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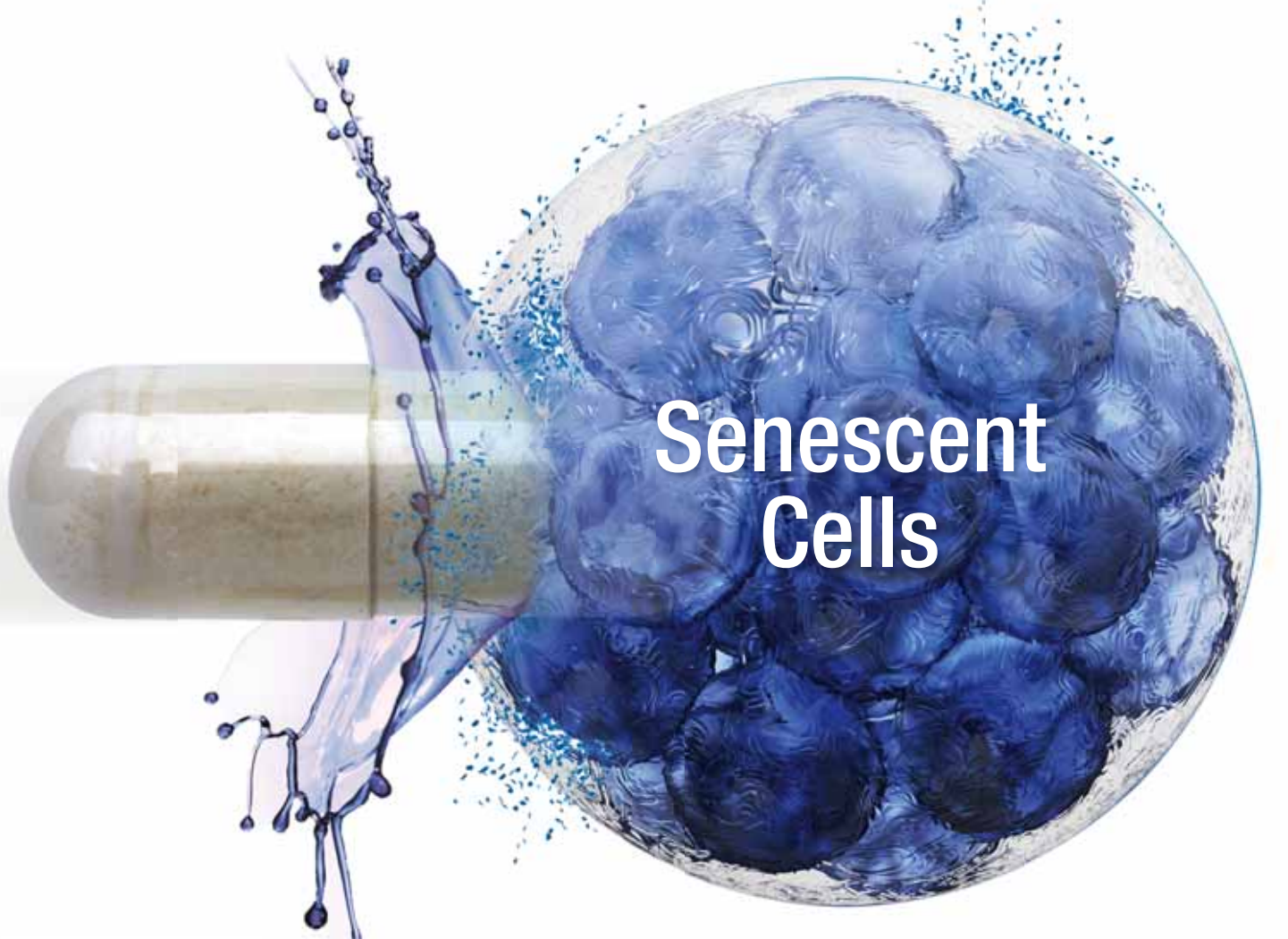
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November 2022

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## What is Delaying Senolytics?

Exciting data about the ability of **senolytics** to delay and reverse **aging** processes continue to emerge.

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# What is Delaying Senolytics?



WILLIAM FALOON

When we wrote about the dangers of **senescent cells** in **2015**, few had ever heard about this aspect of pathologic **aging**.

Move forward to **2022** and there are hundreds of published papers in the **National Library of Medicine** describing compounds that remove these worn-out cells.

Agents that delete **senescent cells** are called "**senolytics**."<sup>1,2</sup>

In coming years, **senolytics** will likely become standard care for all individuals over age 40.

The reason is that **senescent cells** release toxic factors that accelerate degenerative processes throughout our bodies.<sup>1,3-8</sup>

When **senolytics** were administered to old mice (the **human** equivalent of **75-90 years**), lifespans

increased roughly **36%** along with better physical function.<sup>9</sup>

In **2018** and **2019**, mainstream medical journals described the potential of **senolytics** to "**transform medical care**."<sup>10,11</sup>

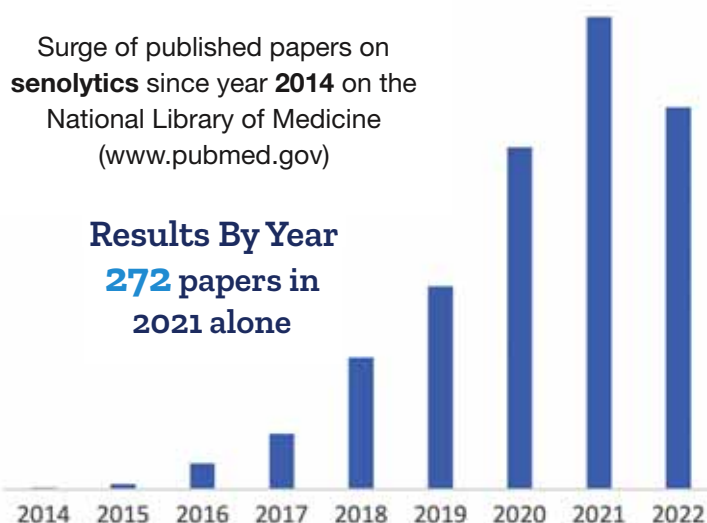
A huge review article published in **August 2022** described many promising **animal** and **human** studies. The authors advocated for large, randomized, placebo-controlled **clinical trials** using **senolytics** to combat **age-related** disorders.<sup>12</sup>

We concur about more extensive research, but this begs the question, what are people over age 40 supposed to do now to reduce their **senescent cell** burden?

This editorial describes what's holding back rapid clinical research and what people are practicing today to selectively remove **senescent cells**.

Surge of published papers on **senolytics** since year **2014** on the National Library of Medicine (www.pubmed.gov)

Results By Year  
**272** papers in 2021 alone



August 24, 2022

## "Senolytics"

The term "senolytic" in published papers increased from near zero in **2013** to over **850** by mid-2022.

<https://pubmed.ncbi.nlm.nih.gov/?term=senolytics>

A major factor in **old-age decline** is the accumulation of **senescent cells** that:

- **Impede Organ Function**
- **Ignite Chronic inflammation**
- **Emit Protein-Destroying Enzymes**
- **Shorten Healthy Lifespan**

Diabetes, obesity, stroke, vision loss, neurodegenerative disorders, osteoarthritis, and cancer can be connected to the presence of **senescent cells**.<sup>13-17</sup>

**Senolytic** compounds selectively *destroy* **senescent cells**.

Numerous studies about **senolytics** have been published in recent years.<sup>18-20</sup>

This research provides evidence that **senolytics** could contribute to better clinical outcomes against age-associated disorders. They show promise in combating heart failure, type II diabetes, Alzheimer's, vascular insufficiency, and lung impairment.

## Senolytic Properties of Fisetin

**Fisetin** is a flavonoid found in various plants including strawberries, apples, grapes, and onions.

Researchers have found that **fisetin** is an exceptionally powerful senolytic.

When compared to other plant compounds, fisetin was the most effective at removing **senescent cells**, both in cell culture and in mice.<sup>21</sup>

The impact is dramatic. Mice given **fisetin** lived an average of about 2.5 months *longer*, an almost **10%** extension of lifespan—even when treatment was started at the human equivalent of **75** years of age.<sup>21</sup>

The Mayo Clinic has been at the forefront in initiating **clinical trials** to ascertain the ability of **fisetin** to reduce the **senescent cell** burden in aging **humans**.

**Mayo Clinic** researchers, however, ran into an obstacle.

## Government Impedes Human Research

Professor **James Kirkland** at the **Mayo Clinic** is spearheading multiple **senolytic** studies.

On **December 9, 2021**, Dr. Kirkland described a clinical trial where he had to complete a **450-page** detailed **Investigational New Drug** application. He submitted this to the **FDA** for **approval** to do a **human** study using **fisetin**.<sup>22</sup>

The **FDA** then mandated that Dr. Kirkland do preclinical (animal and pharmacology) studies before “allowing” a **senolytic** clinical trial to commence. It took **2.5 years** to gather this information, and only then could they begin the **human** study.



What's irrational about this **delay** is that **fisetin** has long been ingested by people in various fruits and vegetables (albeit at lower potencies). It's also been used for years as a **dietary supplement**.

Bureaucratic barriers like this impede **rapid testing** of senolytic and other compounds that may slow or reverse certain **aging** processes.

It's a major reason why most practicing physicians remain in the dark about **senolytics**, despite favorable reviews published in the *New England Journal of Medicine*, *JAMA*, and other respected medical journals.

## Congress Needs to Amend Regulations

In this instance, I am not criticizing the **FDA** for intentionally committing wrongdoing.

The problem is an antiquated system that erects so many bureaucratic hurdles that many promising **clinical trials** never commence.

**Congress** needs to amend requirements for studying compounds (like repurposed medications) so that **clinical trials** can be initiated without the strict regulatory requirements for testing a brand-new **drug**.

## Senolytic Drug and Nutrient Options



The first clinically tested **senolytic** approach combined a cancer drug called **dasatinib** with high-dose **quercetin** on an intermittent basis (several dosing periods within a year).

