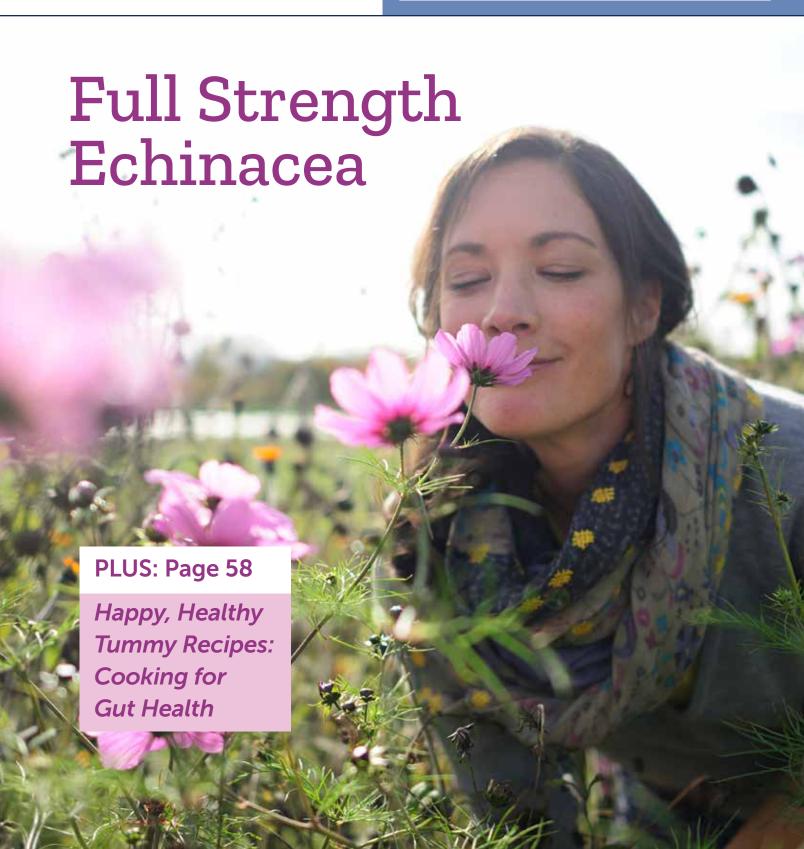


The Science of a Healthier Life®

November/December 2022

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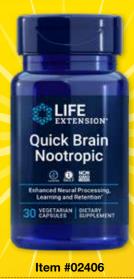
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\*Br J Pharmacol. 2004 Mar;141(5):825-30.



#### The Science of a Healthier Life®

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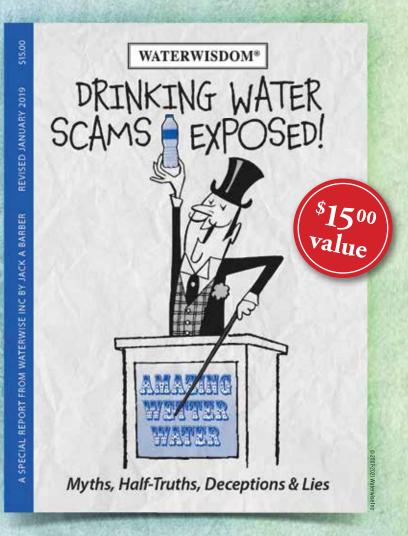
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Richard Black, DO, is a dedicated nuclear medicine physician practicing as an independent contractor out of Cleveland, Ohio. Dr. Black is board certified in internal medicine and nuclear medicine, and is licensed to practice medicine in multiple states throughout the United States.



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Aubrey de Grey, PhD, is a biomedical gerontologist and Editor-in-Chief of Reiuvenation Research, the world's highest-impact, peer-reviewed journal focused on intervention in aging. He received his BA and PhD from the University of Cambridge in 1985 and 2000 respectively. Dr. de Grey is a Fellow of both the Gerontological Society of America and the American Aging Association and sits on the editorial and scientific advisory boards of numerous journals and organizations.



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Ralph W. Moss, PhD, is the author of books such as Antioxidants Against Cancer, Cancer Therapy, Questioning Chemotherapy, and The Cancer Industry, as well as the award-winning PBS documentary The Cancer War. Dr. Moss has independently evaluated the claims of various cancer treatments and currently directs The Moss Reports, an updated library of detailed reports on more than 200 varieties of cancer diagnoses.



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



#### In the News

#### **Resveratrol Supplementation Improves Glucose Regulation in Type II Diabetics**

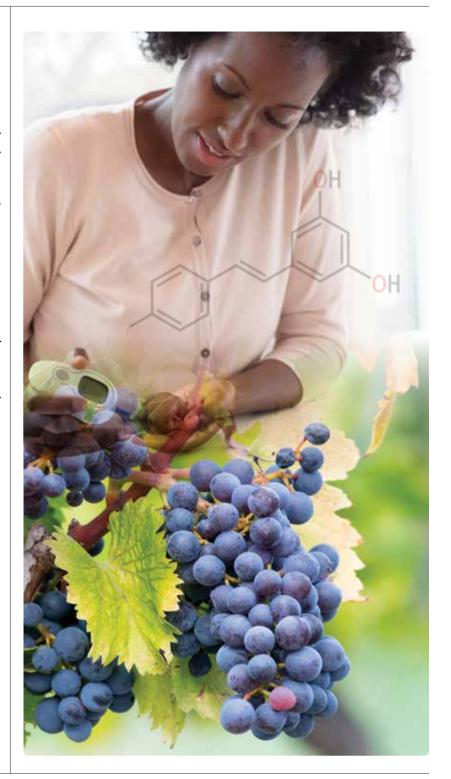
Supplementing with resveratrol showed positive effects in the regulation of glucose and the maintenance of healthy levels of inflammation and oxidative stress in type II diabetics, according to an article in Complementary Therapies in Medicine.\*

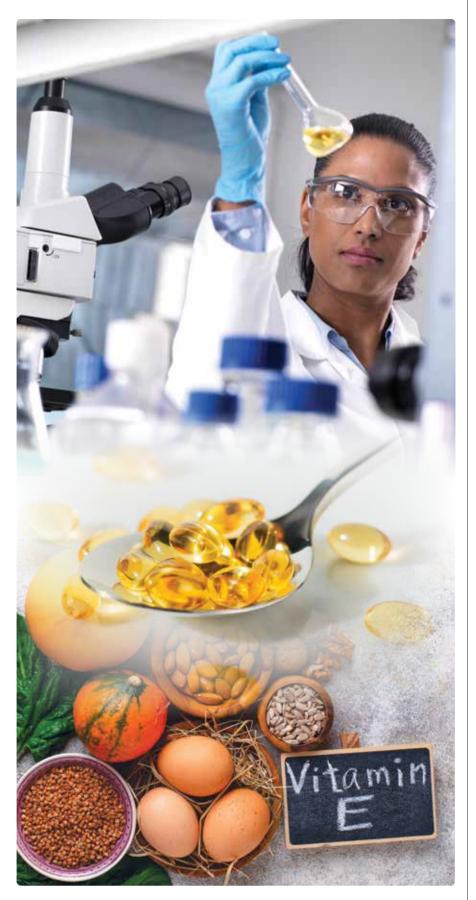
The participants who completed the trial were being treated with drugs for type II diabetes. One group received 200 mg of resveratrol daily for 24 weeks and another was given a placebo.

The resveratrol recipients had reductions in glucose and insulin, as well as reduced insulin resistance, compared to the beginning of the trial and to the placebo group.

Editor's Note: The authors concluded that, "Supplementation of resveratrol along with oral hypoglycemic agents may be useful in the reduction of diabetic-associated complications."

\* Complement Ther Med. 2022 Mar 1;66: 102819.





#### **Vitamin E Helps People with** Leukoaraiosis, a Brain Condition

A study published in the International Journal of Neuroscience found improvements in factors related to leukoaraiosis, an abnormality in the brain's white matter, among adults given supplements containing vitamin E.\*

The study included 160 men and women diagnosed with leukoaraiosis by MRI who had undergone testing for cognitive function. Participants received either 200 IU, 400 IU or 600 IU of vitamin E or a placebo daily for 12 weeks. At the end of the treatment period, blood samples were evaluated for inflammatory factors as well as for markers of oxidative stress and endothelial function.

Inflammation, oxidative stress, and endothelial function improved in all individuals in vitamin E-treated groups compared with the placebo. Cognitive function scores also significantly improved in the vitamin E-treated groups. Improvement in all measured factors was correlated with higher doses of vitamin E.

Editor's Note: "Vitamin E could be a potential drug for the clinical treatment of leukoaraiosis patients," the authors concluded.

\* Int J Neurosci. 2022 Jun 2;1-9.

#### **Branched Chain Amino Acid Supplements Raise Level** of Physical Function in **Stroke Patients**

Stroke patients who supplemented with branched chain amino acids (BCAAs) showed improvement in muscle and functional status compared to those who did not, the journal Frontiers in Neurology reported.\*

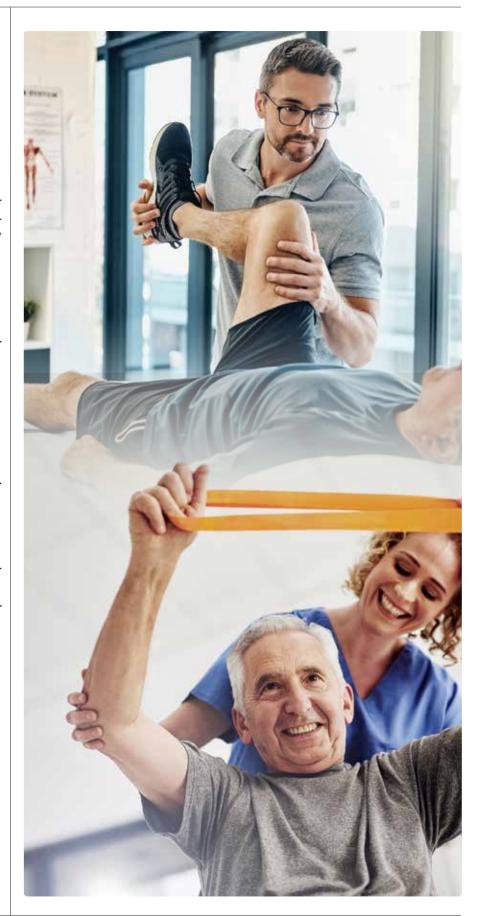
The study included 54 patients who had recently suffered a stroke and were receiving intensive therapy at a rehabilitation center. Most had muscle tissue loss. Half of the participants received a supplement that contained 6 grams of a blend of the branched chain amino acids leucine. isoleucine, and valine, twice per day for four weeks.

Among those who received BCAAs, handgrip strength and skeletal muscle mass improved after treatment, while in the control group, muscle mass decreased.

In the BCAA group, 46% of the individuals regained the ability to walk by the study's conclusion, compared to 37% in the placebo group.

Editor's Note: Both groups experienced improvement in physical function such as balance, gait, and swallowing, but the group that received BCAAs improved to a greater extent.

\* Front Neurol. 2022 Mar 11;13:744945.





#### People with *Higher* **Carotenoid Levels Have** Lower Dementia Risk

An article published in Neurology®, the medical journal of the American Academy of Neurology, reported an association between higher levels of several carotenoids and a lower risk of developing Alzheimer's disease and other dementias during an average follow-up period of 16 to 17 years.\*

Carotenoids are a family of yellow to red plant pigments, including betacarotene, which have an antioxidant effect.

Researchers examined data from 7,283 men and women who were aged 45 years and older upon enrollment in the third National Health and Nutrition Examination Surveys 1988-1994. Participants' serum levels of antioxidant vitamins A, C and E, and the carotenoids were determined from blood samples collected at the beginning of the study.

Among those aged 65 and older at enrollment, each approximate 15.4 micromols/liter increase in lutein and zeaxanthin was associated with a 7% decrease in dementia risk during follow-up. For beta-cryptoxanthin, each 8.6 micromols/liter increase was associated with a 14% reduction among those older than 45 at the beginning of the study.

Editor's Note: "Antioxidants may help protect the brain from oxidative stress, which can cause cell damage," stated study author May A. Beydoun, PhD, MPH, of the National Institutes of Health's National Institute on Aging.

\* Neurology. 2022 May 24;98(21):e2150-e2162.

