

The Science of a Healthier Life[®] LifeExtension.com December 2024 FEATURE ARTICLES

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Combined with other compounds this may help protect **brain health**.

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34 EFFECTS OF MUSHROOMS ON IMMUNITY Combining beta glucans with mushroom

extracts can *enhance* **immune functions** and *reduce* **upper respiratory infections**.

46 ASTAXANTHIN'S SYSTEMIC EFECTS

In human studies, **astaxanthin** has been shown to benefit the **eyes**, while helping to *protect* against **skin aging**, cardiometabolic risks, and age-associated **cognitive decline**.

58 HEALTHY DIETS PROTECT THE BRAIN

Numerous studies show that consuming more <u>un</u>processed and plant foods, such as those found in the **Mediterranean** and **MIND diets**, may *improve* **brain health** and *lower* **dementia risk**.

68 CLEAN UP YOUR CELLS WITH CURCUMIN

In preclinical models, **curcumin** *activated autophagy*, the internal **cellular cleansing** process that declines with age.



ALZHEIMER'S REVERSAL MOVES TO THE CLINIC

For <u>decades</u>, *Life Extension*[®] readers have been educated on ways to delay and reverse earlystage cognitive deficits. Now, a new clinical trial has suggested reductions in cognitive decline with comprehensive lifestyle interventions that include **diet**, **exercise**, and supplemental **nutrients**.

15 IN THE NEWS

Higher levels of nutrients in the blood may delay brain aging; salting food at the table linked to gastric cancer; female military recruits taking multivitamins suffer fewer injuries; flavonoid-rich diet lowers dementia risk.





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Alzheimer's Reversal Moves to the Clinic



WILLIAM FALOON



Until recently, an **Alzheimer's** diagnosis was viewed as a terminal illness with no current cure.

The families are told to expect continued deterioration of **brain function** until the patient drifts into a vegetative state.

Readers of *Life Extension Magazine*[®] have been educated about different approaches that can help <u>reverse</u> *early*-stage Alzheimer's cognitive deficits. Much of this is now being implemented in varying ways by mainstream medicine.

As reported in the **Wall Street Journal**, a revolution is happening in the way some doctors diagnose and treat early-stage disease. This is enabling Alzheimer's victims to live relatively normal lives several years *longer* compared to when they were told to go home and prepare for the worst.¹

Progressive neurologists are improving Alzheimer's victims' lives by emphasizing the cognitive benefits of **healthy lifestyles** and avoiding behaviors that hasten mental decline. Patients are encouraged to eat better, exercise, stop smoking, moderate alcohol intake, correct hearing loss, sleep issues, and depression...and keep their brains <u>active</u>.

Patients are also warned about the neurotoxicity of chronic use of certain medications (like protonpump inhibitors), environmental pollutants, and heavy metals.

Expensive new drugs can slow cognitive decline but require close monitoring due to side effects like brain edema and bleeding.² The **Wall Street Journal** described Alzheimer's patients who slow their disease course and boost overall well-being by managing their disease in an upbeat, positive manner while avoiding negative connotations about **aging**.¹

Just two months later, a new **clinical trial** was published that involved participants with mild cognitive impairment or early-stage Alzheimer's dementia. It suggested potential <u>reductions</u> in **cognitive decline** in response to comprehensive lifestyle interventions that included diet, exercise, and supplemental **nutrients.**³

I felt a sense of vindication when reading about these clinical benefits but regret that they have been overlooked by mainstream neurology for so long.

This article describes published findings about diet and lifestyle patterns associated with **delay** and **reversal** of age-related cognitive decline.



Encouraging findings from large **human trials** reveal methods to protect cognitive function even into our advanced years. One study found that modest dietary changes can slash **Alzheimer's** risk by **35%** when a healthy diet is consistently followed.⁴

Aging is associated with **mild cognitive impairment** that can progress to full-blown **Alzheimer's**.^{5,6,7}

An analysis from the 2020 U.S. census found that a startling **34.6%** of adults 85 years and older were living with clinical Alzheimer's disease.⁸

The good news is that decades of research have led to practical approaches that aging individuals can adopt to reduce their senility risk.