**Quercetin** and **dasatinib** each have unique **senolytic**-targeting properties. Taking **dasatinib** + **quercetin** together is a validated approach to removing **senescent cells**.<sup>9,23</sup>

Obtaining a prescription for **dasatinib** is challenging, the cost per pill is high, and some people don't want to take a cancer drug, even though it is only being used several times a year in many cases.



Fortunately, an extract from black tea called **theaflavins** has been shown to have a similar **senolytic** mechanism (decrease activity of **tyrosine kinase** receptors) as **dasatinib** in preclinical research.<sup>24</sup>

**Theaflavins** have also been shown to inhibit the **BCL-2** family of proteins.<sup>25</sup> Compounds that inhibit BCL-2 might help prevent some malignancies in addition to removing certain types of **senescent cells**.

**Fisetin** is a broad-spectrum bioactive plant flavonoid with potent senolytic activity.

**Fisetin** has been shown to:

- Function as a targeted senolytic agent,<sup>21</sup>
- Protect the brain in various models of neurodegenerative disorders,<sup>26-32</sup>
- Improve outcomes in people who suffered strokes,<sup>33</sup>
- Help prevent malignant changes in cells,<sup>34-37</sup> and
- Help fight obesity and type II diabetes in animal and experimental models.<sup>38-40</sup>

The initial challenge was that **fisetin** is mostly, and rapidly, converted to different metabolites in the **liver**.

Two years ago, scientists developed a method to increase **fisetin** bioavailability up to **25 times higher**,<sup>41</sup> thus enabling it to reach *higher* concentrations in the blood, and then to stay there longer, compared to ordinary fisetin.

A current nutritional **senolytic** strategy is to take, just once per week, the following:

### Theaflavins + Quercetin + Fisetin

Many readers of this publication already do this, using a formula that combines all three of the above nutrients.

## Mainstream Recognizes Potential of Senolytics

Here are a few quotes from research published in the *Journal of the American Medical Association*:

*"...many human pathologic conditions are associated with the presence of senescent cells."*<sup>42</sup>

*"Interventions aimed at eliminating those senescent cells, commonly called senolytic, have also been shown to improve health and extend life in various mouse disease models."*<sup>42</sup>

*"If senolytics are shown to be safe and effective in humans, they could transform care of older adults and patients with multiple chronic diseases."*<sup>10</sup>



### In this month's issue...

In a recent interview, **Dr. James Kirkland** at the **Mayo Clinic** elaborated on the multiple ways that **senolytics** can potentially combat a host of degenerative disorders.

The article on page 30 of this month's issue provides an update on Dr. Kirkland's research at the **Mayo Clinic**.

People with *higher* intake of **black tea** have *lower* incidences of **cancer**. This may be due to a **senolytic** compound in black tea called **theaflavins**.

The article on page 38 describes how **theaflavins** activate a beneficial **cancer-suppressing** gene named **p53**.

**Theaflavins** may play a dual role by removing **senescent cells** and protecting normal cells.

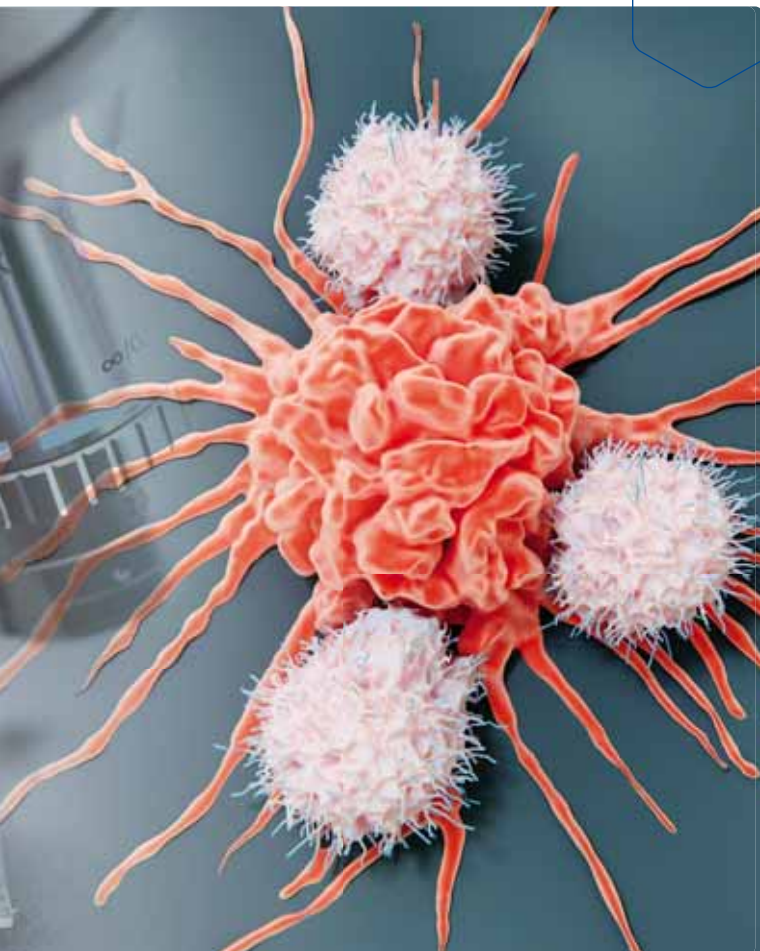
We at **Life Extension** continue to advocate for rapid-fire clinical testing of compounds that may delay and reverse toxic mechanisms that underlie biological aging.

For longer life,

William Faloon, Co-Founder  
Life Extension Buyers Club

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HIGHLY ABSORBABLE

# ASTAXANTHIN

SUPPORTS  
HEART  
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**ASTAXANTHIN** is a carotenoid that benefits the brain, heart, skin, and immune system. Research suggests that astaxanthin can play a role in promoting cardiovascular health.<sup>1</sup>

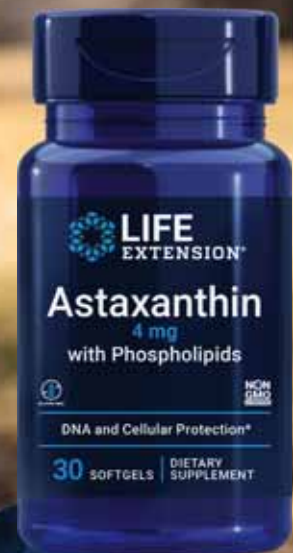
Found naturally in seafood and algae, as little as **50%** of **astaxanthin** is normally **absorbed** in the bloodstream.<sup>2,3</sup>

**Life Extension®** combines **4 mg** of **astaxanthin** with a blend of four different **phospholipids**, which has been shown to enhance carotenoid **absorption** by **several-fold**.<sup>4</sup>

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For full product description and to order **ASTAXANTHIN 4 mg with Phospholipids**, call **1-800-544-4440** or visit **www.LifeExtension.com**



Item #01923 • 30 softgels  
1 bottle \$12

4 bottles \$10.50 each





"I feel like I will be healthy for the long haul."

Wendy

VERIFIED CUSTOMER REVIEW

# Clean

## Your House at the Cellular Level

### Ever heard of **cell senescence**?

It's when some of your body's cells no longer function optimally and emit toxic **compounds** that affect healthy cells.

#### COMPREHENSIVE SENOLYTIC SUPPORT

**Senolytic Activator**® can help manage pesky **senescent cells** with the following nutrients:

- **THEAFLAVINS** (polyphenols from black tea)
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- **APIGENIN** (a natural flavonoid)
- **BIO-FISETIN** (up to **25 times** greater bioavailability)

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



Item #02301 • 36 vegetarian capsules

1 bottle \$19.50 | 4 bottles \$18 each

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

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



# In the News



## 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.

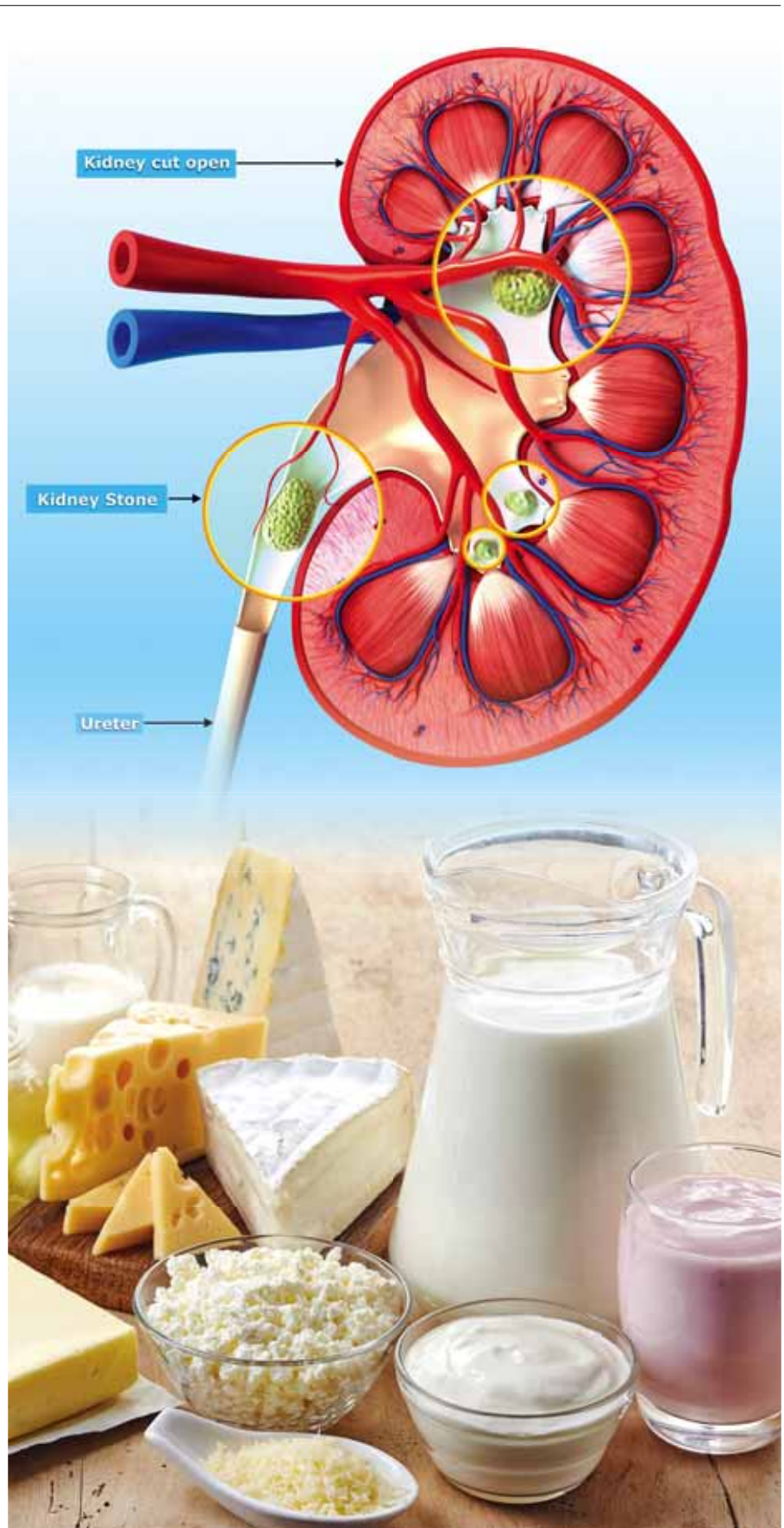
A recurrence of kidney stone symptoms was experienced by 73 of the stone formers. After adjustment for various factors, lower dietary calcium intake remained a significant predictor of recurrent symptoms.