#### Vitamin D Levels Linked to **Better Cognitive Function in** Parkinson's Disease

Higher levels of vitamin D are associated with better cognitive function in Parkinson's disease, according to a study published in the Journal of Clinical Neuroscience.\*

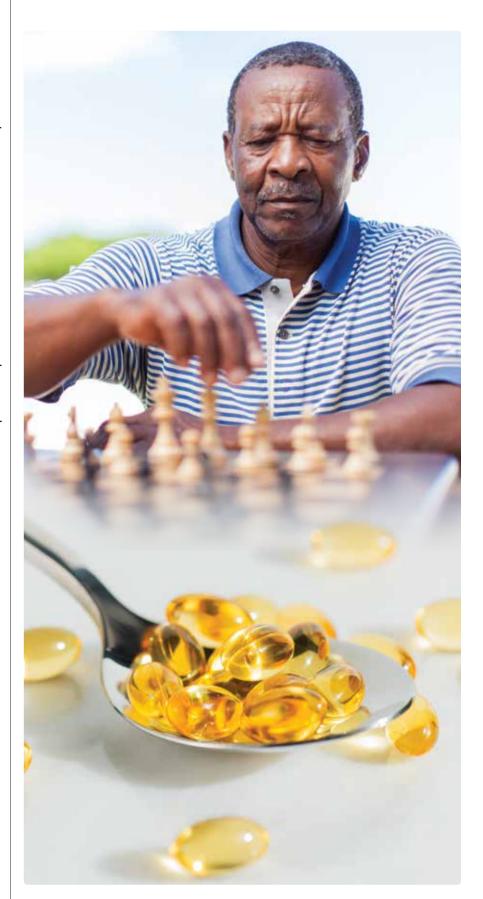
Compared to healthy controls, levels of vitamin D were significantly lower in patients with Parkinson's disease.

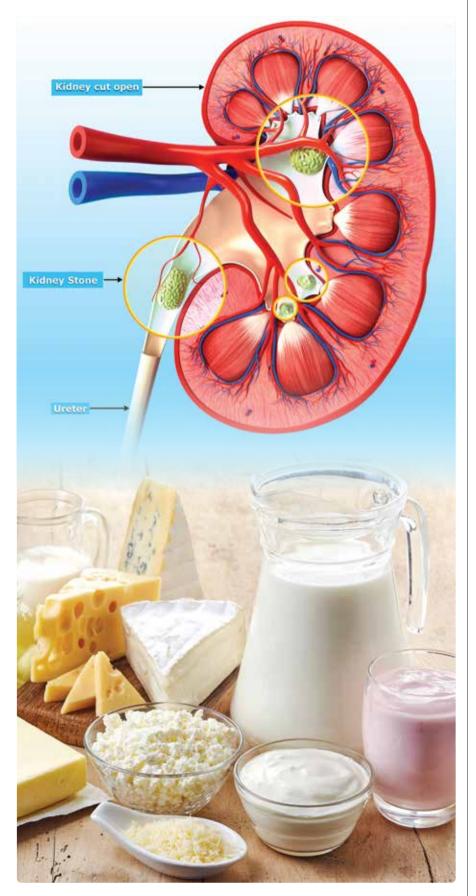
Differences were also noted in the levels of cognitive function within Parkinson's disease patients.

For example, the highest levels of vitamin D were seen in those with normal cognition. Those with Parkinson's dementia had the lowest vitamin D levels.

Editor's note: The researchers concluded that, "These findings support the relationship between cognitive impairment and vitamin D in Parkinson's disease patients."

\* Journal of Clinical Neuroscience 100 (2022) 192-195.





#### **Calcium Intake May Protect Against Kidney Stones'** Recurrence

A study reported in Mayo Clinic Proceedings revealed a lower risk of recurrent kidney stone symptoms in people who had higher dietary intake of calcium.\*

The study enrolled 411 individuals who were symptomatic kidney stone formers and 384 control patients who did not have the condition, following them for a median of 4.1 years. Responses to questionnaires about diet at the beginning of the study were analyzed for the intake of various nutrients.

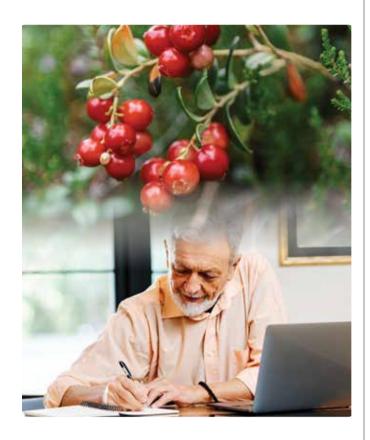
A recurrence of kidney stone symptoms was experienced by 73 of the stone formers. After adjustment for various factors, lower dietary calcium intake remained a significant predictor of recurrent symptoms.

Editor's Note: Life Extension considers an optimal calcium intake of 1,200 mg from both diet and supplements together. Many women supplement with 700 mg of calcium daily.†

† This dose assumes daily calcium dietary intake of 300-500 mg.

A man may require less supplemental calcium, but aging men need skeletalsupport nutrients, like calcium.

\* Mayo Clin Proc. 2022 Aug;97(8):1437-1448



#### **Cranberry Supplement Boosts Memory**

Frontiers in Nutrition reported the finding of a brain benefit among a group of older men and women who consumed a supplement containing powdered cranberries.\*

Sixty participants between the ages of 50 to 80 were given a supplement that contained the equivalent of one cup of fresh cranberries (providing 281 mg of proanthocyanidins) or a placebo daily for 12 weeks. Blood chemistry and cognitive function were assessed, and magnetic resonance imaging (MRI) scans of the brain were conducted before and after the treatment period.

Participants who received the supplement showed improved episodic memory performance and neural functioning compared to placebo.

Editor's Note: Additionally, researchers reported the observation that there was a decrease in low-density lipoprotein (LDL) cholesterol during the course of the study. Cranberry juice or concentrated cranberry anthocyanin capsules have long been used to prevent urinary tract infections.

\* Front Nutr. 2022 May 19;9:849902.

#### **Colorectal Cancer Risk Reduced with Higher Folate Intake**

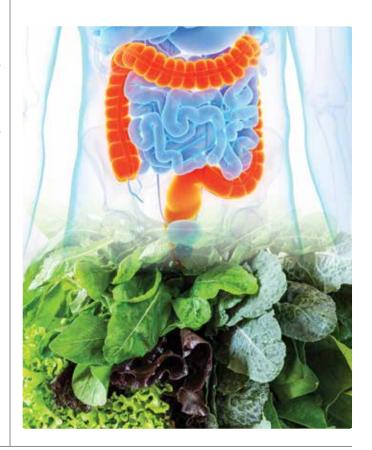
Higher intake of **folate** and its synthetic form, folic acid, is associated with a lower risk of colorectal cancer (CRC), The American Journal of Clinical Nutrition reported.\*

Based on data collected from more than 85,000 individuals who participated in the Nurses' Health Study, folate intake was assessed using dietary questionnaires, with follow-up lasting from 1980-2016.

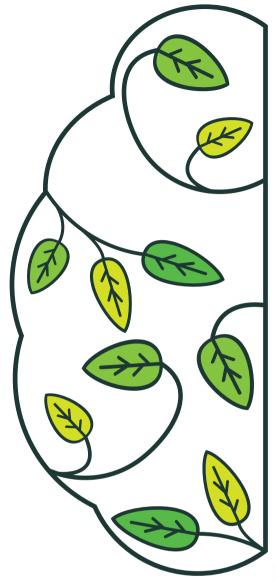
Greater folate intake 12-24 years before diagnosis was associated with a 7%-17% lower risk of colorectal cancer, and greater intake of folic acid 16-20 years before diagnosis was associated with a 9% reduced risk.

Editor's Note: "Folate intake, both total and from synthetic forms, was associated with a lower risk of overall CRC after long latency periods. There was no evidence that high folate intake in the postfortification period [the 1998 institution of mandatory folic acid fortification in the U.S.] was related to increased CRC risk in this U.S.... population," the authors concluded.

\* Am J Clin Nutr. 2021 Jul 1;114(1):49-58.



#### MANAGE STRESS





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- Support a healthy response to everyday stress
- Promote emotional well-being
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## Body & Brain

"Felt a renewed energy."

Alan

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### **NUTRIENTS** that IMPACT IMMUNITY BY MICHAEL DOWNEY Normal aging results in a progressive decline in immune function with a sharp fall occurring after age 65-70 years. Experimental studies seek to restore stem cells in bone marrow, where all immune cells originate. 1,2 The dilemma is that these stem cell renewal therapies are not yet available outside research settings. Healthy immunity at any age, however, can be supported using nutrients that function via multiple pathways. This article summarizes what many readers of this publication are doing to optimize their immune function. Garlic NOVEMBER/DECEMBER 2022 | LIFE EXTENSION | 21

#### **Garlic**

A recent review found that **garlic** compounds show strong **antibacterial** activity against a wide range of harmful bacteria, including drug-resistant strains.<sup>3</sup>

Another review reported that **garlic** offers **antimicrobial**, antifungal, anticancer, wound-healing, antioxidant, anti-inflammatory, and other protective effects.<sup>4</sup>

Compounds in garlic boost proliferation of **T cells** and function of **natural killer** cells.<sup>5-8</sup>

Garlic's **antiviral** defense was demonstrated when volunteers took **oral garlic** containing the protective garlic compound **allicin** from November through February.<sup>9</sup>

The garlic group suffered **63% fewer cold infections** than the placebo group. Those in the garlic group who *did* catch colds had symptoms for just **1.52 days** on average, compared to **5.01 days** for the placebo group.<sup>9</sup>

Although it contains no allicin, aged garlic extract has demonstrated potent **antiviral** and **immune-enhancing** properties.

In individuals taking an **aged garlic extract**, T cells and NK cells showed greater proliferation, compared to individuals taking placebo. After 90 days, the garlic group had experienced **21**% fewer cold and flu symptoms and **58**% fewer work/school days missed due to illness.<sup>5</sup>



#### Lactoferrin

Lactoferrin is a protein found in milk and produced in tears, saliva, mucus, and by some immune cells. 10 It helps *prevent* a wide range of pathogens from entering through the linings of the oral cavity, nasal cavity, airways, and digestive system. This includes viruses that cause the common cold, flu, and hepatitis B and C.10

Lactoferrin *disrupts viruses' ability to bind to cells*. 

If a virus cannot attach to cells, it cannot cause illness.

Lactoferrin's *indirect* antiviral effects include:

- Activating and increasing natural killer cells, which eliminate abnormal cells, 12,13 and
- Stimulating production of other antiviral compounds, including interferons, which trigger immune mechanisms.<sup>10,14</sup>

If viruses are already *inside* body cells, lactoferrin may block these pathogens from **reproducing**, limiting the spread of an illness and reducing its severity.<sup>10,15</sup>

Lactoferrin also enhances the immune system's ability to monitor for potential **carcinogenic** cells.<sup>12</sup>

A **2022** study concluded that, by **sequestering iron**, lactoferrin reduces the pathogenic potential of microorganisms, which *require* iron to grow and reproduce. The study concluded that lactoferrin may help maintain health at *all stages* of life.<sup>16</sup>

#### **Vitamin D**

**Vitamin D** fortifies immunity and has anti-microbial effects. 17-21

Published studies show that vitamin D:

- Interferes with some forms of viral replication,
- Helps repair cell linings, including those in the lung airways,
- Boosts production of proteins that protect against infection, and
- Helps prevent production of excess proinflammatory compounds in the lungs.

Meta-analyses of clinical trials have shown that vitamin D helps protect against **respiratory tract infections.**<sup>22,23</sup>

Low vitamin D levels have been associated with higher rates of many **chronic diseases**, including cancer.<sup>24</sup>

In **2022**, two reviews were published documenting vitamin D's capacity to enhance protection against both **infections** and **cancer.**<sup>25,26</sup>

The first review noted that studies support vitamin D's role in preventing *and* reducing the severity of several **infectious diseases**.<sup>25</sup>

It also found that *higher* blood *25-hydroxyvitamin D* levels (a measure of vitamin D levels in the body) may benefit some **autoimmune rheumatic diseases.**<sup>25</sup>

The second review found that vitamin D provides *multi-level anti-cancer action* and protects against several **cancer** types.<sup>26</sup>

#### **Zinc**

**Zinc deficiency**, which is common among the elderly,<sup>27</sup> may compromise immune function and contribute to atherosclerosis, **cancer**, autoimmune diseases, and other age-related conditions.<sup>28,29</sup>

Aging adults who *replenish* zinc levels may slow normal immune decline and protect against **chronic inflammation**.<sup>30</sup>

Oral zinc intake in the elderly boosts the stress response of **white blood cells**, providing an immune anti-aging mechanism.<sup>31</sup>

A **2022** review study found that zinc's **anti-viral** properties can *disrupt* the **replication** and **infectivity** of some respiratory viruses and help regulate immune response in the respiratory tract.<sup>32</sup>

#### **Mushrooms**

A **2022** review article concluded that medicinal **mushrooms** possess anticancer, anti-aging, antiviral, anti-parasitic, antimicrobial, and other beneficial properties.<sup>33</sup>

Another recent review concluded that mushrooms' ability to inhibit **tumor** cells makes them a "**natural pharmaceutical**."<sup>34</sup>

Among the most powerful of mushrooms' immunesupporting compounds are **beta glucans**.