Impact of Diet on Brain Health

Diet is a powerful factor that affects whether we develop **dementia**.

A randomized controlled trial published in **2015** corroborates the **brain-boosting** benefits that occur in response to healthier dietary choices.⁹ I suspect most of you reading this have been following at least some of these beneficial eating patterns.

A 2016 publication titled "*Dietary Patterns and Risk of Dementia: A Systematic Review and Meta-Analysis of Cohort Studies*" revealed:¹⁰

- 12% <u>decreased</u> risk with higher antioxidant intake,
- 16% <u>decreased</u> risk with higher unsaturated fat intake,



- 28% <u>decreased</u> risk with higher vitamin B intake,
- 31% <u>decreased</u> risk with greater adherence to the **Mediterranean diet**,

and conversely:

- 43% increased risk in cigarette smokers,
- 52% increased risk in people with low vitamin D levels,
- 224% increased risk in people with higher aluminum levels,

and need to further investigate:

- Fish consumption: 21% decreased risk, and
- Fruit and vegetable intake: 54% decreased risk.

The authors concluded this meta-analysis with the following:

...the Mediterranean diet and higher consumption of unsaturated fatty acids, antioxidants, and B vitamins decrease the risk of dementia, while smoking and higher consumption of aluminum increase the risk of dementia. Low levels of vitamin D were associated with cognitive decline. The effect of [consuming] fish, vegetables, fruits, and alcohol needs further investigation. The findings will be of great significance to guide people to prevent dementia.¹⁰ What impressed me about these **human** studies is that they show **reversals** of cognitive dysfunction even in the elderly.

In one study conducted at Rush University, the average age of the subjects was **81** years, showing that it may never be too late to alter one's dietary patterns to protect brain function.⁴

Role of Magnesium

Intriguing discoveries over prior decades associate greater **magnesium** intake with <u>lower</u> **dementia** risk.¹²⁻¹⁴

Findings from a **2022** published study suggest that *higher* **magnesium** intake <u>alone</u> may **improve** cognition in older Americans...<u>if</u> they have sufficient blood levels of **vitamin D**. (Magnesium is needed to <u>activate</u> vitamin D in the body.)¹³

A **2023** published study showed *higher* **magnesium** intake is related to larger brain volumes and reduced pathologies that predispose people to dementia.¹⁴

Yet most Americans do <u>not</u> obtain enough dietary **magnesium**.

Combining **lifestyle** and **dietary** factors shown to protect against cognitive decline with adequate **nutrient** intake may yield remarkable neuro-protective results.

New Clinical Trial

As I was finishing this editorial, results from a new randomized controlled **clinical trial** by Dean Ornish's research group were published.³

Patients with mild **cognitive impairment** or *early-stage* dementia were randomized to either a comprehensive lifestyle intervention program **or** a control group.

After only 20 weeks, the comprehensive lifestyle **intervention group** (e.g. diet, exercise, stress management, dietary supplements) showed evidence of statistically significant, beneficial changes in cognitive function in several validated tests of cognition.

These findings were further supported by observed changes in the **microbiome** and improvements that correlate with the degree of lifestyle changes. Those who better <u>adhered</u> to the multiple **interventions** showed *greater* **improvement** in <u>all</u> four measures of **cognition** and **function**.

And the degree of Alzheimer's blood biomarker improvements (such as the A β 42/40 ratio) correlated with the **degree of compliance** with the **interventions**.



Olive Oil Lowers Dementia Death Risk

A study published by the **American Medical Association** (May 6, 2024) showed a correlation between modest **olive oil** intake and <u>reduced</u> risk of **dementia death**.

