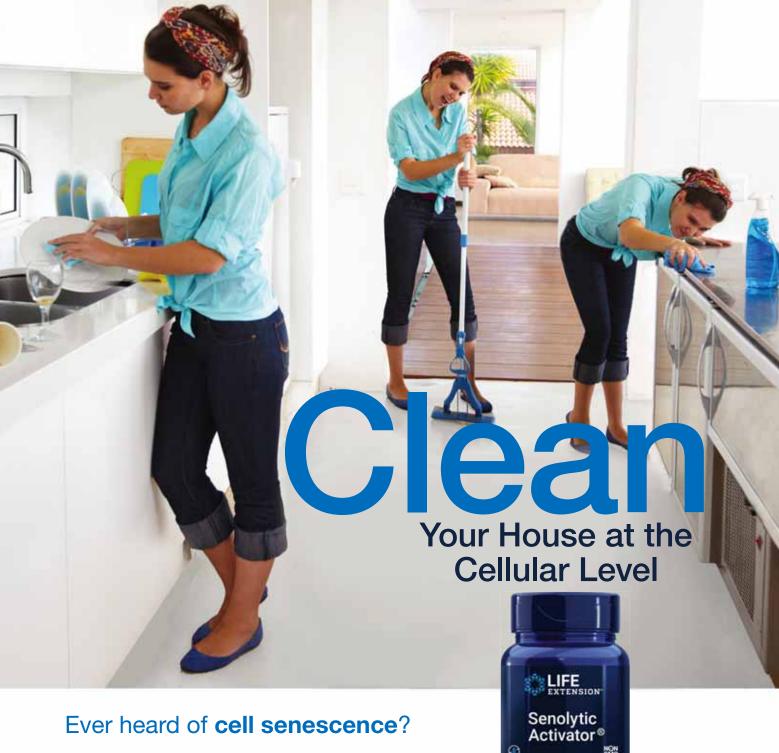
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## **Apples**

#### BY LAURIE MATHENA



When it comes to superfoods, it doesn't get much more nutrientdense, tasty, portable, or versatile than apples.

Eating just one apple per day has been associated with a lower risk of dying from cardiovascular disease, cancer, or all-cause mortality.1

But eating more could be even better.

According to a study published in the American Journal of Clinical Nutrition, eating two apples per day reduced LDL cholesterol and triglyceride levels in people with slightly elevated levels.2

Higher apple consumption has been tied to a lower risk of numerous types of cancer,3 along with a lower risk of cardiovascular disease, asthma, and type II diabetes.4

A review of human, culture, and animal studies has also demonstrated that frequent apple consumption has beneficial effects on lipid metabolism, vascular function, and inflammation.5

This could be due in part to their high level of phytochemicals such as quercetin, flavonoids, and carotenoids.4

These studies prove the truth of the popular adage: An apple a day really can keep the doctor away. •

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- 01932 Cat Mix
- 01931 Dog Mix

#### **PROBIOTICS**

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

#### SKIN CARE

- 80157 Advanced Anti-Glycation Peptide Serum
- 80165 Advanced Growth Factor Serum
- 80170 Advanced Hyaluronic Acid Serum
- 80154 Advanced Lightening Cream
- 50154 Advanced Lightening Cream
- 80155 Advanced Peptide Hand Therapy
- 80175 Advanced Probiotic-Fermented Eye Serum
- 80177 Advanced Retinol Serum
- 80152 Advanced Triple Peptide Serum
- 80140 Advanced Under Eye Serum with Stem Cells
- 80137 All-Purpose Soothing Relief Cream
- 80139 Amber Self MicroDermAbrasion
- 80118 Anti-Aging Mask
- 80151 Anti-Aging Rejuvenating Face Cream