**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 skeletal-support 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 post-fortification 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.



"Mainstay in my prostate health regimen."

**Rick**

VERIFIED CUSTOMER REVIEW

# PROSTATE HEALTH

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- Promote healthy prostate function
- Support healthy prostate cell division

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"Great product—don't want to be without it."

Ingrid

VERIFIED CUSTOMER REVIEW

# HIGHER POTENCY CARNOSINE



**Carnosine** is a unique dipeptide that can inhibit *glycation* throughout the body, thereby helping to slow normal aging processes. Suggested dose is one **500 mg** Carnosine capsule taken once or twice daily.

**Item #01829** • 60 vegetarian capsules

1 bottle **\$27** • 4 bottles \$24 each

Life Extension® was the **first** to introduce high-dose (**500 mg**) carnosine back in **1999**.



**Super Carnosine** provides **500 mg** of carnosine per capsule along with fat-soluble vitamin B1 (**benfotiamine**) to further impede glycation reactions.

**Item #02020** • 60 vegetarian capsules

1 bottle **\$30** • 4 bottles \$27 each

Life Extension® **carnosine** is available in *different* formulas including **Mitochondrial Energy Optimizer** to allow you to customize your longevity program

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



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

"I believe this product is another arrow in my quiver of products I use to be my best."

Raymond

VERIFIED CUSTOMER REVIEW



# Fisetin

## The Longevity Flavonoid

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

In preclinical studies, fisetin:

- Mimics effects of **calorie reduction**<sup>2</sup>
- Targets longevity pathways<sup>2-6</sup>
- Extends lifespan of mice by about **10%**<sup>7</sup>
- Removes **senescent** cells through **senolytic** action<sup>7</sup>
- Suppresses excess **mTOR** activation<sup>8</sup>

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

**Bio-Fisetin** solves this problem by enclosing **fisetin** with a compound from the fenugreek herb.

A **human** trial showed **bioavailability** of this **fisetin** compound increased up to **25 times** compared to fisetin by itself.<sup>9</sup>

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

**Item #02414**

30 vegetarian capsules

1 bottle **\$11.25**

4 bottles \$10 each

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For full product description and to order **Bio-Fisetin**, call **1-800-544-4440** or visit [www.LifeExtension.com](http://www.LifeExtension.com)





# 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 one 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 different parts of the plant (the roots, flowers, leaves, and others) and in different 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).<sup>8</sup>
- 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.<sup>9</sup>
- 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.<sup>6</sup>

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**.<sup>6</sup>

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:<sup>6</sup>

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

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.

WHAT  
YOU  
NEED  
TO  
KNOW

## 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.
- Studies suggest that to receive echinacea's complete spectrum of immune-boosting and antiviral benefits, it is critical to select a product that contains **extracts** from various parts of the plant, as well as more than one **plant species**.



## 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. •

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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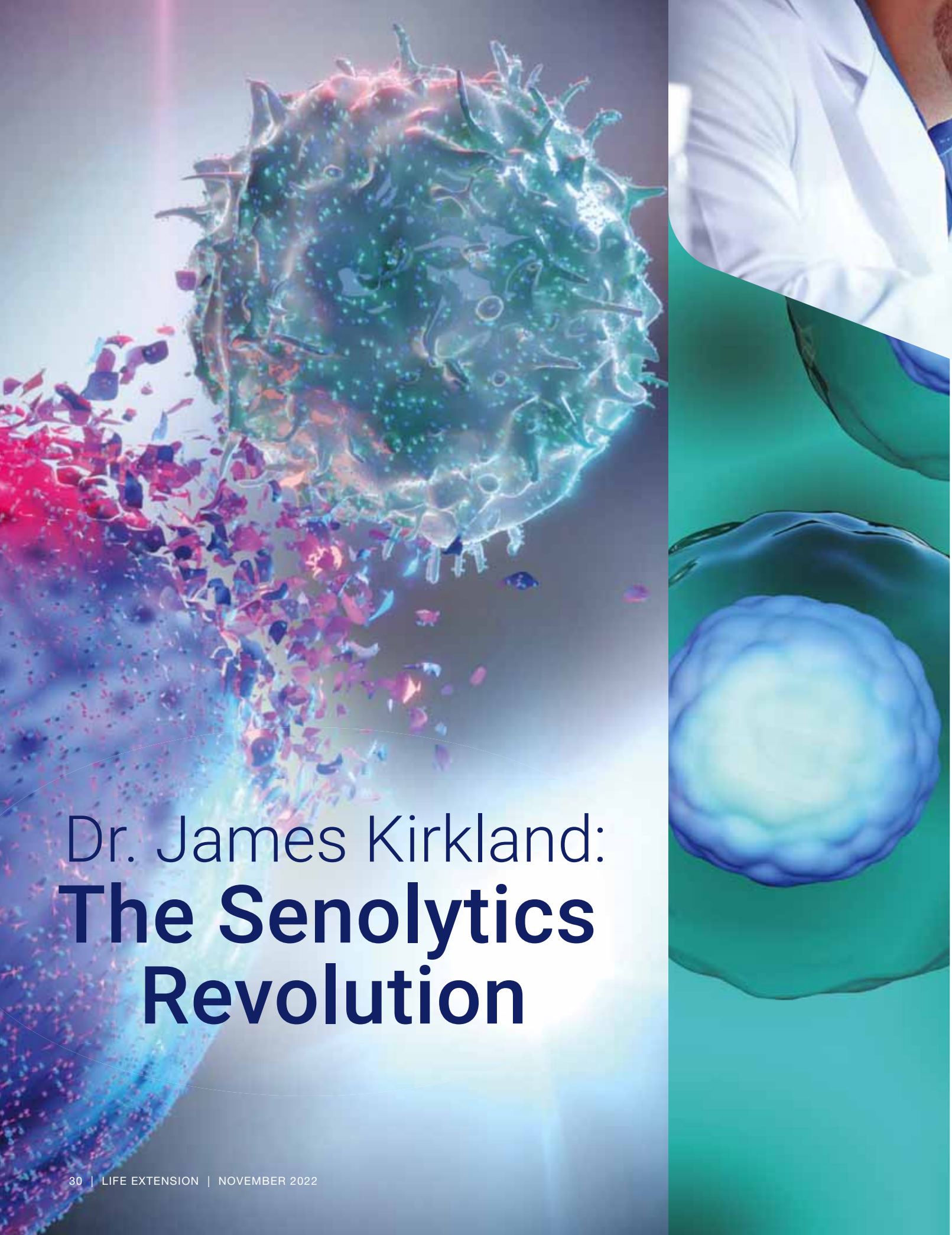
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Dr. James Kirkland:  
**The Senolytics  
Revolution**





James Kirkland, MD, PhD

BY MICHAEL DOWNEY

**James Kirkland, MD, PhD**, and his **Mayo Clinic** team are spearheading research that aims to prevent or reverse multiple diseases of aging.

Compounds known as **senolytics** are being tested in 16 clinical (**human**) trials.<sup>1</sup>

Early evidence suggests they may do *more* than target chronic diseases. They may also counteract certain **aging processes**.

Dr. Kirkland, along with a growing number of scientists, believes the body's accumulation of **senescent cells** is a critical factor in disease, frailty, and aging.

His research is focused on identifying and testing agents that safely *remove* these toxic, old cells.