They bind to receptors on cells important for **immunity**, 35,36 boosting their function and helping defend against infection. Beta glucans activate *both* the **innate** (the immediate, general defense) and **adaptive** (a later defense against specific threats) immune responses. 35,37-40



## Support Immunity as You Age

- The immune system weakens with age, increasing risk of infectious disease, cancer, and other life-shortening illnesses.
- Oral intake of vitamin D, zinc, lactoferrin, mushrooms, garlic, melatonin, and vitamin C has been shown to enhance immune function.
- Daily use of these nutrients may help fight disease and maintain health well into old age.



Preclinical studies show that melatonin improves immune response to infection by viruses, bacteria, and parasites by stimulating production and activity of **T cells**, **natural killer** cells, and **macrophages** that engulf and destroy invaders.<sup>54</sup>

**Melatonin** has also been found to support the immune system's protection against **cancer**, inhibiting it at **every stage**. 62-66

A recent review study concluded that melatonin was a potential *oncostatic*, an agent that blocks cancer spread.<sup>67</sup> Another **2022** report found that **melatonin** could mitigate cancer's development, growth, *and* spread.<sup>68</sup>

In animal models of aging, **beta glucans** help prevent or *reverse* **immunosenescence**.<sup>39,41</sup>

They boost immune cell numbers and improve their function.<sup>41</sup>

In **humans**, beta glucans demonstrate **infection-fighting** effects, particularly against upper respiratory tract infections like cold and flu.<sup>42</sup>

Ragweed **allergy** sufferers also had significant reductions in symptoms and severity after **beta glucans** intake.<sup>43</sup>

Four mushroom strains that support the immune system are **shiitake**, **maitake**, **reishi**, and **chaga**.<sup>38,44-52</sup>

Combining **beta glucans** with immune-supporting **mushrooms** may maximize immune support.

#### Melatonin

With aging, the **thymus gland**—which produces **T cells**—shrinks, diminishing immune function.

But in aged mice, the hormone **melatonin** stimulates *new* thymus growth, producing *new T cells*.<sup>53</sup>

Melatonin also counters immune decline by: 54-61

- Enhancing responses of antibodies that "tag" viruses, bacteria, and other invaders for destruction by immune system components,
- · Improving T cell activity, and
- Reducing chronic inflammation, a cause of most age-related, chronic disease.

#### **Vitamin C**

The activity of **phagocytes** (cells that surround and kill invaders), **T cells**, and many other immune cells is closely tied to their **vitamin C** content.<sup>69</sup>

So, it makes sense that **immune functions** are improved by taking **vitamin C**.<sup>70,71</sup>

A clinical trial showed that oral vitamin C reduced duration of **colds** by **9.4**% on average and may decrease the severity of **respiratory tract infections**. <sup>72</sup> (Not all studies show vitamin C to be effective against the common cold.)

Researchers have found that vitamin C:

- Boosts function, growth, and survival of infection-fighting cells,<sup>73,74</sup>
- Increases levels of immune-activating interferons, 75,76
- Neutralizes excess free radicals caused by infections, reducing illness severity,<sup>77</sup>
- Promotes production of collagen, which maintains a barrier against infection, <sup>76</sup>
- Reduces histamine, a pro-inflammatory compound<sup>76</sup> that plays a role in infections<sup>78</sup> and causes allergy symptoms,<sup>79</sup> and
- Lowers pro-inflammatory compounds caused by infection, promoting tissue healing.<sup>80</sup>

Optimal immunity requires **daily** intake of vitamin C and other immune-supporting nutrients.



#### **Summary**

Age-related immune system dysfunction increases risk of infectious disease, cancer, and chronic inflammatory conditions.

Oral intake of the key immune-supporting nutrients vitamin D, zinc, lactoferrin, mushrooms, garlic, melatonin, and vitamin C can enhance immune function and partially offset age-related immune decline.

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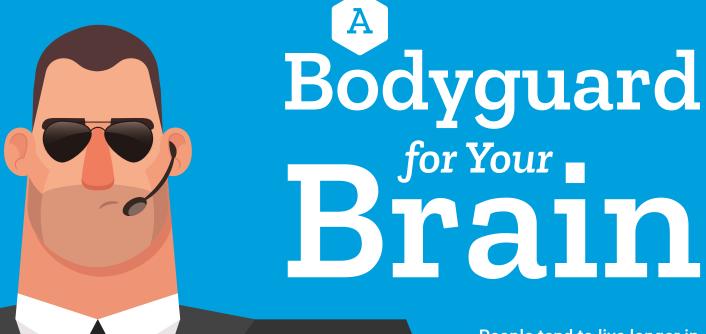
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## FULL-STRENGTH ECHINACEA

BY MICHAEL DOWNEY

Echinacea is an immune enhancing plant.

Clinical studies have shown that compared to placebo, **echinacea** use can lead to an improvement in cold symptoms, **fewer** days with severe symptoms, and **reduction** in cold incidence and severity.<sup>1-3</sup>

But not all echinacea is the same.

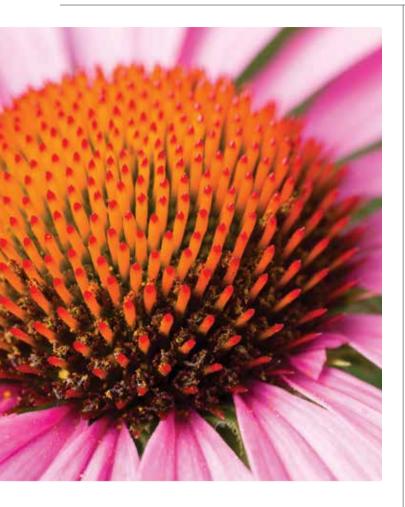
Different active components are found in different **species** of echinacea *and* in different **parts** of the plant.

Many echinacea supplements contain only <u>one</u> **species**, with **80**% of products relying solely on *Echinacea purpurea*.

Not all contain *standardized* ingredients. This results in inconsistent potency.<sup>4</sup>

To maximize echinacea's full immune supportive potential, look for supplements containing *extracts* from various parts of the plant, as well as more than one *plant species*.

This can deliver echinacea's spectrum of immune-boosting benefits.



#### What is Echinacea?

**Echinacea** is a plant native to central and eastern North America. It was used as folk medicine by Native Americans to **reduce cold symptoms** and treat coughs, sore throat, and headaches.

When explorers **Lewis** and **Clark** learned about the uses of this medicinal plant in **1805**, they considered it one of their most important finds, mailing its seeds and roots back to President Thomas Jefferson.<sup>5</sup>

Today, echinacea extracts are used to boost **immune function** and treat flu, colds, and other **upper respiratory tract infections**. It is also an anti-inflammatory.

Echinacea's effects derive from its bioactive compounds, including **phenolics**, **polysaccharides**, **alkamides**, **caffeic acid** derivatives, and others.

These active components are found in <u>different</u> parts of the plant (the roots, flowers, leaves, and others) and in <u>different</u> echinacea species. Research suggests that the clinical effects are likely due to these multiple bioactive compounds which may have a synergistic effect.<sup>6,7</sup>

#### **How Echinacea Works**

The compounds in **echinacea** work in different ways to enhance **immune function** and deliver other benefits. For example:<sup>7</sup>

- Phenolic compounds provide antiviral, antitumor, and antioxidant activity.
- Polysaccharides provide immunomodulating and anti-inflammatory effects. They stimulate macrophages (immune cells that destroy harmful microorganisms), which in turn secrete signaling proteins that enhance virus-killing natural killer (NK) cells.
- Alkamides provide immunomodulating, anti-inflammatory, and antifungal effects, and protect NK cells against compounds that can inhibit their activity.

#### **Boosting Immunity**

Preclinical studies support echinacea's use for **immune** support:

- One study found that echinacea produced a two-fold increase in natural killer cell activity in a type of human immune cell known as peripheral blood mononuclear cells (PBMCs).8
- In another study on human PBMCs, compared to baseline, echinacea resulted in a reduction in pro-inflammatory compounds of up to 24% and a 13% increase in interleukin 10 (IL-10), an anti-inflammatory factor.9
- A study on aging mice showed that echinacea increased NK cell numbers by 30% and activity by 20%.<sup>10</sup>
- Studies on mice found that echinacea boosted NK cell activity<sup>11</sup> and that lifelong echinacea use significantly increased lifespan.<sup>12</sup>
- A systemic review of preclinical and clinical studies found that echinacea may decrease pro-inflammatory cytokines and increase levels of anti-inflammatory cytokines.<sup>13</sup>

This immune support explains how echinacea may defend against illnesses like the common **cold** and **flu**.

#### Fighting Upper **Respiratory Tract Infections**

To evaluate the ability of **echinacea** to help prevent upper respiratory tract infections, researchers conducted a meta-analysis of 24 controlled trials. involving a total of 4,631 participants.6

These clinical trials had used various echinacea preparations from different species, with dosages ranging anywhere from 40 mg to 4,000 mg per day.

The meta-analysis found that echinacea use was associated with an absolute reduction of 10% in the risk of contracting a cold, compared to placebo.6

When the clinical trials included in the study are examined individually, the effects of echinacea on the common cold are more dramatic.

These individual studies document an array of improvements with echinacea use compared to placebo, including:6

- 58.7% improvement in symptoms compared to 33.6% with placebo,1
- 33.3% fewer days with severe symptoms,<sup>2</sup>
- 36% relative reduction in cold incidence and severity following travel,3 and
- 3.4 days duration of upper respiratory tract infection, versus 8.6 days with placebo.14

These human studies used different echinacea species and different echinacea plant parts, and each trial demonstrated a different type or level of protection against upper respiratory tract infections.

This suggests that using *more than one echinacea* species and multiple parts of the plant is the best way to maximize echinacea defense.

#### Getting the Most from Echinacea

- The immune supportive effects of echinacea help it defend against upper respiratory tract infections. Clinical studies have shown that compared to placebo, echinacea use can lead to an improvement in cold symptoms, fewer days with severe symptoms, and reduction in cold incidence and severity.
- Different active components are found in different species of echinacea and in different parts of the plant. Many echinacea products contain only one species and one plant part.



#### **Summary**

Echinacea delivers immune support and varying degrees of protection against colds, flu, and other upper respiratory tract infections.

Different bioactive compounds behind this immune support are found in different echinacea species and different parts of the plant.

Many echinacea supplements contain only one species and provide only one part of the plant. This diminishes the wide range of biologically active components and their immune-supporting effects.