- 01786 Melatonin 6 Hour Timed Release 3 mg, 60 veg tablets 80153 Anti-Aging Rejuvenating Scalp Serum 80179 Brightening Peptide Serum 01721 Optimized Tryptophan Plus 01444 Quiet Sleep 80176 Collagen Boosting Peptide Cream 01445 Quiet Sleep Melatonin 80156 Collagen Boosting Peptide Serum 02502 Rest & Renew 02408 Collagen Peptides for Skin & Joints 80180 CoQ10 and Stem Cell Rejuvenation Cream **VITAMINS** 80169 Cucumber Hydra Peptide Eye Cream 01533 Ascorbyl Palmitate 02423 Daily Skin Defense 00920 Benfotiamine with Thiamine 80141 DNA Support Cream 00664 Beta-Carotene 80163 Eye Lift Cream 01945 BioActive Complete B-Complex 80123 Face Rejuvenating Anti-Oxidant Cream 00102 Biotin 80109 Hyaluronic Facial Moisturizer 00084 Buffered Vitamin C Powder 80110 Hyaluronic Oil-Free Facial Moisturizer 02229 Fast-C® and Bio-Quercetin Phytosome 80138 Hydrating Anti-Oxidant Facial Mist 02075 Gamma E Mixed Tocopherol Enhanced with 00661 Hydroderm Sesame Lignans 55495 Instensive Moisturizing Cream 80103 Lifting & Tightening Complex 01913 High Potency Optimized Folate 80168 Melatonin Advanced Peptide Cream 01674 Inositol Caps 80114 Mild Facial Cleanser 02244 Liquid Vitamin D3 • 50 mcg (2000 IU) 80172 Multi Stem Cell Hydration Cream 80159 Multi Stem Cell Skin Tightening Complex 01936 Low-Dose Vitamin K2 80122 Neck Rejuvenating Anti-Oxidant Cream 00065 MK-7 80174 Purifying Facial Mask 00373 No Flush Niacin 80150 Renewing Eye Cream 01939 Optimized Folate (L-Methylfolate) 80142 Resveratrol Anti-Oxidant Serum 01217 Pyridoxal 5'-Phosphate Caps 01938 Shade Factor™ 01400 Super Absorbable Tocotrienols 02129 Skin Care Collection Anti-Aging Serum 02334 Super K 02130 Skin Care Collection Day Cream 02335 Super K Elite 02131 Skin Care Collection Night Cream 01863 Super Vitamin E 80166 Skin Firming Complex 02422 Vegan Vitamin D3 02096 Skin Restoring Ceramides 02028 Vitamin B5 (Pantothenic Acid) 80130 Skin Stem Cell Serum 01535 Vitamin B6 80164 Skin Tone Equalizer 00361 Vitamin B12 Methylcobalamin 80143 Stem Cell Cream with Alpine Rose 01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges 80148 Tightening & Firming Neck Cream 80161 Triple-Action Vitamin C Cream 80162 Ultimate MicroDermabrasion 80173 Ultimate Peptide Serum 80178 Ultimate Telomere Cream 01751 Vitamin D3 • 25 mcg (1000 IU), 250 softgels 80160 Ultra Eyelash Booster 80101 Ultra Wrinkle Relaxer 80113 Under Eye Refining Serum 01758 Vitamin D3 with Sea-lodine™ 80104 Under Eye Rescue Cream 02040 Vitamins D and K with Sea-lodine™ 80171 Vitamin C Lip Rejuvenator 80129 Vitamin C Serum 80136 Vitamin D Lotion 80102 Vitamin K Cream 01509 Advanced Anti-Adipocyte Formula 01807 Advanced Appetite Suppress **SLEEP** 02207 AMPK Metabolic Activator 01512 Bioactive Milk Peptides 02504 Body Trim and Appetite Control 02300 Circadian Sleep 02478 DHEA Complete 01551 Enhanced Sleep with Melatonin 01738 Garcinia HCA
- 01511 Enhanced Sleep without Melatonin
- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 02308 Herbal Sleep PM
- 01722 L-Tryptophan
- 01668 Melatonin 300 mcg, 100 veg capsules
- 01083 Melatonin 500 mcg, 200 veg capsules
- 00329 Melatonin 1 mg, 60 capsules
- 00330 Melatonin 3 mg, 60 veg capsules
- 00331 Melatonin 10 mg, 60 veg capsules
- 00332 Melatonin 3 mg, 60 veg lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release
  - 300 mcg, 100 veg tablets
- 01788 Melatonin 6 Hour Timed Release 750 mcg, 60 veg tablets

- 02070 Gamma E Mixed Tocopherol & Tocotrienols
- 02232 Liquid Vitamin D3 (Mint) 50 mcg (2000 IU)

- 01537 Vitamin B12 Methylcobalamin 5 mg, 60 veg lozenges
- 02228 Vitamin C and Bio-Quercetin Phytosome 60 veg tablets
- 02227 Vitamin C and Bio-Quercetin Phytosome 250 veg tablets
- 01753 Vitamin D3 25 mcg (1000 IU), 90 softgels
- 01713 Vitamin D3 125 mcg (5000 IU), 60 softgels
- 01718 Vitamin D3 175 mcg (7000 IU), 60 softgels

#### **WEIGHT MANAGEMENT & BODY COMPOSITION**

- 02479 7-Keto® DHEA Metabolite 100 mg, 60 veg capsules
- 01908 Mediterranean Trim with Sinetrol™-XPur
- 01432 Optimized Saffron
- 00818 Super CLA Blend with Sesame Lignans

#### **WOMEN'S HEALTH**

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

# PROTECT & ENERGIZE Your Aging Cells



#### **SUPER SALE PRICE**

Mitochondrial Energy Optimizer with PQQ Item #01868 | 120 vegetarian capsules 1 bottle \$45.90 | 4 bottles \$40.50 each

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Carnosine, benfotiamine, and pyridoxal-5-phosphate are powerful anti-glycation nutrients.

**PQQ** and **R-lipoic** acid promote healthy cell energizing **mitochondria** function.

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

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#### **SUPER OMEGA-3 PLUS**

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

#### **SUPER SALE PRICE**

Item #01988 • 120 softgels

1 bottle \$30.38 • 4 bottles \$28.35 each







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Sesame Lignans & Olive Extract
(2,400 mg of EPA + DHA in four softgels)

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1 bottle \$21.60 • 4 bottles \$18.90 each

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

These products have been tested to the quality and purity standards of the IFOSTM program conducted at Nutrasource Diagnostics, Inc.



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