In the **August 2022** issue of ***Nature Medicine***, Dr. Kirkland and two Mayo Clinic colleagues note that **senescent cells** are a target for "**disorders across the lifespan.**"<sup>2</sup>

## 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 **protein-degrading enzymes** that damage healthy cells. They also secrete **pro-inflammatory** factors that contribute to chronic low-grade inflammation.<sup>3</sup>

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 short-lived mice have more **senescent cells**.<sup>4</sup>

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

Senescent cells also *increase* in a number of **chronic diseases**.<sup>6</sup>

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.<sup>9,10</sup>

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**.<sup>11</sup>

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

**Clinical trials** currently underway for senescence-related 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.<sup>12</sup>

## 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.<sup>2</sup>

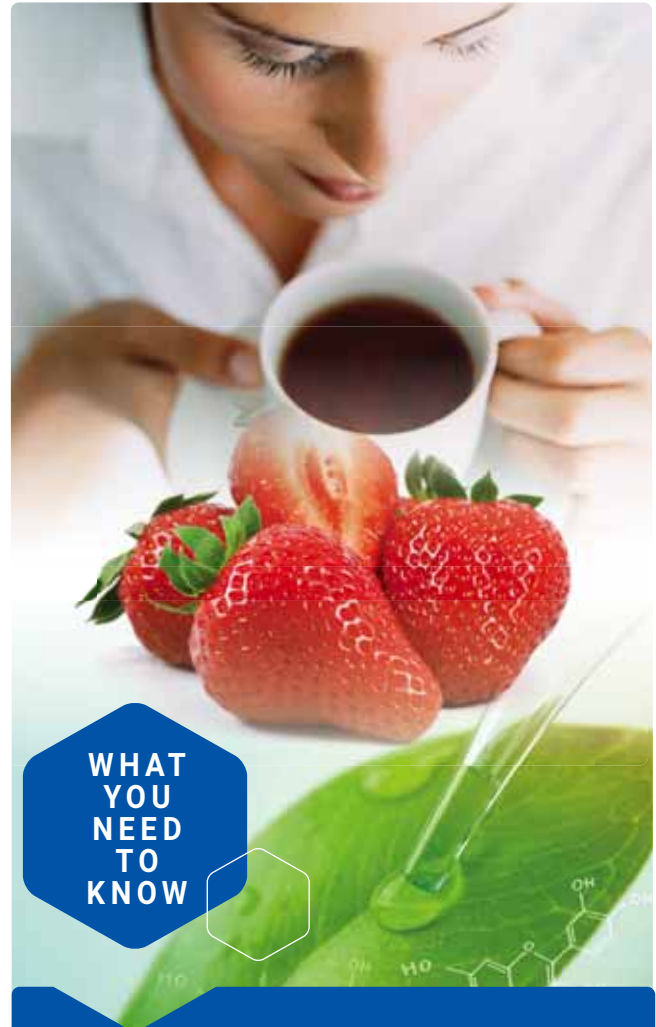
Even more daunting, bureaucratic mandates and **regulatory red tape** are proving to be the greatest roadblock.

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.



WHAT  
YOU  
NEED  
TO  
KNOW

## 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**. •

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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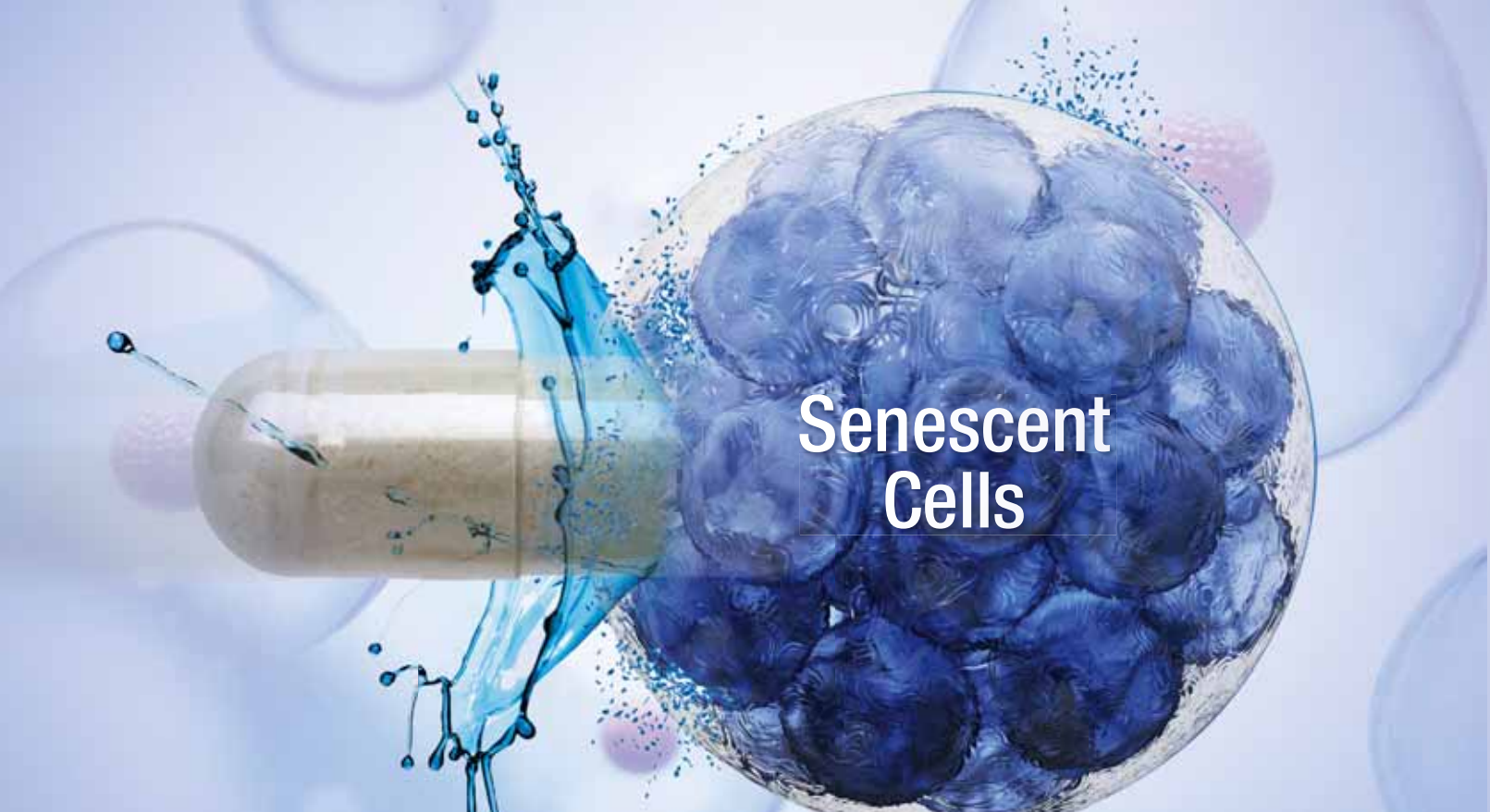
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# CANCER-FIGHTING EFFECTS OF THEAFLAVINS







BY BRUCE EDWARDS

It has been observed that people with *higher* intake of **black tea** have *reduced* rates of cancers.<sup>1</sup>

That may be due to a compound found in black tea called **theaflavins**.

In cell culture and animal models, theaflavins have demonstrated **anti-cancer** effects, working in multiple ways to slow the spread and progression of many types of cancer.<sup>1-5</sup>

One group of scientists has dubbed black tea "***the future panacea for cancer.***"<sup>2</sup>

## Systemic Effects of Theaflavins

When **green tea** leaves are fermented to make **black tea**, compounds called **theaflavins** are formed.<sup>6</sup>

These **black tea polyphenols** (theaflavins) have shown body-wide health benefits.

In particular, research has uncovered specific ways that **theaflavins** play a role in fighting **cancer**.

By interacting with cellular pathways and processes critical to cancer development and progression, theaflavins **beat back cancer cells** and make it hard for them to survive and spread.

One review paper noted that an **ideal cancer therapy** would:<sup>2</sup>

- Shrink tumors by inducing cancer cell death, blocking the growth of new blood vessels in tumors, and slowing or stopping the spread of cancer in the body,
- Boost immune system function to aid in the fight against cancer, and
- Reduce the systemic toxic effects that cancer creates.

These scientists believe that **black tea theaflavins** accomplish *all* these actions. Several reviews of the anti-cancer actions of theaflavins provide evidence to support this belief.<sup>1-5</sup>

## A “Guardian Angel” Against Cancer

A **gene** is critically involved in halting the progress of a wide range of human cancers.

Known as **p53**, this gene has long been recognized as a **tumor suppressor**, inhibiting both the formation and progression of tumors. In fact, **p53** has earned the nickname “**the guardian of the genome**.”<sup>7,8</sup>

**Tumor suppressor genes** are parts of the genetic code that prevent and interrupt malignant changes in cells.

In approximately half of **all human malignancies**, the p53 gene is mutated, thus impairing the cell protective role of **p53**.<sup>9</sup>

When **p53** is functional, it defends the health of cells by **repairing damage to DNA** that can cause mutations that contribute to cancer.<sup>9</sup>

The **p53** gene also acts as a **master regulator** of cell pathways that are involved in cancer development. Active p53 helps starve cancer cells of fuel, prevent new blood vessel formation, halt spread and metastasis, block cancer cell proliferation, and induce cancer cell death.<sup>3</sup>

It even helps improve the success of **chemotherapy** and **radiation** in attacking existing cancer cells.

In many tumors, however, **p53** is mutated. This is a driver of cancer risk and progression.<sup>3</sup>

Research on **theaflavins** suggests the **activation of p53** as an important mechanism in inducing many of its anti-cancer actions.<sup>3</sup>





## WHAT YOU NEED TO KNOW

### Anti-Cancer Activity of Theaflavins

- **Theaflavins** are nutrients found in **black tea**. These compounds work in different ways to prevent cancer development, block its ability to grow and spread, and directly kill cancer cells.
- These **anti-cancer** effects of theaflavins have been demonstrated for many forms of cancer in both cell cultures and animal models.

#### Additional Anti-Cancer Action

Theaflavins *regulate* a protein called **mTOR**, which can cause cells to excessively propagate.

Theaflavins also inhibit an **inflammation-inducing** complex called **NF-kB** that is involved in cancer development and progression.<sup>1,4,7,10</sup>

In cell cultures and animal models, theaflavins have demonstrated the ability to impair cancer by:<sup>1-5</sup>

- Reducing the **initial development** of cancers,
- Arresting the cancer **cell cycle**, halting cancer cells' ability to grow and proliferate,
- Reducing cancer cell viability, making them less robust and resilient,
- Inducing the **death** of cancer cells,
- Inhibiting the formation of new blood vessels in the tumor, **starving the cancer** of oxygen and nutrients,
- Impairing the ability of cancer cells to spread and metastasize, and
- Boosting the **immune system** to join the fight against cancer.