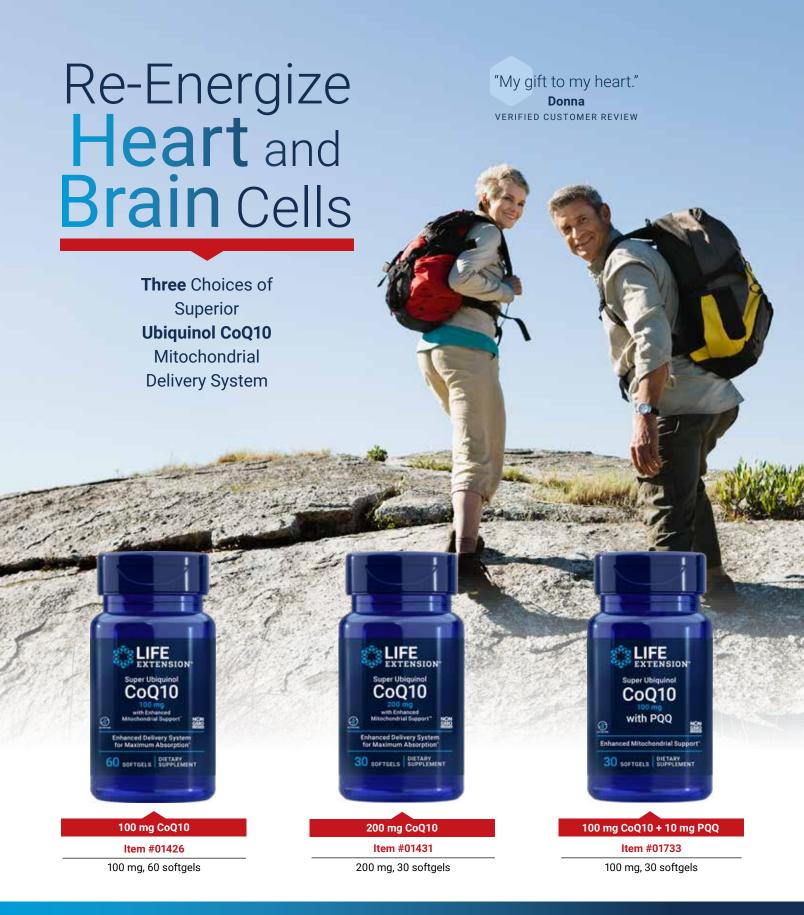
The best way to obtain echinacea's full immune support and anti-viral power is by taking extracts from various parts of the plant, as well as more than one plant species. •

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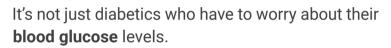






# Manage After-Meal Blood Sugar Spikes

BY JASON GREEN



According to the *National Diabetes Statistics Report*, an estimated **38**% of Americans aged 18 years or older have **blood glucose** levels that are *higher than normal* but not high enough to meet the threshold for **type II diabetes**.<sup>1</sup>

Our longstanding position is that anyone with lessthan-optimal glucose, insulin and hemoglobin A1c (HbA1c) should aggressively intervene to optimize these glycemic markers.

Scientists have identified two **plant extracts** that can help maintain normal blood sugar levels, particularly **after meals** when spikes typically occur.

In human trials, a **clove extract** and a **maqui berry extract**<sup>2-5</sup> each helped prevent harmful after-meal leaps in blood sugar.

These extracts can aid in maintaining healthy aftermeal blood glucose levels.



#### The Danger of Elevated Blood Sugar

More than 48% of all U.S. adults aged 65 and over have prediabetes. About 25% have a formal diagnosis of type II diabetes.1

Those with prediabetes may have normal resting levels of glucose, but their levels can get out of control after a meal. These cases often go unnoticed because they're not apparent on standard fasting blood tests.

That's a huge problem. After-meal elevated glucose levels alone are associated with higher rates of cardiovascular disease, impaired cognitive function, and death.6-14 Almost a third of those with prediabetes could go on to develop diabetes within five years if no corrective actions are taken.15

#### **Benefits of Plant Extracts**

Higher intake of polyphenols, health-promoting compounds found in plants, is associated with protection from disease. Low polyphenol intake is associated with increased risk of chronic disease, including type II diabetes.4

Two specific polyphenol-rich plant extracts have been found to have beneficial effects on the control of glucose levels, particularly following a meal: maqui berry extract and clove extract.

#### **Maqui Berry Extract**

Magui berry is a fruit native to South America. Extracts of these berries are high in polyphenols known as delphinidins.16

These nutrients have been shown to lower aftermeal glucose levels. They do this by stimulating a peptide produced in the intestines that improves glucose metabolism. 16,17

A study published in 2022 in the medical journal Frontiers in Nutrition found that a single dose of maqui berry extract before intake of sugars was associated with a decreased risk of high blood glucose levels in people with prediabetes.5

Patients showed reductions of the risk of dysglycemia (abnormal blood sugar levels) at the different doses tested, with the greatest impact seen with the highest dose of 180 mg.

In another human study, 200 mg of magui berry extract taken before a meal helped lower after-meal glucose by more than 15% while also reducing aftermeal insulin levels.3 (Excess secretion of insulin is associated with insulin resistance and future diabetic risks.)

Another study of subjects with a new diagnosis of prediabetes<sup>2</sup> found that **180 mg** of magui berry extract significantly reduced levels of HbA1c (hemoglobin A1c) over 90 days.





#### After-Meal Glucose Control

- Elevations of blood sugar following a meal are associated with poor health outcomes.
- Scientists have found that polyphenolrich clove and maqui berry extracts help control blood glucose, reducing aftermeal spikes.
- In human studies, maqui berry extract reduced high glucose levels after meals in those with prediabetes.
- A clove extract lowered after-meal glucose levels in subjects with prediabetes and healthy adults with normal fasting glucose levels. It also reduced fasting glucose in prediabetics.

HbA1c is a commonly used blood marker of **long-term** blood glucose control. *Lower* levels indicate *better* long-term glucose control and *less risk* of diseases related to elevated glucose levels.

Overall, these studies suggest that an early intervention with maqui berry extract might help prevent prediabetes from progressing into full-blown **diabetes**.

#### **Clove Extract**

**Cloves** are dried flower buds of the *Syzygium aromaticum* tree. They have been widely used as a spice for centuries.

A **clove extract** has been produced that is standardized to at least **30% total polyphenols**, a powerful mixture of bioactive compounds. 18-20



The most compelling evidence of **blood sugar control** using **clove extract** was seen in a clinical trial published in **2019**.<sup>4</sup> This pilot study enrolled healthy young adults with **normal** fasting glucose levels *and* prediabetics with **elevated** fasting glucose.

All subjects were given **250 mg** of **clove extract** daily, following a meal, for 30 days. On various days during this month, subjects had their blood glucose levels tested before and after a meal.

The extract led to improvements in **both groups** as follows:

- Reduced after-meal blood glucose levels by 22% in those with normal fasting glucose, and
- <u>Reduced</u> after-meal blood glucose levels by 27% in prediabetics with *elevated* fasting glucose.

In the group with **prediabetes**, the clove extract also helped maintain healthy levels of glucose throughout the day. That means their **fasting glucose levels** were also significantly reduced.

Cell culture experiments reveal three ways that clove extract<sup>4</sup> helps maintain normal blood glucose and prevent after-meal spikes:

- It enhances uptake of glucose into muscle cells by 63%.
- It inhibits excess production of glucose by liver cells, and
- It reduces the activity of two digestive enzymes that break down more complex sugars such as starch, preventing a spike in glucose.

Taking clove and magui berry extracts together may reduce after-meal glucose spikes and help with overall glucose control.

#### Summary

Typical aging people have higher than ideal levels of glucose, insulin, and A1C.

Clove extract and maqui berry extract have been shown to reduce after-meal blood glucose levels in individuals with prediabetes.

Even in adults with normal fasting glucose, clove extract reduces after-meal glucose levels. •



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# The Problem with Sleep-Aid Drugs

#### BY BARRY MICHAELS

More than **30 million** adults in the U.S. rely on **Xanax**<sup>®</sup>, **Valium**<sup>®</sup>, **Ativan**<sup>®</sup>, or other prescription **benzodiazepine** drugs to cope with sleep disorders.<sup>1-3</sup>

These drugs come with side effects, and long-term use can lead to addiction.

Benzodiazepines cause another issue. Their use is associated with <u>reduced</u> **melatonin** levels.<sup>4-6</sup>

In one study, a *single* dose of a benzodiazepine derivative (which is metabolized into active benzodiazepines) before bedtime significantly *suppressed the production of melatonin*.<sup>4</sup>

Melatonin helps regulate our **sleep cycles**. This means that benzodiazepines *interfere* with the body's natural ability to initiate healthy sleep.

Clinical trials show that melatonin intake can **improve sleep** quality in many people and appears to help reduce dependence on benzodiazepine **drugs**.

#### **Dangers of Benzodiazepines**

More than 50 million U.S. adults suffer from a sleep disorder like insomnia or sleep apnea.7,8

Poor sleep has been linked with health problems, including type II diabetes, obesity, and injuries. In the elderly, sleep problems are associated with increased risk of falls, frailty, and death.9-14

Many people turn to benzodiazepine drugs for help. 15 These drugs enhance sleep onset, reduce the number of times waking at night, and improve total sleep time and sleep quality with **short-term** use. 16 Too often, these drugs are taken longer than needed, increasing their addictive potential.

Well-known downsides to regular benzodiazepine use:17-19

- They are heavily sedating, impairing the ability to think clearly and increasing risk for accidents.
- They can lead to **tolerance**, which means users need to take higher and higher doses to get the same effect.
- They can lead to **dependence** or **addiction**.
- They come with common side effects including dizziness, weakness, depression, and confusion.



What's less well-known is that benzodiazepines **interfere** with how the **brain** naturally promotes healthy sleep.

#### **Benzodiazepines Deplete Melatonin**

Melatonin is a hormone secreted by the brain's pineal gland. Often called the "sleep hormone," it is central to regulating the body's natural sleep-wake cvcle.20

Benzodiazepines interfere with the body's natural melatonin production.4

As early as 1986, scientists found that even a single dose of a benzodiazepine derivative (which is metabolized into active benzodiazepines) before bedtime significantly suppresses the production of melatonin.4 When scientists administered a drug that blocked the action of benzodiazepines, melatonin was restored to normal levels.

Larger studies have confirmed this finding. For example, after a single nighttime dose of alprazolam (Xanax®), peak levels of melatonin in the bloodstream are roughly half what they would be normally.5,6

By trying to improve sleep quality with benzodiazepines, people are impeding their body's natural ability to regulate sleep.

#### **How Oral Melatonin Improves Sleep**

A meta-analysis of **19** studies found that melatonin improves sleep in multiple ways, including:21

- Reducing the time it takes to fall asleep,
- Improving sleep quality, and
- Extending the *duration* of sleep.

Melatonin promotes relaxation and sleep, without side effects or the risk of dependence associated with benzodiazepines.

For example, an observational study of patients undergoing kidney dialysis—which is often associated with sleep disturbances-found that taking 3 mg of **melatonin** before bedtime was *more effective* than Xanax® in improving sleep quality as shown in multiple subjective sleep assessment scales.<sup>22</sup>

Regrettably, not all sleep-deprived sufferers find complete relief using melatonin alone.

#### **Reduce Dependence** on Drugs

Melatonin is safer than benzodiazepines and has side benefits that include potential to reduce risks of certain cancers.23

It is not addictive or sedating, and melatonin supports the brain's natural ability to promote sleep instead of interfering with it.

In elderly insomniacs who use benzodiazepines to be able to sleep, adding melatonin significantly improved sleep quality and time.<sup>24</sup> In a follow-up study, scientists evaluated whether taking melatonin could help people stop using benzodiazepines.25

They randomized elderly insomniacs on benzodiazepines to receive either 2 mg of controlled-release melatonin before bed or a placebo. During the six weeks of the study, participants were encouraged to try to wean themselves off benzodiazepines.

By the end of the study, 79% of those taking melatonin were able to completely discontinue benzodiazepine use. In the placebo group, only 25% were able to stop using benzodiazepines.

Life Extension advises not to discontinue any medication without prior approval from your treating physician.

#### **Summary**

The use of benzodiazepines to promote sleep comes with potential side effects and may lead to dependence.

Clinical trials show that melatonin improves sleep quality, helps people fall asleep faster, helps them stay asleep longer, and can help benzodiazepine users discontinue their use of these drugs.

The dilemma is that melatonin does not work for everyone and better methods to improve sleep quality, especially in older individuals, is urgently needed.

Please consult with your treating physician before discontinuing use of any medication. •



#### Melatonin Compared to Prescription Sleep Medications

- Many people turn to benzodiazepine drugs to help promote sleep. But benzodiazepines cause sedation and are often addictive.
- Research has revealed that even a single dose of a benzodiazepine significantly lowers levels of melatonin, the sleep hormone that is integral to sleep control in the body.
- Trials show that **oral melatonin** promotes sleep without side effects or the risk for dependence associated with benzodiazepines.



#### Common Benzodiazepines

The benzodiazepines, often referred to as "benzos," are a group of drugs that induce sedation and sleep.

Below is a list of the most commonly used benzodiazepines:<sup>26</sup>

Alprazolam (Xanax®)

Diazepam (Valium®)

Lorazepam (Ativan®)

Clonazepam (Klonopin®)

Chlordiazepoxide (Librium®)

Temazepam (Restoril®)

Clorazepate (Tranxene®)

Halazepam (Paxipam®)

Estazolam (ProSom®)

Flurazepam (Dalmane®)

Triazolam (Halcion®)

Oxazepam (Serax®)

Prazepam (Centrax®)

Quazepam (Doral®)

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### **Bloated?** Get Relief

BY LAURIE MATHENA

Sometimes, the foods you love don't love you back.