This study observed over **92,000** adults over **28 years** and found that consuming just over half a tablespoon a day of **olive oil** was linked to a **28%** <u>lower</u> risk of dementiarelated death.¹¹

The authors of this study, mostly from Harvard, concluded "Opting for olive oil... instead of fats such as margarine and commercial mayonnaise, is a safe choice and may reduce the risk of fatal dementia."

Even those with a strong genetic predisposition to Alzheimer's (APOE e4 gene carriers) reduced their dementia death risk by consuming **olive oil** instead of unhealthy fats.

The greatest risk reduction (28%) compared those who rarely or <u>never</u> ingested **olive oil** to those who consumed a modest half tablespoon or more a day.

This may be the <u>first</u> major study to investigate whether this staple of the **Mediterranean diet** (olive oil) reduces dementia death risk. In addition to diet, exercise, and stress management, the following daily doses of **dietary supplements** were used in the **intervention** group:

- Coenzyme Q10: 200 mg
- Curcumin: 800 mg
- Omega-3 fatty acids: (1680 mg of EPA/DHA)
- Multivitamin and Minerals (without iron)
- Vitamin C: 1000 mg
- Vitamin B12: 500 mcg
- Magnesium L-Threonate: 144 mg
- Lion's Mane: 2000 mg
- Probiotic blend: 471 mg

These are preliminary findings in a small, controlled clinical trial. They nevertheless are promising, and support other, previously published evidence that in some patients with mild cognitive impairment and/or early-stage dementia, their condition may be partially **reversible**. Longer, larger multi-center clinical studies should be conducted to ascertain sustainable success with confidence.

Although prevention is not necessarily the same as actual treatment (of pre-existing dementia), these results are also consistent with prior studies suggesting **healthy lifestyles** to be associated with <u>reduced</u> dementia or cognitive impairment.¹⁵⁻¹⁹

Take Charge of your Brain Health!

While some enlightened clinicians seek to correct Alzheimer's risk factors, most lack the time to fully engage with an individual patient's needs.

This is where the concept of being a "**proactive patient**" becomes apparent.

Those concerned about cognitive decline today can take an <u>active</u> role in managing their health, treatment decisions, and overall well-being.

We encourage supporters to educate themselves when confronted with neurological deficits, ask questions, seek out second opinions, and participate in discussions with their healthcare providers. Rather than being passive victims, proactive patients are empowered to make informed decisions that are more likely to achieve better outcomes.

And coincidentally, the process of **patient empowerment** keeps one's brain <u>active</u>, which is another factor that helps combat neurological decline.

The article on page 58 of this month's issue describes dietary patterns shown in multiple studies to be associated with **improved** cognitive functions.

For longer life,

William Faloon, Co-Founder Life Extension





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In the News



Delayed Brain Aging Linked with *Higher* Nutrient Blood Levels

A recent study revealed an association between blood nutrient biomarkers and differences in indicators of **brain aging**.*

In people with delayed brain aging, compared to those with accelerated brain aging, blood nutrient biomarker assessment revealed *higher* levels of **omega-3** and other fatty acids, lutein, zeaxanthin, vitamin E, and choline.

Women and men with *delayed* brain aging performed <u>better</u> in tests of intelligence, executive function, and memory.

Individuals with <u>accelerated</u> brain aging had an average brain age of **65.1** years compared to people with <u>delayed</u> brain aging who had an average brain age of about **59.7** years.

Editor's Note: Participants included 100 older men and women who also received magnetic resonance imaging (MRI) of the brain to measure structure, metabolism, and functional connectivity. A total of 139 brain health variables were measured.

* npj Aging 10, 27 (2024).

Always Adding Salt to Food? You Could be Adding Risk of Gastric Cancer

Individuals who always add salt to their food at the table have an increased risk of gastric cancer, according to a study published in the journal *Gastric Cancer*.*

Using data collected from the UK Biobank, which included 471,144 people, researchers obtained information on the frequency of adding salt to food. They compared these findings to cancer incidence from national cancer registries.