A wealth of pre-clinical data has found that **theaflavins** offer protection against mechanisms involved in cancer development and progression.<sup>11-15</sup>

These beneficial actions have been seen in cancers of the breast, prostate, lung, ovaries, cervix, skin, colon, liver, esophagus, stomach, and hematological malignancies like leukemia.<sup>1-5</sup>

#### Human Studies

There are **human** data to support this. One study recruited men with **prostate cancer** who were scheduled for surgery.<sup>16</sup> Some consumed **black tea** for five days *prior* to **surgery** while others received a **placebo** drink.

After surgery, levels of **tea polyphenols** were significantly **higher** in the removed tumor tissues of men who received black tea.

Scientists then attempted to grow the prostate cancer cells in a cell culture containing blood serum from the patients. In these cultures, cancer cell growth was significantly **reduced** in those who drank **black tea** five days prior to surgery.

## Summary

Preclinical studies have found that **theaflavins** from black tea exert **anti-cancer** effects.

Cell culture and animal models have demonstrated multiple ways that theaflavins **block cancer development and progression**, and epidemiological studies show that people with *higher* intake of black tea **theaflavins** have reduced rates of cancers.

We hope the data presented in this article will motivate oncology researchers to initiate **clinical trials** to assess whether adding **theaflavins** to conventional cancer treatments improves patient outcomes. •



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



## Theaflavins Fight Cancer by Some of the Same Mechanisms as Statin Drugs

Recent research has found that some common medications possess anti-cancer activity. For example, the **statin** drugs used to treat abnormal cholesterol levels have been found in some studies to reduce risk for cancer. This effect is believed to be attributable to various mechanisms including modulation of **mTOR** and associated **PI3K/Akt**.

These cellular signaling pathways are intertwined with many other mechanisms of cancer development and progression. Theaflavins have been found to share many of these mechanistic targets.<sup>1,4,5,17</sup>

**Theaflavins** are not a substitute for conventional cancer treatment. They may later demonstrate efficacy as an adjuvant nutrient analogous to doctors who recommend **vitamin D** to patients with diseases like type II diabetes and cancers today.

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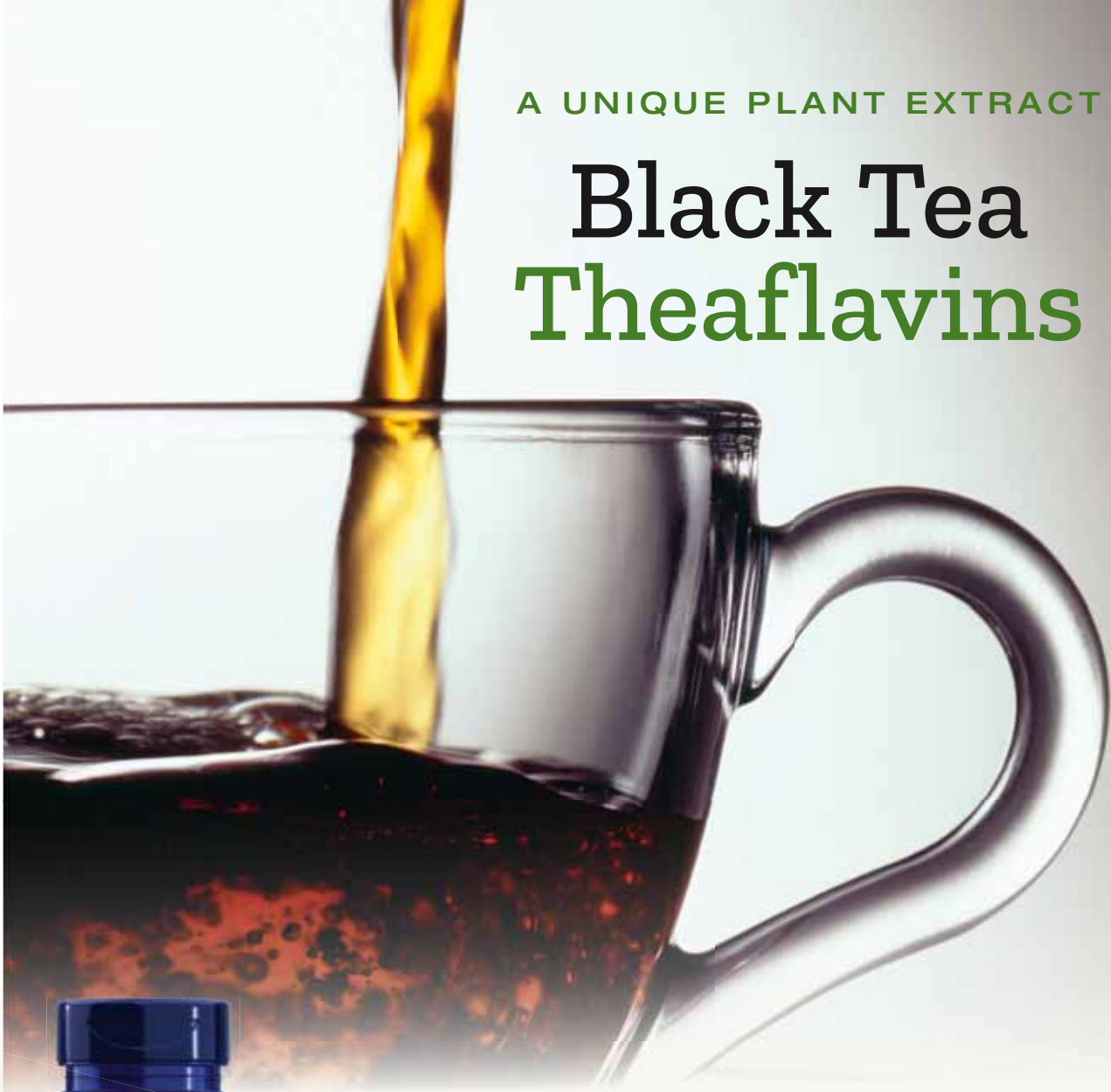
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- Promote normal cell division
- Activate the **p53 gene** known as the “*guardian of the genome*”
- Scavenge free radicals
- Help inhibit inflammation to support whole-body health

**Theaflavin Standardized Extract** is a convenient way to obtain the benefits that come from the theaflavins found in black tea—just take one capsule daily.



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

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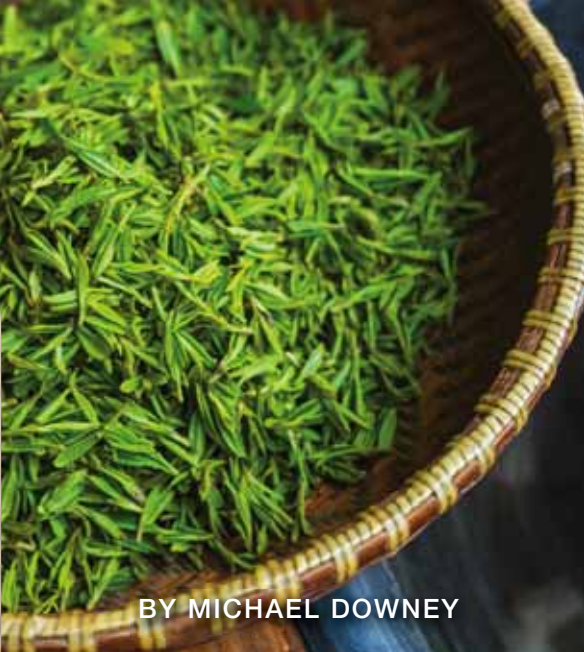
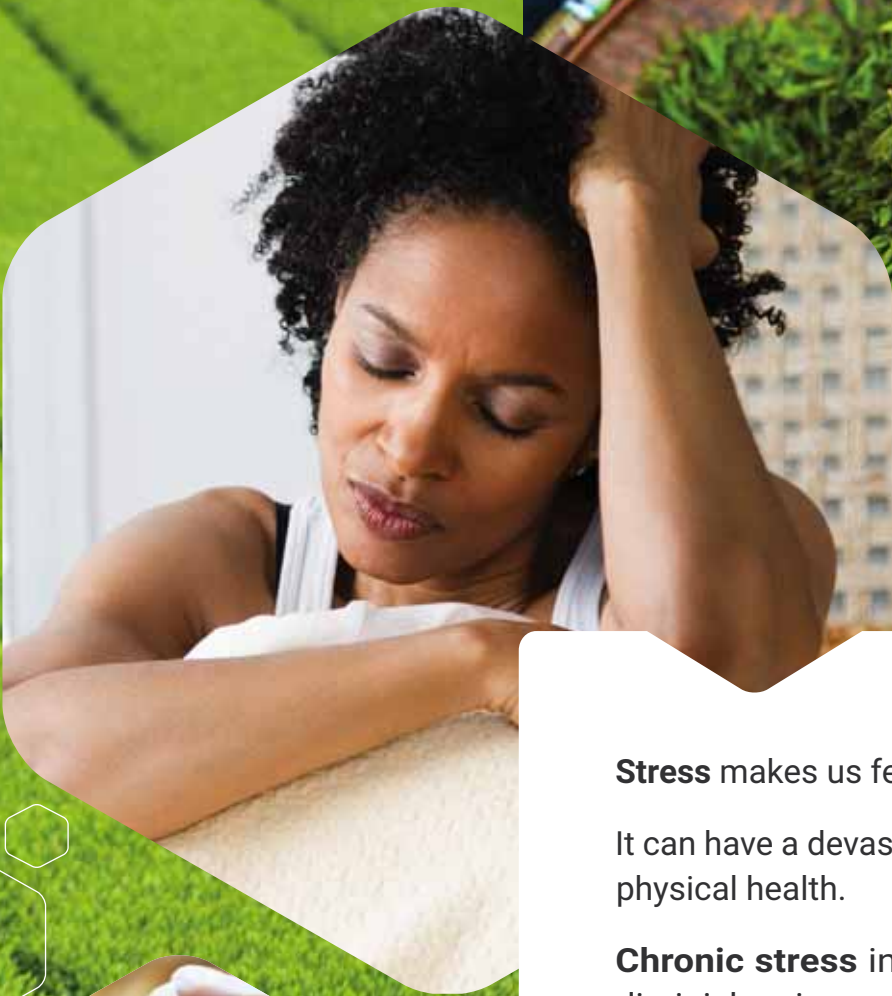
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A high-angle photograph of a tea plantation. The rows of tea bushes are vibrant green and stretch across the frame. A person wearing a light-colored bucket hat, a white protective vest over an orange long-sleeved shirt, and dark gloves is bent over, working in one of the rows. The overall scene is bright and lush.