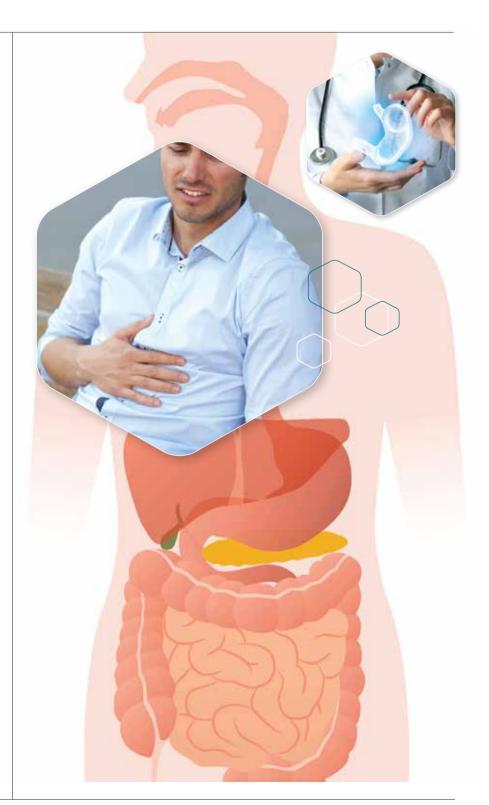
Between 16% to 31% of adults complain of **bloating**, which produces uncomfortable feelings of excessive fullness, gas, abdominal pressure, and pain. A whopping 66% to 90% of those with irritable bowel syndrome (IBS) suffer from the same symptoms.<sup>1</sup>

Bloating also often goes hand-inhand with other gastrointestinal disorders, such as **dyspepsia** (indigestion), celiac disease, and constipation.<sup>1</sup>

Fortunately, **four plant compounds** have been shown to provide effective relief from occasional digestive discomfort.

#### **Decreased Bloating**

Fennel and curcumin have traditionally been used to aid digestion. In a clinical trial, researchers combined fennel seed oil and low-dose curcumin to test their effect in patients with irritable bowel syndrome.<sup>2</sup>



After 30 days, those taking the **fennel-curcumin** blend reported an average 50% decrease in a rating score of bloating, abdominal pain, and other irritable bowel syndrome symptoms. This was nearly double the 26.1% decrease in the placebo group.

Even better, all symptoms were improved by treatment with fennel and curcumin, and 25.9% of the fennel-curcumin group became com*pletely symptom-free* (compared to just **6.8%** of placebo recipients).

The treated group also reported a significant improvement in irritable bowel syndrome-related quality of life, with no adverse effects.

#### **Improved Digestive Symptoms**

Two additional extracts, artichoke and ginger, have been shown to substantially improve digestive symptoms like bloating, nausea, vomiting, upper abdominal pain, and feeling overly full after eating only a small amount of food.

In a clinical trial, 126 patients with functional dyspepsia (recurring and unexplained indigestion) received either 20 mg of ginger root extract and 100 mg of artichoke leaf extract or a placebo.3

In just two weeks, 44.6% of participants taking the artichoke-ginger blend had significant improvement in digestive symptoms, compared to 13.1% of placebo recipients.

After four weeks, 63.1% of those in the treatment group reported marked reductions in digestive symptoms, compared to only 24.6% in the placebo group.

#### Summary

After-meal bloating and other gastrointestinal disturbances can impair our quality of life.

Ginger, artichoke leaf, fennel, and curcumin have shown clinical effectiveness in decreasing bloating, gas, nausea, abdominal pain, and other symptoms typical of irritable bowel syndrome as well as other gastrointestinal problems.

Together, extracts from these four plants may promote a healthier digestive system. •

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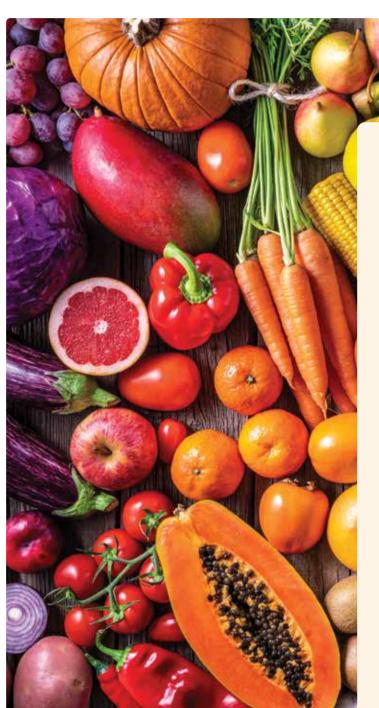
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#### Cook for Your Gut Health:

Quiet Your Gut, Boost Fiber, and Reduce Inflammation



Gut health is vital to your overall health and longevity. Beyond influencing your digestive system, it plays a role in immunity, emotions, and in how well you absorb nutrients from food.

The cookbook. Cook for Your Gut Health, from America's Test Kitchen, provides recipes designed to encourage a healthy microbiome.

These recipes are packed with fiber to help keep you regular, provide prebiotics that help feed the good bacteria in your gut, and help prevent chronic inflammation in your GI tract.

All the recipes can be adjusted to be gluten-free, lactose-free, or wheat-free. And 60 of the recipes in Cook for Your Gut Health are naturally low FODMAP. while others can be easily customized to be low FODMAP.

FODMAPs are fermentable carbohydrates that are notorious for triggering digestive symptoms like pain, gas, and bloating. A low-FODMAP diet is recommended for anyone suffering from irritable bowel syndrome (IBS) and other digestive disorders.

In addition to its gut-friendly recipes, Cook for Your Gut Health provides an in-depth education on the science of gut health, how to eat to support a healthy gut, and information on the low-FODMAP diet.

The following recipes from the book prove that you don't have to sacrifice flavor or variety to support a healthy gut.

-LAURIE MATHENA

#### Pea and Feta Frittata

#### **SERVES 4**

12 large eggs

<sup>1</sup>/<sub>3</sub> cup whole milk

- ½ teaspoon plus pinch table salt, divided
- 2 ounces feta cheese, crumbled into ½-inch pieces (½ cup)
- 2 tablespoons minced fresh oregano
- 2 tablespoons extra-virgin olive oil, divided
- 2 cups frozen peas

Pinch red pepper flakes (optional)

- ½ teaspoon grated lemon zest plus 2½ teaspoons juice, divided
- 6 ounces (6 cups) baby arugula
- 1 fennel bulb, stalks discarded, bulb halved, cored, and sliced thin
- 1. Adjust oven rack to middle position and heat oven to 350 degrees. Whisk eggs, milk, and ½ teaspoon salt in bowl until well combined. Stir in feta and oregano.
- 2. Heat 1 teaspoon oil in 12-inch ovensafe nonstick skillet over medium-high heat until shimmering. Add peas, pepper flakes, and ½ cup water. Cover and cook until peas are bright green and just tender, 3 to 5 minutes. Uncover, stir in lemon zest and ½ teaspoon juice and cook until skillet is dry, about 1 minute.
- 3. Add egg mixture and cook, using rubber spatula to stir and scrape bottom of skillet until large curds form and spatula leaves trail through eggs but eggs are still very wet,



about 30 seconds. Smooth curds into even layer and cook, without stirring, for 30 seconds. Transfer skillet to oven and bake until frittata is slightly puffy and surface bounces back when lightly pressed, 6 to 9 minutes.

4. Using rubber spatula, loosen frittata from skillet and transfer to cutting board. Let sit for 5 minutes. Meanwhile, whisk remaining 5 teaspoons oil, remaining 2 teaspoons lemon juice, and remaining pinch salt together in large bowl.

Add arugula and fennel and toss to coat. Season with salt and pepper to taste. Serve.

Make it Low FODMAP Substitute dairy-free or lactose-free milk for whole milk. Substitute 2 cups frozen broccoli florets, thawed and chopped, for peas. Increase arugula to 8 ounces and reduce fennel to ½ bulb.

Make it Dairy Free Substitute dairyfree milk for the whole milk. Omit feta.

#### Salmon, Avocado, Orange, and Watercress Salad

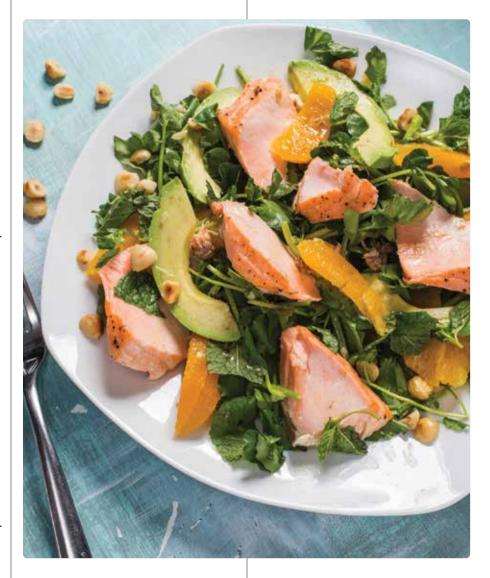
#### **SERVES 4**

- 2 (6- to 8-ounce) skin-on salmon fillets, 1 inch thick
- 3 tablespoons plus 1 teaspoon extra-virgin olive oil, divided
- 34 teaspoon table salt, divided
- I teaspoon pepper
- 3 oranges
- 1 teaspoon white wine vinegar
- 1 teaspoon Dijon mustard
- 4 ounces (4 cups) watercress, torn into bite-size pieces
- 1 avocado, halved, pitted, and sliced thin
- ¼ cup fresh mint leaves, torn
- 1/4 cup hazelnuts, toasted and chopped
- 1. Adjust oven rack to lowest position, place aluminum foil-lined rimmed baking sheet on rack, and heat oven to 500 degrees. Make 4 or 5 shallow slashes, about 1 inch apart, on skin side of each fillet, being careful not to cut into flesh. Pat salmon dry with paper towels, rub with 1 teaspoon oil, and sprinkle with 1/4 teaspoon salt and pepper.
- 2. Reduce oven temperature to 275 degrees and remove sheet from oven. Carefully place salmon skin side down on hot sheet. Roast until center is still translucent when checked with tip of paring knife and registers 125 degrees (for mediumrare), 8 to 12 minutes. Transfer

- salmon to plate. Let cool completely, about 20 minutes. Using 2 forks, flake salmon into rough 2-inch pieces; discard skin.
- 3. Meanwhile, cut away peel and pith from oranges. Holding fruit over bowl, use paring knife to slice between membranes to release segments. Measure out 2 tablespoons orange juice and transfer to separate bowl.
- 4. Add vinegar, mustard, remaining 3 tablespoons oil, and remaining ½ teaspoon salt to bowl with orange juice and whisk until smooth.

Arrange watercress in even layer on serving platter. Top with salmon pieces, orange segments, and avocado. Drizzle vinaigrette over top, then sprinkle with mint and hazelnuts. Serve.

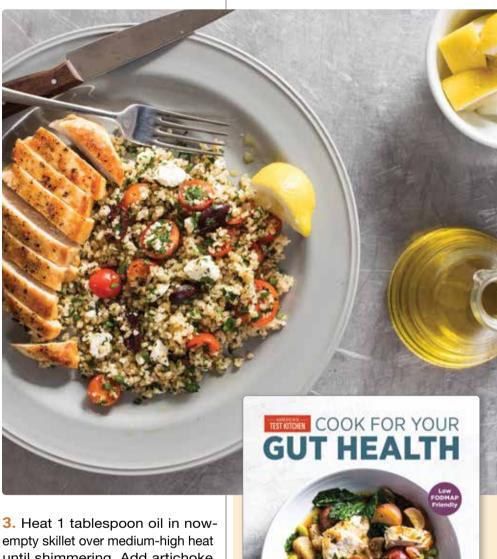
Make it Low FODMAP Reduce avocado to ½ avocado (4 ounces).



#### Pan-Seared Chicken Breasts with Artichoke, Tomato, and Bulgur Pilaf

#### SFRVFS 4

- ½ teaspoon ground cumin
- ¼ teaspoon plus ⅓ teaspoon table salt, divided
- Iteaspoon pepper
- 4 (6-ounce) boneless, skinless chicken breasts, trimmed
- ¼ cup extra-virgin olive oil, divided
- 1½ cups jarred whole baby artichokes packed in water, rinsed, patted dry, and quartered
- 21/4 cups water
- 11/2 cups medium-grind bulgur
- 10 ounces cherry tomatoes, halved
- 3 ounces feta cheese, crumbled (¾ cup)
- 34 cup minced fresh parsley
- 1/3 cup pitted kalamata olives, chopped
- 1 tablespoon lemon juice
- 1. Combine cumin, ½ teaspoon salt, and pepper in bowl. Cover chicken breasts with plastic wrap and pound to uniform thickness as needed. Pat dry with paper towels and sprinkle with cumin mixture.
- 2. Heat 1 tablespoon oil in 12-inch skillet over medium-high heat until just smoking. Cook breasts, turning as needed, until golden brown and register 160 degrees, about 10 minutes. Transfer breasts to plate, tent with aluminum foil, and let rest while preparing pilaf.



empty skillet over medium-high heat until shimmering. Add artichoke hearts and cook, without stirring, until spotty brown, about 2 minutes. Stir in water, scraping up any browned bits, and bring to boil. Stir in bulgur and remaining ½ teaspoon salt. Off heat, cover and let sit until grains are softened and liquid is fully absorbed, about 5 minutes.