Over an average follow-up of 10.9 years, people who reported "always" adding salt to their food had a **41%** *higher* risk of gastric cancer, compared to people who reported "never or rarely" adding salt to their food.

Editor's Note: The American Heart Association recommends limiting daily sodium intake to no more than 2,300 mg but ideally it should be no more than 1,500 mg for most adults.** However, since numbers like these can be difficult to assess, the researchers concluded that using terms like "always adding salt to food" could be a useful indicator of salt intake, as well as a risk assessment of gastric cancer.

* Gastric Cancer. 2024 Apr 17.

** Available at: https://www.heart.org/en/ healthy-living/healthy-eating/eat-smart/ sodium/how-much-sodium-should-i-eatper-day. Accessed September 6, 2024.





Female Military Recruits Who Take Multivitamins have Fewer Injuries

Female military recruits undergoing basic training who received in-person education about **multivitamins** and had better compliance with a multivitamin regimen were found to have significantly <u>fewer</u> overuse musculoskeletal injuries and bone stress injuries compared to those with less knowledge and poorer compliance.*

The study included 159 recruits in the seven-and-a-half-week initial entry training for all enlisting U.S. Air Force and Space Force recruits. They all received multivitamins. Seventy-nine trainees viewed an educational video created by dieticians concerning the subject of multivitamins and also received an in-person briefing by a group of experts. The remaining 80 women were only shown the video.

Women who received the in-person briefing concerning multivitamins reported greater **compliance** with **multivitamin** use.

In the group that received the briefing, musculoskeletal injuries were diagnosed among **17.72%** of the recruits and bone stress injuries among **5.06%**. In participants who viewed the video only, **31.25%** were diagnosed with musculoskeletal injuries and **15%** with bone stress injuries.

This study demonstrates the benefits of **in-person** learning as opposed to watching videos.

Editor's Note: The multivitamin formula provided to the recruits included vitamins A, B complex, C, D, and E, calcium, iron and zinc.

Mil Med. 2024 Aug 19;189(Supplement_3): 93-98.

High Intake of Flavonoid-Rich Foods Reduces Dementia Risk

A flavonoid-rich diet has been associated with a lower risk of dementia—especially among those with a high genetic risk or depressive symptoms—according to a study published in JAMA Network Open.*

Flavonoids are beneficial plant compounds found in common foods such as tea, red wine, and berries.

Compared to those in the lowest quintile of flavonoid intake, those in the *highest* quintile (which was defined as **six** additional servings of flavonoids per day) had a **28%** lower risk of dementia. The highest intake of flavonoids was associated with a **43%** <u>lower</u> risk among those with a high genetic risk of dementia, and a **48%** <u>lower</u> risk among those with depressive symptoms.

Consuming at least <u>two</u> of the following per day was connected to the greatest risk reduction: five servings of tea, one serving of red wine, or half a serving of berries.

Editor's note: This cohort study included 121,986 participants from the UK Biobank aged 40-70. Data were collected from 2006 to 2010, with an average follow-up of 9.2 years.

* JAMA Netw Open. 2024;7(9):e2434136.





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

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Support BRAIN Health and COGNITIVE Function



ASHWAGANDHA

PERIWINKLE

BY RANDY STEVENS

Several plant extracts have been found to benefit **brain health** and boost **cognitive function** in <u>human</u> studies.¹⁻⁵

In a clinical trial of older adults, taking a specific **sage extract** led to a roughly **60%** improvement in measures of **memory** and a **2.5-fold** enhancement in accuracy of **attention**, compared to a **placebo**.⁶

Scientists have <u>combined</u> this extract with other compounds to support optimal brain function and potentially ward off neurological dysfunction.