# A Single Dose of L-THEANINE Safely Lowers Stress





BY MICHAEL DOWNEY

**Stress** makes us feel miserable.

It can have a devastating impact on emotional and physical health.

**Chronic stress** increases cardiovascular risk, diminishes immune function, impairs cognition, induces gastrointestinal problems, contributes to depression, and more.<sup>1</sup>

A compound found in **green tea** can help. This amino acid, named **L-theanine**, promotes **stress relief**, calm, and relaxation—*without* causing drowsiness.<sup>2</sup>

**L-theanine** is rapidly absorbed and cleared from the body. This causes some people to take multiple doses throughout the day to achieve sustained levels.

Using an *immediate- and extended-release technology*, scientists have found a way to allow **L-theanine** to stay in the body for **up to six hours**.

One study in **moderately stressed** adults found that a **single dose** of this form of L-theanine led to a greater *increase* in indicators of **relaxation** compared to placebo.<sup>3</sup>



## 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.<sup>6</sup>

Most anti-stress or anti-anxiety drugs cause **sedation** and other side effects and can be addictive.<sup>7</sup> 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.<sup>2</sup>

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.<sup>8</sup>

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

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

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**.<sup>3,19</sup>

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.<sup>9</sup>

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.<sup>19</sup>

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.



## WHAT YOU NEED TO KNOW



## 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.

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:<sup>19</sup>

- **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.<sup>3</sup>

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

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 self-reported 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.<sup>3</sup>

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**. ●

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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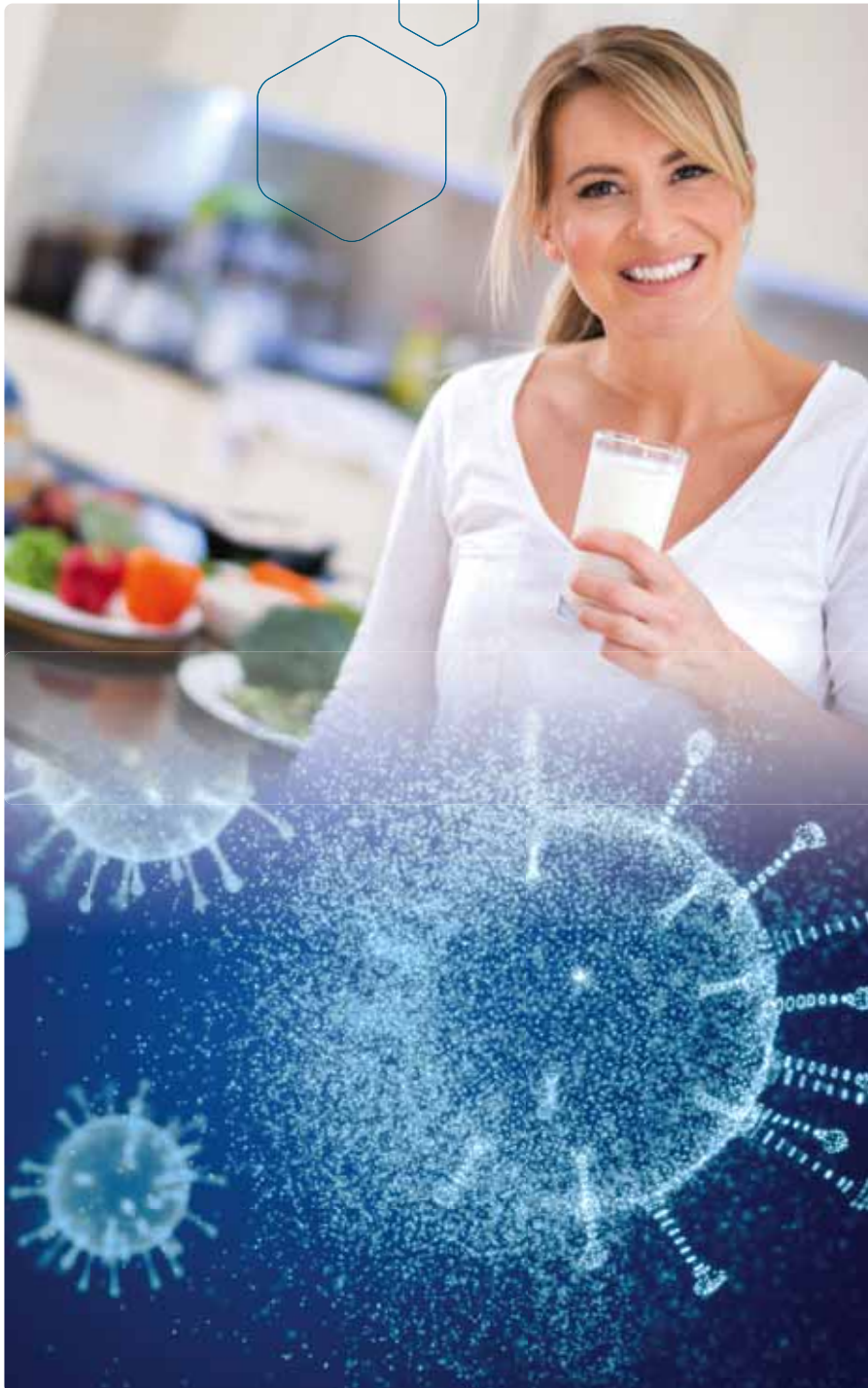
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# What Is LACTOFERRIN?

BY LAURIE MATHENA



Lactoferrin is a protein found in milk that provides antimicrobial activity and has immunomodulatory properties.<sup>1</sup>

It is present in many tissues and required for effective protection against external threats.<sup>2</sup>

While some lactoferrin is produced in the body, it can also be absorbed from oral intake, bolstering the body's defenses.<sup>3</sup>

Laboratory, animal, and clinical research demonstrates lactoferrin's activity against a wide range of viruses, including those that cause the **common cold** and **flu**.<sup>1</sup>

## Lactoferrin Fights Common Viral Illnesses

Lactoferrin is an important component of the body's defense against infections. It works by helping to block viral invasion of cells and by amplifying the immune system's power to eliminate viral infection from the body.<sup>1</sup>

Found in mucous, saliva, and other secretions, lactoferrin helps prevent pathogens from gaining entry through the linings of the oral cavity, nasal cavity, airways, and digestive system.<sup>4</sup>

One unusual feature of **lactoferrin** is the diversity of viruses it can shield against. It possesses robust **antiviral** activity against viruses that cause the **common cold** and **flu**, gastroenteritis (stomach flu), hepatitis B and C, herpes simplex, Epstein-Barr virus, and more.<sup>1</sup>

In one study, healthy women taking **oral lactoferrin** experienced a reduced onset of symptoms of both the common cold and gastroenteritis.<sup>5</sup>

In another, oral lactoferrin was shown to reduce the *incidence* and *severity* of the symptoms of viral gastroenteritis.<sup>4</sup>

### How Lactoferrin Works

Lactoferrin works several ways to defend against viral infections.

First, it disrupts viruses from binding to cells.<sup>6</sup> This can stop the virus in its tracks, before it has a chance to enter cells and cause illness.



Second, it activates specific **immune** functions, such as **natural killer** (NK) cells and increases NK cell numbers. This can help prevent the spread of a virus in the body.

Lactoferrin may also help block the ability of viruses to **reproduce** even if they're already inside cells.<sup>1</sup> This helps limit the spread of the virus, potentially reducing the severity of the resulting illness.

### Added Benefits

Lactoferrin has shown great promise in fighting against age-related bone loss.<sup>8</sup>

It can also help prevent “dry eyes” after cataract surgery. This loss of tear film and quality can produce symptoms such as pain, irritation, and poor vision.

When patients were given lactoferrin one day after surgery, they showed a **95%** improvement in tear quality and quantity after **60 days** of supplementation compared to controls.<sup>9</sup>



### Supplementing with Lactoferrin

Lactoferrin is a versatile substance with a wide range of benefits. A typical dose of lactoferrin is **300 mg** once or twice daily.

Taken orally, lactoferrin is readily absorbed and can play an important role in bolstering defenses against viral illnesses. •