**4.** Add tomatoes, feta, parsley, olives, lemon juice, and remaining 2 tablespoons oil to pilaf and gently fluff with fork to combine. Season with pepper to taste. Serve chicken with pilaf.

Make It Dairy Free Omit feta.

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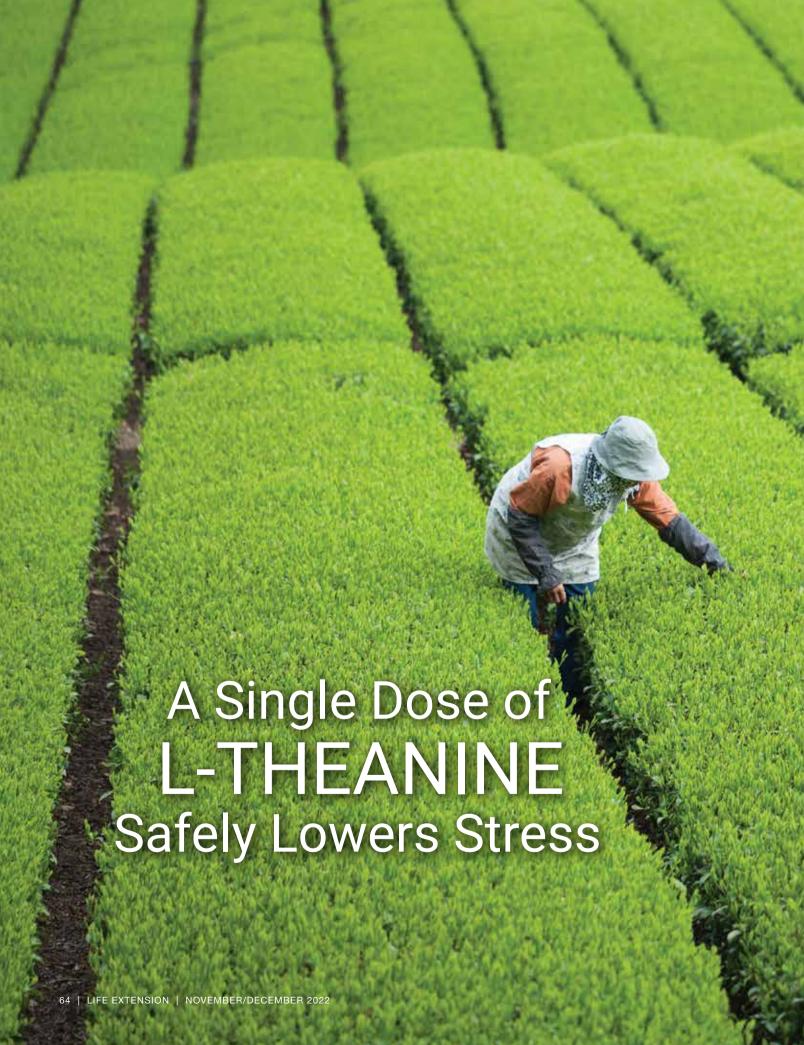
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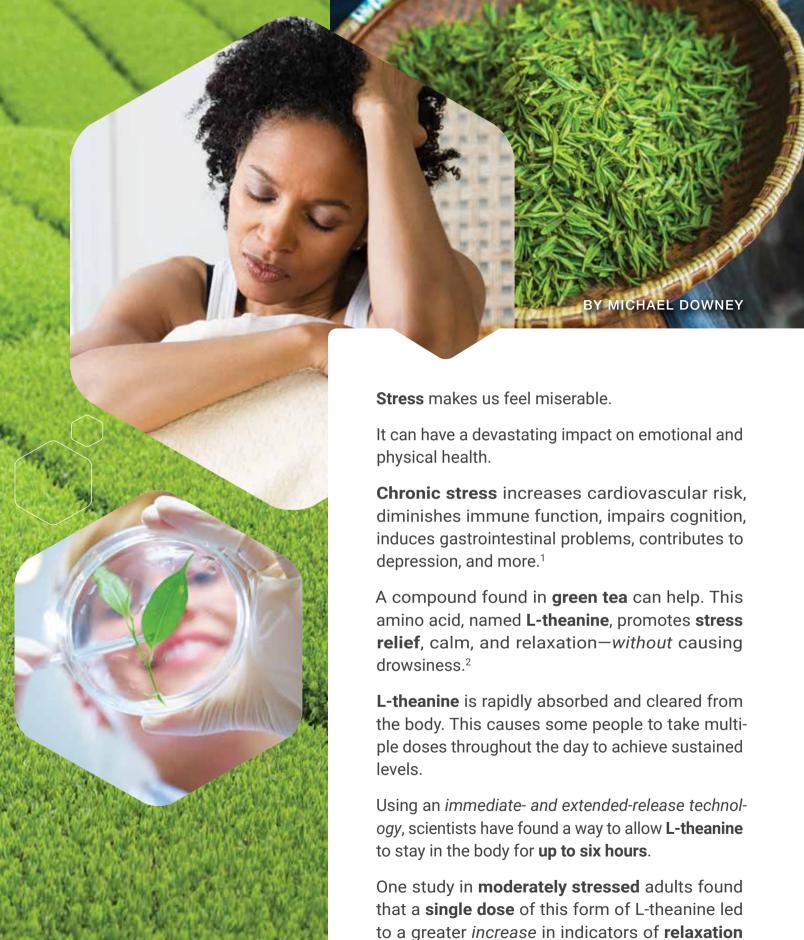


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compared to placebo.3

#### **Deadly Effects of Chronic Stress**

Repeated or unrelenting stress leads to a higher risk for cardiovascular disease, diminished immune function, and damaging inflammation.<sup>1,4</sup>

One of the most widely recognized health effects of chronic stress is an increased risk of heart disease.

Chronic stress has been shown to impair cardiac<sup>5</sup> function and can cause high blood pressure, arrhythmia, and vascular inflammation leading to atherosclerosis and stroke.6

Most anti-stress or anti-anxiety drugs cause sedation and other side effects and can be addictive.7 So, scientists have been investigating plant extracts that may safely reduce stress and anxiety without side effects.

#### L-Theanine Lowers Stress

Researchers have long been investigating an amino acid called L-theanine that is found primarily in the leaves of green tea. Studies show it is able to cross the blood-brain barrier.2

L-theanine has demonstrated anti-stress effects. including reductions in perceived stress and markers of stress response like blood pressure, heart rate, cortisol, and patterns of brain activity.8

This confirms earlier work that showed subjects taking **L-theanine** reported significantly less subjective stress than those taking placebo.9

Research has revealed that L-theanine generates a sense of relaxation, with alertness, through at least two mechanisms: 10-18

- 1. Enhances production of the inhibitory (relaxing) neurotransmitter GABA, or gamma amino butyric acid.
  - (GABA then influences levels of dopamine and serotonin that also produce relaxing effects.)
- 2. L-theanine increases the brain's production of alpha brain waves. This creates a state of deep relaxation with mental alertness.

#### Results of Human Studies

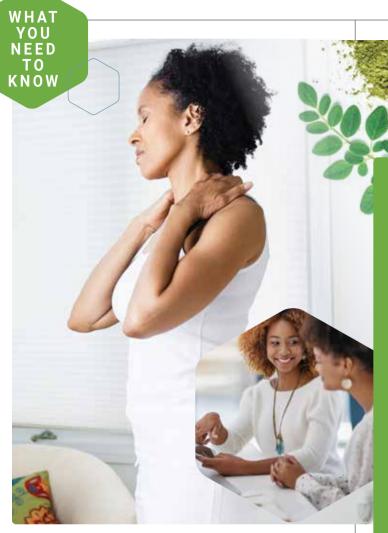
Human trials confirm that L-theanine has relaxing properties that relieve stress. 3,19

In one study, pharmacy students undergoing high-stress clinical training who took 200 mg of L-theanine twice daily reported feeling significantly less stress than those who took a placebo.9

Another clinical trial was done with healthy men and women, aged 21 to 47, who were not considered to be particularly stressed before the study.19

Each volunteer was subjected to alpha brain wave testing, which measures wakeful relaxation, and heart rate measurements. Then, a stress test was given and measurements were retaken.





Next, half the group was given 200 mg of L-theanine, and half was given a placebo. The stress test was conducted twice more over the following 90 minutes. The alpha brain wave and heart rate tests were also repeated. Results showed that:19

- Relaxed wakefulness (measured by alpha brain wave activity) increased with L-theanine but not with the placebo,
- Tension and anxiety were reduced to a greater degree in the L-theanine group, and
- Heart rates were lowered by L-theanine, compared to placebo, a further sign of stress reduction.

A randomized, triple-blind, placebo-controlled, crossover study was done on healthy but moderately stressed adults aged 19 to 60 years.3

Study subjects took a single dose of 200 mg of an extended-release form of L-theanine, or placebo.

#### Stress Relief Without Sedation

- Stress and anxiety can reduce emotional well-being, increase risk for many diseases, and shorten healthy lifespan.
- Anti-stress medications are often sedative and can be addictive.
- Clinical studies show that an amino acid found in green tea, **L-theanine**, promotes calm and relaxation and safely reduces stress without causing drowsiness.
- People taking just *one dose* of **200 mg** of L-theanine had reduced physiological indicators of stress.

All these volunteers took a mental arithmetic test in order to induce mental stress. There was a seven-day washout period between the L-theanine test and the placebo test.

Alpha brain wave activity, salivary cortisol levels, and vital signs were recorded before and after participants took the arithmetic test.

Increases in heart rate, blood pressure, and selfreported stress and anxiety confirmed that subjects experienced stress during the stressful mental test. However, compared to the placebo, 200 mg of L-theanine led to greater alpha wave activity, indicating a higher level of relaxation without drowsiness, just three hours later.3

The "calming response" in brain activity was further supported by greater decreases in salivary cortisol levels, compared to placebo.

In other words, **L-theanine** reduced feelings of stress and physical markers of stress in the body.

#### **Summary**

Stress reduces quality of life and boosts the risk of chronic disorders and premature death.

L-theanine, an amino acid found in green tea, lowers stress and promotes relaxation while maintaining alertness.

Unlike anti-anxiety drugs, L-theanine safely relieves stress without causing drowsiness.

L-theanine is rapidly absorbed, but then rapidly cleared from the body. Using an immediate- and extended-release technology, scientists have found a solution to this, allowing L-theanine to stay in the body for up to six hours.

**Human** trials have shown that L-theanine reduces signs of stress after just a single 200 mg dose.

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#### **Cancer-Fighting Compounds**

**Gynostemma pentaphyllum** contains more than **230** different compounds in multiple classes, including saponins, sterols, flavonoids, and others.<sup>1</sup>

Dozens of these nutrients have been studied and most have demonstrated **anti-cancer** activities against different cancer types.

One review article listed **28 specific compounds** in *Gynostemma* that have **anti-cancer activity** in vitro. That *doesn't* include the flavonoids and carotenoids it contains, which *also* have **cancer-fighting** properties in vitro.<sup>1</sup>

#### **Reducing Cancer Growth**

Studies in cell cultures and animal models have demonstrated this plant's **anti-cancer** properties.<sup>1</sup>

In animals given *Gynostemma*, the **size** and **weight** of tumors is significantly reduced.<sup>2-5</sup>

Some of these studies found that *Gynostemma* attacked **cancer cells** *and* boosted the animals' **immune response** to the tumor.<sup>3,6-8</sup>

*Gynostemma* also appears to have synergistic effects with other anti-cancer compounds. For example, in a mouse model of **colorectal cancer**, co-treatment with the chemotherapy drug **5-fluorouracil** enhanced the drug's effectiveness.<sup>9</sup>

#### **Early Human Trials**

Evidence from studies in the 1990s mentions that *Gynostemma* intake enhances **immune function** even when patients are undergoing chemotherapy, which *impairs* immune function.<sup>1</sup>

An early observational study showed <u>lower</u> rates of cancer relapse and metastasis as well as <u>lower</u> **mortality rates** and improved **immune function**.

Research interest on the benefits of *Gynostemma* has increased markedly over the past decades. We await and look forward to reporting new evidence as it becomes available.

#### How Gynostemma Works

With its many bioactive compounds, *Gynostemma* induces several beneficial mechanisms all at once.

In general, *Gynostemma* modulates the activity of several cellular *signaling* pathways tied to cancer formation and progression.

For example, it activates **AMPK**, while blocking **mTOR** and the associated **PI3K/Akt**.<sup>1,10-12</sup>

These pathways are involved in many aspects of cancer progression. These same mechanisms are found for other anti-cancer compounds being explored, such as the drug **metformin**.





*Gynostemma's* mechanisms are associated with effects that have been observed in various studies. Some of the most notable include:<sup>1</sup>

- Cell cycle arrest. When cancer cells grow and reproduce, they pass through a complex pathway known as the cell cycle. In multiple cancer types, studies have shown that Gynostemma modulates the activity of several proteins involved in cell cycle regulation, stopping the growth of cancer cells.
- Induction of cell death. When normal cells are aged or damaged, they die off through a beneficial process called apoptosis. Cancer cells shut off this process, evading death. Gynostemma acts to re-activate apoptosis, killing off these abnormal cells.
- Inhibition of invasion and metastasis. The lethality of cancers lies mainly in their ability to invade surrounding healthy tissues and metastasize (spread) to distant sites in the body. Gynostemma blocks several pathways involved in invasion and metastasis.

### Gynostemma's Cancer-Fighting Actions

- Gynostemma pentaphyllum, also known as jiaogulan, is an Asian plant containing hundreds of different bioactive compounds. Many have been studied and found to have anti-cancer activities.
- In cell culture and animal models, Gynostemma has been shown to stop the growth and spread of cancer, cause cancer cells to die off, and help the immune system attack cancer.
- Gynostemma acts by modulating the activity of several cellular signaling pathways tied to cancer formation and progression.
- Interfering with cancer cell metabolism.
   Cancer cells need nutrients and energy to grow. Gynostemma has been found to alter the function of key enzymes involved in cancer cell metabolism, starving cancer cells of energy and further blocking their ability to grow and reproduce.
- Immune support. Gynostemma has been found to support key immune system functions, giving a boost to immune cells such as macrophages, T cells, and NK cells. This helps the body more effectively fight and attack cancer.

This wide range of mechanistic effects makes *Gynostemma* a potential adjuvant weapon in the battle against cancer.

#### **Summary**

**Gynostemma pentaphyllum** and its extracts contain hundreds of compounds, many of which have demonstrated, in pre-clinical studies, **anti-cancer** activities against a range of human cancer types.

By acting on different *signaling* pathways associated with cancer formation and progression, *Gynostemma* adds yet another ingredient with promising results in the fight against cancer.

Most people use *Gynostemma pentaphyllum* today to <u>activate</u> cellular **AMPK**, which suppresses excess **mTOR1**. This enables many people to lose excess **belly fat**.

The anti-cancer findings provide another reason for people to include *Gynostemma pentaphyllum* in their supplement program.

We look forward to new evidence on *Gynostemma*, which has attracted growing interest in recent decades. •

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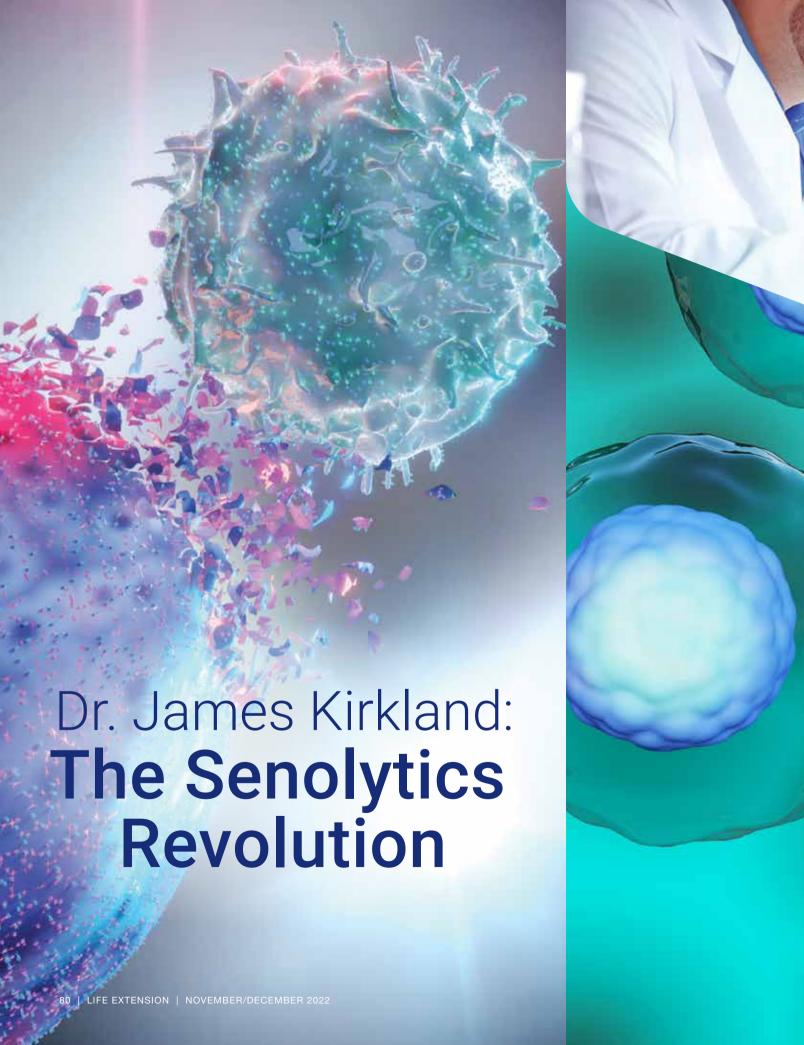




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#### **Senescent Cells**

Ideally, old cells begin a programmed sequence of self-destruction, known as apoptosis, and are cleared away by the immune system.

But senescent cells behave differently. They don't self-destruct.

Instead, they linger and emit a toxic mix of proteindegrading enzymes that damage healthy cells. They also secrete **pro-inflammatory** factors that contribute to chronic low-grade inflammation.3

Dr. Kirkland attributes the accumulation of senescent cells to be causative factors of degenerative aging and chronic diseases.

These senescent cells are what Dr. Kirkland and others seek to safely eliminate.

#### **Dangers of Senescence**

The idea that removing senescent cells could boost longevity was based partly on the observation that mice with mutations that increase lifespan have fewer senescent cells than normal mice. Similarly, very shortlived mice have more senescent cells.4

In studies in some human cell and animal models, removing senescent cells from the body improves markers of aging and prolongs lifespan. 5-9

Senescent cells also increase in a number of chronic diseases 6

Dr. Kirkland and his collaborators are investigating the effects of eliminating senescent cells in models of Alzheimer's disease, arthritis, osteoporosis, frailty, and other disorders.

#### **Senolytics**

Compounds called senolytics have the capacity to safely sweep away senescent cells.9,10

They work by reactivating the **apoptosis** switch in senescent cells, causing these toxic cells to die off, and provide room for healthy, functioning cells.

Dr. Kirkland has worked intensively on the potential for senolytics to reverse a range of chronic diseases and increase human longevity.

Senolytics being tested include the anticancer drug dasatinib, the plant-based nutrients quercetin, theaflavins, and fisetin, and a growing list of related compounds.

The senolytic effects of these compounds have been documented in rodents and human cultured cells.



Compared to untreated mice, those that started a dasatinib-quercetin mix at an age equivalent to 75 to 90 years in humans ended up living about 36% longer, with better physical function.11

Senolytics have effectively prevented, delayed, or alleviated a variety of conditions and diseases in mice.

Clinical trials currently underway for senescencerelated diseases have shown early but clear signs of promise.

In humans, a brief course of senolytics enhanced several measures of physical activity in patients with idiopathic pulmonary fibrosis, a progressive lung disease.12

#### **Daunting Roadblocks**

**Human trials** of senolytics could change medicine forever. They could allow us to switch from treating symptoms to circumventing root causes of aging and age-related disease.

Of course, these trials can take many years, given the timeframe needed to observe a significant change in longevity.

Lack of funding delayed getting senolytic trials started. As Dr. Kirkland noted in the review of which he was a co-author, companies and entrepreneurs are generally uninterested in funding studies of nutrients or existing drugs because they're unable to patent them.2

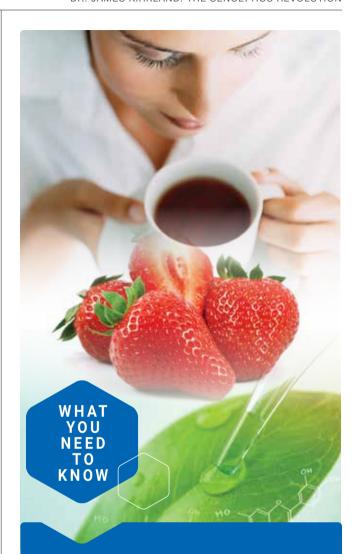
Even more daunting, bureaucratic mandates and regulatory red tape are proving to be the greatest roadblock.

In a recent interview, Dr. Kirkland described the voluminous paperwork and endless regulatory hoops holding his team back.

Dr. Kirkland and his team wanted to study the plant compound fisetin, known to be a promising senolytic. Before getting approval, however, the U.S. Food and Drug Administration (FDA) forced them to compile a highly technical, 450-page Independent New Drug report on fisetin.

Preparing this one document for FDA submission required 2.5 years.

These roadblocks were erected despite over 5,000 Americans a day perishing from an age-related pathology.



### The Promise of Senolytics

- Senescent cells cause damage that drives chronic disease and aging.
- **Senolytics** are compounds that safely cause senescent cells to die off. Known senolytics include the drug dasatinib and the nutrients quercetin, theaflavins, and fisetin.
- Dr. James Kirkland and his colleagues are leaders in the research into senolytics. Their research shows promise in boosting human lifespan.

#### **Summary**

Senescent cells are a major cause of accelerated aging and the development of chronic age-related disorders.

The research into senolytics by Dr. Kirkland and his colleagues at the Mayo Clinic seeks to delay the onset of multiple degenerative illnesses and increase healthy human lifespans. •

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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 pentaphyllum + hesperidin** formula is designed to support healthy **AMPK** cellular activation.

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30 vegetarian tablets

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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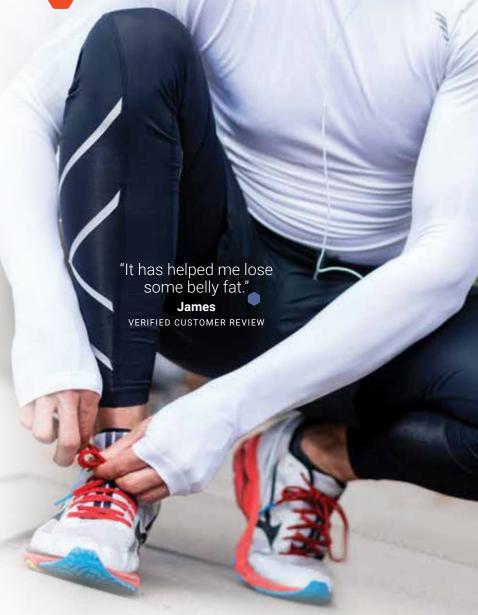




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60 capsules







### The Secret to Longevity in Life and Love



At 95 years old, Marion Ferdinand Hess, Sr., has lived a life that has defied the odds.

He survived a premature birth, fighting in World War II, and two deadly hurricanes in his hometown of New Orleans.

He has been married to his wife. Jean, for 75 years.

And he is in the 10% of men over 90 years old who do not have prostate

Now, Marion attributes his longevity to the vitamins he and his wife started taking for prevention over 25 years ago.

#### **The Early Years**

At age 17, Marion enlisted in the army to fight in World War II. He was immediately deployed to Germany, where he landed under fire, and he served under General Patton until the end of the war.

Soon after returning home from the war, Hess met his future wife, Jean Catherine Meliet.

On September 20, 1947, Marion and Jean tied the knot just one day after one of the deadliest hurricanes to hit the gulf coast slammed into New Orleans, a category 2 hurricane with sustained winds of 110 mph.