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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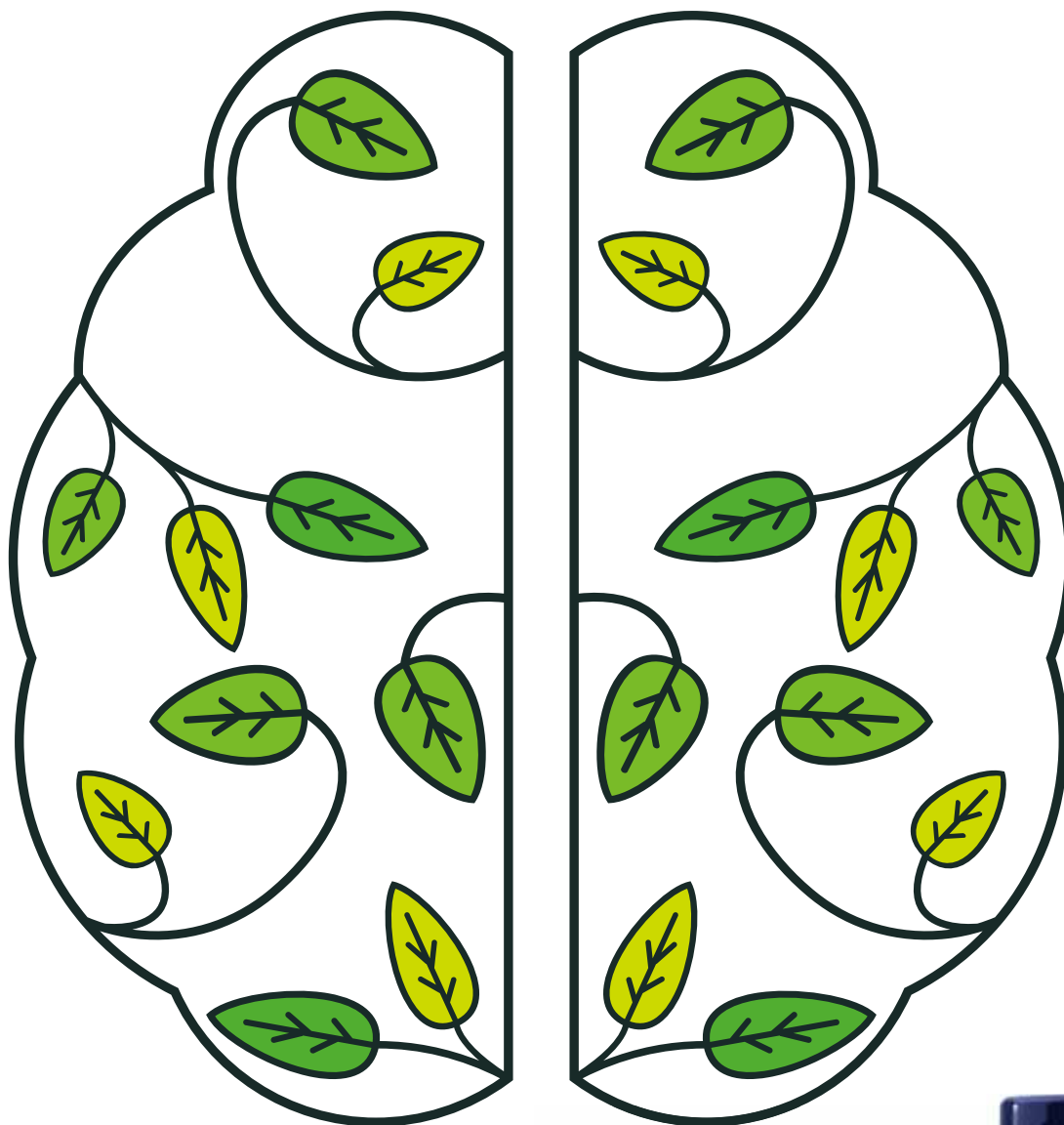


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# Manage After-Meal Blood Sugar Spikes

BY JASON GREEN



MAQUI BERRIES



CLOVES

It's not just diabetics who have to worry about their **blood glucose** levels.

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 less-than-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 after-meal 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**.<sup>1</sup>

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.<sup>6-14</sup> Almost a **third** of those with prediabetes could go on to develop **diabetes** within **five years** if no corrective actions are taken.<sup>15</sup>

## 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**.<sup>4</sup>

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

**Maqui berry** is a fruit native to South America. Extracts of these berries are high in polyphenols known as **delphinidins**.<sup>16</sup>

These nutrients have been shown to **lower after-meal glucose levels**. They do this by stimulating a peptide produced in the intestines that improves glucose metabolism.<sup>16,17</sup>

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**.<sup>5</sup>

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 maqui berry extract taken before a meal helped lower after-meal **glucose** by more than **15%** while also reducing after-meal **insulin** levels.<sup>3</sup> (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 maqui berry extract significantly *reduced* levels of **HbA1c (hemoglobin A1c)** over 90 days.



WHAT  
YOU  
NEED  
TO  
KNOW



## After-Meal Glucose Control

- Elevations of **blood sugar** following a meal are associated with poor health outcomes.
- Scientists have found that polyphenol-rich **clove** and **maqui berry** extracts help control blood glucose, reducing after-meal 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.<sup>18-20</sup>

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
- **Reduced** 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.

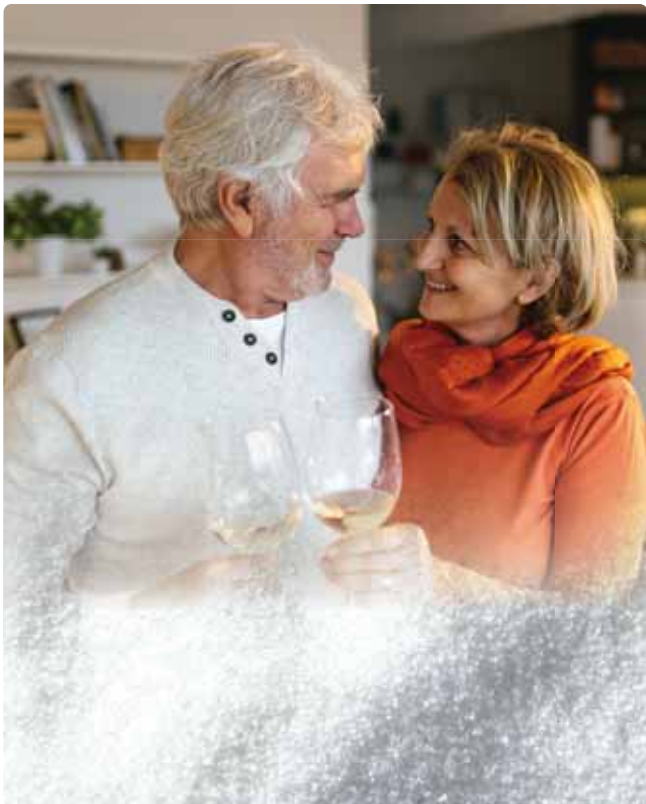
Taking **clove** and **maqui berry extracts** together may reduce after-meal glucose spikes and help with overall glucose control.

### 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. •



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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1. Akay Internal Study. Liposomal hydrogel vitamin C pharmacokinetics. Data on file. 2021.

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# The Secret to Longevity in Life and Love

BY LAURIE MATHENA



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 cancer.

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 17<sup>th</sup> 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!”

### Their Life Extension Journey

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 arose.

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-year-old. 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 multi-vitamin, 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

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### 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.” •

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

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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- 01394 Optimized Garlic
- 01309 Optimized Quercetin
- 01811 Peony Immune
- 00525 ProBoost Thymic Protein A
- 01708 Reishi Extract Mushroom Complex
- 01906 Standardized Cistanche
- 13685 Ten Mushroom Formula®
- 01097 Ultra Soy Extract
- 01561 Zinc Lozenges

**INFLAMMATION MANAGEMENT**

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

**JOINT SUPPORT**

- 02404 Arthro-Immune Joint Support
- 02238 ArthroMax® Advanced NT2 Collagen™ & AprèsFlex®
- 01617 ArthroMax® with Theaflavins & AprèsFlex®
- 02138 ArthroMax® Elite
- 00965 Fast-Acting Joint Formula
- 02430 Fast Acting Relief
- 00522 Glucosamine/Chondroitin Capsules
- 02420 Glucosamine Sulfate
- 02424 Joint Mobility
- 01600 Krill Healthy Joint Formula
- 01050 Krill Oil
- 00451 MSM (Methylsulfonylmethane)
- 02231 NT2 Collagen™

**KIDNEY & BLADDER SUPPORT**

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

**LIVER HEALTH & DETOXIFICATION**

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

**LONGEVITY & WELLNESS**

- 00457 Alpha-Lipoic Acid
- 01625 AppleWise
- 02414 Bio-Fisetin
- 01214 Blueberry Extract
- 01438 Blueberry Extract and Pomegranate
- 02270 DNA Protection Formula
- 02431 Essential Youth - L-Ergothioneine
- 02119 GEROPROTECT® Ageless Cell™
- 02415 GEROPROTECT® Autophagy Renew
- 02401 GEROPROTECT® Stem Cell
- 02211 Grapeseed Extract
- 00954 Mega Green Tea Extract (decaffeinated)
- 00953 Mega Green Tea Extract (lightly caffeinated)
- 01513 Optimized Fucoidan with Maritech® 926
- 02230 Optimized Resveratrol Elite™
- 01637 Pycnogenol® French Maritime Pine Bark Extract
- 02210 Resveratrol Elite™
- 00070 RNA (Ribonucleic Acid)
- 02301 Senolytic Activator®
- 01208 Super R-Lipoic Acid
- 01919 X-R Shield

**MEN'S HEALTH**

- 02209 Male Vascular Sexual Support
- 00455 Mega Lycopene Extract
- 02306 Men's Bladder Control
- 01789 PalmettoGuard® Saw Palmetto and Beta-Sitosterol
- 01790 PalmettoGuard® Saw Palmetto/Nettle Root Formula and Beta-Sitosterol
- 01837 Pomi-T®
- 01373 Prelox® Enhanced Sex for Men
- 01940 Super MiraForte with Standardized Lignans
- 02500 Testosterone Elite
- 01909 Triple Strength ProstaPollen™
- 02029 Ultra Prostate Formula

**MINERALS**

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

**MISCELLANEOUS**

- 00577 Potassium Iodide
- 00657 Solarshield® Sunglasses

**MOOD & STRESS MANAGEMENT**

- 02434 Calm-Mag
- 02312 Cortisol-Stress Balance
- 00987 Enhanced Stress Relief
- 01074 5 HTP
- 01683 L-Theanine
- 02175 SAMe (S-Adenosyl-Methionine)  
200 mg, 30 enteric coated vegetarian tablets
- 02176 SAMe (S-Adenosyl-Methionine)  
400 mg, 30 enteric coated vegetarian tablets
- 02174 SAMe (S-Adenosyl-Methionine)  
400 mg, 60 enteric coated vegetarian tablets
- 02429 Theanine XR™ Stress Relief

**MULTIVITAMINS**

- 02199 Children's Formula Life Extension Mix™
- 02354 Life Extension Mix™ Capsules
- 02364 Life Extension Mix™ Capsules without Copper
- 02356 Life Extension Mix™ Powder
- 02355 Life Extension Mix™ Tablets
- 02357 Life Extension Mix™ Tablets with Extra Niacin
- 02365 Life Extension Mix™ Tablets without Copper
- 02292 Once-Daily Health Booster • 30 softgels
- 02291 Once-Daily Health Booster • 60 softgels
- 02313 One-Per-Day Tablets
- 02428 Plant-Based Multivitamin
- 02317 Two-Per-Day Capsules • 60 capsules
- 02314 Two-Per-Day Capsules • 120 capsules
- 02316 Two-Per-Day Tablets • 60 tablets
- 02315 Two-Per-Day Tablets • 120 tablets