Fifty-eight years before the infamous Hurricane Katrina, Hurricane George breached the 17th Street Canal, flooding buildings, causing massive power outages, and leaving standing water for weeks.

But Marion and Jean refused to cancel their wedding, and they were married the following night.

"There was no electricity," recalled Jean, "so my mother placed lanterns around the church for lighting. She also hired a band for dancing and entertainment, and she placed lanterns all around the reception hall. From that day on, my mother treated Marion like her son."

#### **Overcoming Family Medical History**

Marion and Jean did not have an encouraging family medical history. Many of their family members had passed away at a young age from conditions like cancer, heart attack, and stroke.

It appeared as if Jean might follow in their footsteps.

In 2005, at the age of 76, Jean was diagnosed with type II diabetes. She was overweight, and her hemoglobin A1C level was over 6.6.

That's when their daughter, Melissa Hess, stepped in and took Jean to see Dr. Samuel Andrews. an endocrinologist in New Orleans and author of the well-known diet book, Sugar Busters.

Dr. Andrews told Jean that the only way to control her diabetes was to lose weight. Melissa took it a step further and told Dr. Andrews that her mother would not only lose the weight but would reverse her diabetes.

Jean lost 40 pounds in one year, changed her diet, and at her daughter's recommendation, she started taking targeted supplements for diabetes and glucose control from Life Extension.

Before long, her Hemoglobin A1c level dropped down to below 6.0.

Jean said, "After taking these supplements for quite a while-and losing weight-I went back to see Dr. Andrews. He said, 'Mrs. Hess, I'm proud to say that you're not a diabetic anymore.' I couldn't believe it!"



Since 1996, Marion and Jean have taken Life Extension® supplements every day as part of their personal prevention protocol.

They had learned that in order to maintain their cognitive function and prevent conditions like cancer and heart disease, they had to take action long before those conditions

They now believe their efforts have paid off.

"I attribute my longevity to my vitamins." said Jean.

Between the two of them, Marion and Jean take over 50 supplements every day, and they get their blood tested every other month to stay on top of any health problems that might arise.

The blood tests continue to show that Marion's bloodwork looks more like a 30-year-old than a 95-yearold. Marion has very little gray hair and looks younger than his age, which he attributes to his daily supplements.

In addition, a recent biopsy revealed that Marion is free of prostate cancer, a claim only 10% of men in their 90s can make.

Even their dog, Lucki, a Hurricane Katrina survivor that was rescued from a rooftop in a flooded area of New Orleans, is given supplements and remains spry at 18 years old.

Every day, Lucki is given a multivitamin, vitamin C, carnitine, taurine, ubiquinol, ginkgo biloba, collagen, calcium, vitamin D, probiotics, lutein, and many more.

"It's all about prevention," said daughter Melissa. "You have to start many years ahead of time to prevent dementia, heart diseases, autoimmune conditions, and cancers."



#### Marion and Jean's Daily Supplements

- · Advanced Milk Thistle
- AppleWise
- · Arterial Protect
- Arthro-Immune Joint Support with PARACTIN®
- · Bifido GI Balance
- · Bone Restore with Vitamin K2
- · Calcium Citrate with Vitamin D
- Cognitex® Basics
- · Cognitex® Elite
- · Daily Skin Defense
- DMAE Bitartrate
- Endothelial Defense Pomegranate Plus
- · Enhanced Stress Relief
- Eye Pressure Support with Mirtogenol®
- · Fast-Acting Joint Formula
- FLORASSIST® Daily Bowel Regularity
- FLORASSIST® GI with Phage Technology
- FLORASSIST® Heart Health
- FLORASSIST® Mood Improve
- · Gamma E Mixed Tocopherols & Tocotrienols
- Ginkgo Biloba Certified Extract<sup>™</sup> 120 mg
- Glycemic Guard™
- · Homocysteine Resist
- MacuGuard® Ocular Support with Saffron & Astaxanthin
- · Magnesium Caps 500 mg
- · Melatonin 6 Hour Timed Release 300 mcg

- · Mitochondrial Energy Optimizer with PQQ
- N-Acetyl-L-Cysteine (NAC)
- Neuro-Mag®
- · Optimized Carnitine
- Optimized Cran-Max® with Ellirose
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- · Quick Brain Nootropic
- Shade Factor
- · Super Carnosine 500 mg
- · Super K Elite
- Super Omega-3 Plus EPA/DHA Fish Oil,
   Sesame Lignans, Olive Extract, Krill & Astaxanthin
- · Super Selenium Complex with Vitamin E
- Taurine 1,000 mg
- Tri Sugar Shield®
- · Two-Per-Day Multivitamin
- Ultra Prostate Formula
- · Vanadyl Sulfate
- Vitamin D3 7000 IU
- VenoFlow
- · Venotone Standardized Horse Chestnut

#### Words of Wisdom

Through decades and wars, natural disasters and pandemics, Marion and Jean have defied the odds in life, in health, and also in their relationship.

In September of 2022, they celebrated 75 years of marriage, and together they have three children, three grandchildren, and four great grandchildren.

Jean says that their secret to staying together is that "You have to agree with each other, enjoy each other, and never go to bed mad at night. Always keep a smile on your face." No doubt Marion has been instrumental in keeping everyone smiling.

When his doctors ask him why he's taking so many vitamins and supplements, he gets a twinkle in his eyes and responds, "My daughter wants me to die healthy."

PHOTO 1: Wedding photo on September 20, 1947. Marion was 20 and Jean was 18.

PHOTO 2: Marion and Jean with daughter, Melissa Hess, at a wedding in New Orleans on May 20, 2006. Marion was 79 and Jean was 77.

PHOTO 3: 60<sup>th</sup> Wedding Anniversary dinner party in New Orleans on September 20, 2007. Marion was 80 and Jean was 78.

**PHOTO 4:** 72<sup>nd</sup> Wedding Anniversary dinner in New Orleans on September 20, 2019. Marion was 92 and Jean was 90.



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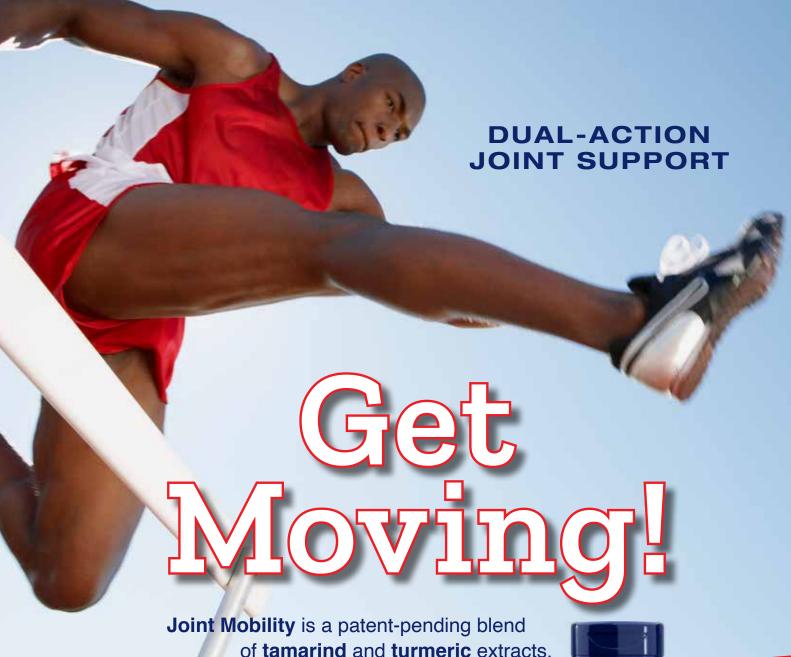






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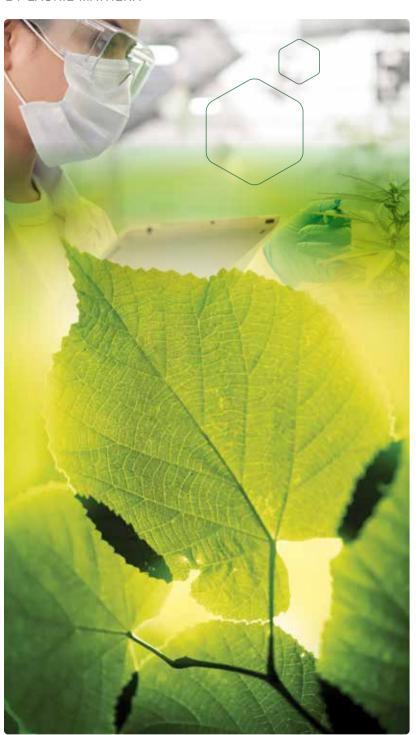
\*Int J Med Sci. 2019;16(6):845-53.





## What Is Chlorophyllin?

BY LAURIE MATHENA



We are surrounded by environmental toxins.

Currently, there are more than **80,000** chemicals registered or listed under the Toxic Substance Control Act.<sup>1</sup>

In 2020, approximately **three bil-lion** pounds of these toxic chemicals—many known carcinogens—were released into the environment.<sup>2</sup>

More disturbing is the fact that most of these chemicals were never adequately tested by any government agency regarding their effects on human health.<sup>3</sup>

Studies now show that these chemicals can contribute to diabetes, heart disease, and cancer by causing **mutations** to our DNA.<sup>4-8</sup>

You can't avoid exposure to these toxins, but you can take steps to minimize their harmful impact on your body.

An inexpensive compound called **chlorophyllin** helps **detoxify** these deadly chemicals from your body, while offering critical protection for your DNA.

#### **Protection Against Numerous Types of Cancer**

Chlorophyllin is a water-soluble derivative of the green plant substance chlorophyll.

Life Extension® reported on the antimutagenic properties of chlorophyllin in the mid-1980s. Since then, numerous studies have been published showing chlorophyllin's ability to protect against multiple types of cancer.

The liver is especially at risk because its job is to cleanse the body of these harmful toxins.

Out of the 600,000 new cases of liver cancer diagnosed yearly. it is estimated that up to 28% of them are caused by aflatoxin, which is found in multiple improperly stored foods, including peanuts, corn, pistachios, and rice.9

Chlorophyllin binds to the carcinogenic byproducts of aflatoxin metabolism, which decreases the bioavailability of these cancer-causing chemicals. 10,11



In this way, chlorophyllin has the potential to significantly reduce the risk of liver cancer induced by aflatoxin

Additionally, chlorophyllin has been shown to protect against the following:

- Oral Cancer: A study in hamsters showed that chlorophyllin can prevent genetic mutations and reverse gene expression linked to oral cancer caused by the chemical dimethylbenzanthracene (DMBA).7,12
- Pancreatic Cancer: Chlorophyllin has antiproliferative effects on pancreatic cells.13
- Colon Cancer: When colon cancer cells were treated with chlorophyllin, it inhibited the enzyme ribonucleotide reductase (RR), which made these cancer cells less able to grow and more receptive to mainstream cancer chemotherapeutic agents.14
- Bladder Cancer: The combination of chlorophyllin with photodynamic therapy resulted in approximately 85% destruction of bladder cancer cells.15
- Breast Cancer: When human breast cells were exposed to the carcinogen dibenzopyrene (DBP), dangerous and unstable DNA adducts were formed. However, adding chlorophyllin to the breast cells led to a 65% decrease in the number of DNA adducts 16 Formation of DNA adducts is an early step in the formation of cancer-causing DNA mutations.17
- Stomach Cancer: Chlorophyllin has been shown to help stop the growth and metastasis of stomach cancer in rats.18

#### **Anticarcinogenic Pathways**

Chlorophyllin protects against many types of cancer because it targets multiple pathways involved in cancer development.

This compound, associated with healthy green plants, has demonstrated anticarcinogenic effects against a variety of widespread environmental toxins. 19

- Chlorophyllin helps prevent carcinogens such as heterocyclic amines from altering DNA to inflict malignant changes.20
- It limits the formation of DNA adducts caused by known carcinogens, including dibenzanthracene, dibenzopyrene and benzophenanthrene.21
- It functions as an antimutagenic agent against chemicals such as PhIP. which are known to be involved in colon, prostate, pancreatic, and breast cancer.21,22
- It protects against mutations of the p53 tumor suppressor gene. Protecting healthy expression of p53 is a critical factor that helps guard against cancerous changes.23

Proper use of chlorophyllin affords considerable defense against the natural and man-made toxins that permeate our food and environment.

Health-conscious individuals sometimes take around 100 mg of chlorophyllin with heavy meals to protect DNA from environmental and dietary mutagens. •



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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



These products are available at fine health food stores everywhere.

- Heterences

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