**NERVE & COMFORT SUPPORT**

- 02202 ComfortMAX™
- 02303 Discomfort Relief

**PERSONAL CARE**

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

**PET CARE**

- 01932 Cat Mix
- 01931 Dog Mix

**PROBIOTICS**

- 01622 Bifido GI Balance
- 01825 FLORASSIST® Balance
- 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
- 02505 FLORASSIST® Probiotic Women's Health
- 01920 FLORASSIST® Throat Health
- 52142 Jarro-Dophilus® for Women
- 00056 Jarro-Dophilus EPS® • 60 veg capsules
- 21201 Jarro-Dophilus EPS® • 120 veg capsules
- 01038 Theralac® Probiotics
- 01389 TruFlora® Probiotics

**SKIN CARE**

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



- 80179 Brightening Peptide Serum
- 80176 Collagen Boosting Peptide Cream
- 80156 Collagen Boosting Peptide Serum
- 02408 Collagen Peptides for Skin & Joints
- 80180 CoQ10 and Stem Cell Rejuvenation Cream
- 80169 Cucumber Hydra Peptide Eye Cream
- 02423 Daily Skin Defense
- 80141 DNA Support Cream
- 80163 Eye Lift Cream
- 80123 Face Rejuvenating Anti-Oxidant Cream
- 80109 Hyaluronic Facial Moisturizer
- 80110 Hyaluronic Oil-Free Facial Moisturizer
- 80138 Hydrating Anti-Oxidant Facial Mist
- 00661 Hydroderm
- 55495 Instensive Moisturizing Cream
- 80103 Lifting & Tightening Complex
- 80168 Melatonin Advanced Peptide Cream
- 80114 Mild Facial Cleanser
- 80172 Multi Stem Cell Hydration Cream
- 80159 Multi Stem Cell Skin Tightening Complex
- 80122 Neck Rejuvenating Anti-Oxidant Cream
- 80174 Purifying Facial Mask
- 80150 Renewing Eye Cream
- 80142 Resveratrol Anti-Oxidant Serum
- 01938 Shade Factor™
- 02129 Skin Care Collection Anti-Aging Serum
- 02130 Skin Care Collection Day Cream
- 02131 Skin Care Collection Night Cream
- 80166 Skin Firming Complex
- 02096 Skin Restoring Ceramides
- 80130 Skin Stem Cell Serum
- 80164 Skin Tone Equalizer
- 80143 Stem Cell Cream with Alpine Rose
- 80148 Tightening & Firming Neck Cream
- 80161 Triple-Action Vitamin C Cream
- 80162 Ultimate MicroDermabrasion
- 80173 Ultimate Peptide Serum
- 80178 Ultimate Telomere Cream
- 80160 Ultra Eyelash Booster
- 80101 Ultra Wrinkle Relaxer
- 80113 Under Eye Refining Serum
- 80104 Under Eye Rescue Cream
- 80171 Vitamin C Lip Rejuvenator
- 80129 Vitamin C Serum
- 80136 Vitamin D Lotion
- 80102 Vitamin K Cream

**SLEEP**

- 01512 Bioactive Milk Peptides
- 02300 Circadian Sleep
- 01551 Enhanced Sleep with Melatonin
- 01511 Enhanced Sleep without Melatonin
- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 02308 Herbal Sleep PM
- 01722 L-Tryptophan
- 01668 Melatonin • 300 mcg, 100 veg capsules
- 01083 Melatonin • 500 mcg, 200 veg capsules
- 00329 Melatonin • 1 mg, 60 capsules
- 02503 Melatonin • 3 mg, 60 gummies
- 00330 Melatonin • 3 mg, 60 veg capsules
- 00331 Melatonin • 10 mg, 60 veg capsules
- 00332 Melatonin • 3 mg, 60 veg lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release  
300 mcg, 100 veg tablets
- 01788 Melatonin 6 Hour Timed Release  
750 mcg, 60 veg tablets

- 01786 Melatonin 6 Hour Timed Release • 3 mg, 60 veg tablets
- 01721 Optimized Tryptophan Plus
- 01444 Quiet Sleep Melatonin • 3 mg, 60 veg capsules
- 01445 Quiet Sleep Melatonin • 5 mg, 60 veg capsules
- 02502 Rest & Renew

**VITAMINS**

- 01533 Ascorbyl Palmitate
- 00920 Benfotiamine with Thiamine
- 00664 Beta-Carotene
- 01945 BioActive Complete B-Complex
- 00102 Biotin
- 00084 Buffered Vitamin C Powder
- 02229 Fast-C® and Bio-Quercetin Phytosome
- 02075 Gamma E Mixed Tocopherol Enhanced with  
Sesame Lignans
- 02070 Gamma E Mixed Tocopherol & Tocotrienols
- 01913 High Potency Optimized Folate
- 01674 Inositol Caps
- 02244 Liquid Vitamin D3 • 50 mcg (2000 IU)
- 02232 Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)
- 01936 Low-Dose Vitamin K2
- 00065 MK-7
- 00373 No Flush Niacin
- 01939 Optimized Folate (L-Methylfolate)
- 01217 Pyridoxal 5'-Phosphate Caps
- 01400 Super Absorbable Tocotrienols
- 02334 Super K
- 01863 Super Vitamin E
- 02422 Vegan Vitamin D3
- 02028 Vitamin B5 (Pantothenic Acid)
- 01535 Vitamin B6
- 00361 Vitamin B12 Methylcobalamin
- 01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges
- 01537 Vitamin B12 Methylcobalamin • 5 mg, 60 veg lozenges
- 02228 Vitamin C and Bio-Quercetin Phytosome • 60 veg tablets
- 02227 Vitamin C and Bio-Quercetin Phytosome • 250 veg tablets
- 01753 Vitamin D3 • 25 mcg (1000 IU), 90 softgels
- 01751 Vitamin D3 • 25 mcg (1000 IU), 250 softgels
- 01713 Vitamin D3 • 125 mcg (5000 IU), 60 softgels
- 01718 Vitamin D3 • 175 mcg (7000 IU), 60 softgels
- 01758 Vitamin D3 with Sea-Iodine™
- 02040 Vitamins D and K with Sea-Iodine™

**WEIGHT MANAGEMENT & BODY COMPOSITION**

- 02479 7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules
- 01807 Advanced Appetite Suppress
- 02207 AMPK Metabolic Activator
- 02504 Body Trim and Appetite Control
- 02478 DHEA Complete
- 01738 Garcinia HCA
- 02506 Mediterranean Weight Management
- 01432 Optimized Saffron
- 00818 Super CLA Blend with Sesame Lignans
- 02509 Waistline Control™

**WOMEN'S HEALTH**

- 01942 Breast Health Formula
- 01626 Enhanced Sex for Women 50+
- 01894 Estrogen for Women
- 01064 Femmenessence MacaPause®
- 02204 Menopause 731™
- 02319 Prenatal Advantage
- 01649 Super-Absorbable Soy Isoflavones
- 02507 Youthful Woman 40+ with B-Complex

**DUAL-ACTION  
JOINT SUPPORT**

# Get Moving!

**Joint Mobility** is a patent-pending blend  
of **tamarind** and **turmeric** extracts.



A placebo-controlled **clinical trial\*** shows these  
**plant extracts** help:

- Support you to walk farther and faster
- Promote knee flexibility and range of motion
- Reduce occasional knee discomfort
- Inhibit inflammation to support continued joint health

**Item #02424** • 60 vegetarian capsules  
Each capsule provides **200 mg**  
of **tamarind-turmeric** extract

1 bottle **\$18.75** • 4 bottles \$17 each

For full product description and to order **Joint Mobility**,  
call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)

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

TamaFlex® is a trademark of NXT USA, Inc. Patents pending.



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



# 45 Times Greater Bioavailability CURCUMIN



Patented **turmeric** and **fenugreek blend** (500 mg) results in **45 times** greater bioavailability of free **curcuminoids**.

**Item #02407**

500 mg, 60 vegetarian capsules

1 bottle **\$24** • 4 bottles \$22 each



Same 500 mg potency of patented **turmeric** and **fenugreek blend** with added benefits of **ginger** and other **turmeric** actives.

**Item #02324**

500 mg curcumin + gingerol, 30 softgels

1 bottle **\$20** • 4 bottles \$18 each

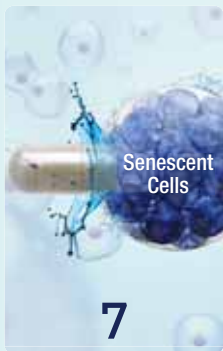
For full product description and to order **Curcumin Elite™** or **Advanced Curcumin Elite™**, call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)



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



## IN THIS EDITION OF *LIFE EXTENSION* MAGAZINE<sup>®</sup>



### 7 WHAT IS DELAYING SENOLYTICS?

**Senolytics** promise to delay and reverse **aging** processes. Bureaucratic barriers are impeding rapid clinical trials of **senolytic** compounds.

### 22 FULL-STRENGTH ECHINACEA

Researchers recommend using *multiple* species and parts of the **echinacea** plant to fully obtain its **immune benefits**.



### 38 CANCER-FIGHTING IMPACT OF BLACK TEA

Preclinical data show that **black tea theaflavins** block cancer development and progression. Human studies are urgently needed.

### 46 SINGLE DOSE OF L-THEANINE LOWERS STRESS

With **extended-release** forms, **L-theanine** can reduce stress for up to **six hours**.



### 55 WHAT IS LACTOFERRIN?

**Lactoferrin**, a protein associated with mother's milk, disrupts viruses from binding to cells and boosts natural killer cell activity.

### 62 MANAGE AFTER-MEAL BLOOD SUGAR SPIKES

Studies show that extracts of **clove** and **maqui berry** can reduce dangerous *after-meal* blood **glucose** spikes.