SAGE

Defend the Brain

Mild cognitive impairment is common with advancing age, and can progress to Alzheimer's and other forms of dementia.⁷

Researchers have found nutrients that may improve and defend **brain health**, providing resources the brain needs to function optimally.

In particular, the Mediterranean herb **sage** can influence biological mechanisms that benefit brain health. Studies have shown promising memory^{1,6,8,9} and cognition-enhancing effects of sage in **human** adults.^{6,8,9}

Optimizing Sage Extract

Sage has long been used for culinary and medicinal purposes. It is rich in compounds with known benefits, including **rosmarinic acid**, **carnosic acid**, and **luteolin**.⁹

In preclinical studies rosmarinic acid has been shown to *increase* **brain-derived neurotrophic factor**, a regulator of neuronal growth and function.⁹

Several studies demonstrate health benefits of sage and its extracts. $^{\mbox{\tiny 1,9}}$

Researchers zeroed in on a **standardized sage extract** from a source of the herb farmed in England.¹⁰

This **sage extract** was tested against others in animal models. It was found to **prolong lifespan** in roundworms by **12%**, while other sources of sage did <u>not</u>.¹¹



Human Studies

Several studies have documented that **sage extract** has a significant impact on human **brain health**.

In acute effects studies of healthy subjects, consuming sage extract led to a boost in **mental performance**, with improved mood,^{8,12} less anxiety, and improvements to memory and attention.¹² In one of these studies participants even reported less mental fatigue.⁸

In a randomized placebo-controlled trial of acute effects of sage extract, 20 healthy older adults were given a standardized extract of sage at doses ranging from **167 mg** to **1,332 mg**. The participants took single doses separated by seven-day washout periods. The **333 mg** dose of standardized sage extract from England led to about **60%** improvement in a composite measure of **memory** and **2.5-fold** enhancement in accuracy of **attention**, compared to a placebo.⁶

Remarkably, these improvements were seen just *hours* after taking the extract.

Studies that used different types of sage extract achieved similar findings in older adults with **cognitive dysfunction**.^{13,14}

For instance, in patients suffering from mild to moderate **Alzheimer's disease**, a different **sage extract** was administered daily for four months and resulted in better **cognitive function** assessment scores than in those who took a placebo.¹³

How Sage Works

Sage helps defend the brain and boost its function in multiple ways, including:

• **Inhibiting acetylcholinesterase.** Preclinical⁹ and clinical^{8,12} research has shown that sage inhibits *acetylcholinesterase*, an enzyme that breaks down the neurotransmitter **acetylcholine**.

Low levels of acetylcholine are tied to cognitive deficits and are seen with cognitive impairment and Alzheimer's disease.¹⁵

In one clinical study of patients with Alzheimer's, *blocking* acetylcholinesterase with drugs was found to be associated with more than **20% lower mortality** overall.¹⁶ Cholinesterase inhibitors are one of the available medication options for cognitive support and delay in the progression of dementia.¹⁷

SUPPORT BRAIN HEALTH AND COGNITIVE FUNCTION

WHAT YOU NEED TO KNOW

Better Brain Health

- Brain function typically declines with age, in many cases leading to cognitive impairment and dementia.
- In an acute effects clinical study of healthy older adults, a standardized sage extract boosted performance of memory tasks by about 60% and improved attention 2.5-fold compared to a placebo.
- A different sage extract also boosted cognitive function scores in adults with mild to moderate Alzheimer's disease.
- Combining sage extract with other compounds and extracts was shown to support brain health and may improve cognitive function.
- Reducing beta-amyloid buildup. In preclinical studies, sage and its components have demonstrated an ability to reduce aggregation of **beta-amyloid**, a protein that forms plaques in the brains of Alzheimer's disease patients.^{9,18,19} This has improved cognitive function and prevented cognitive dysfunction in animal models.⁹
- Supporting neurotrophin levels. Lab experiments have shown rosmarinic acid in sage helps support healthy levels of neurotrophins, including brain-derived neurotrophic factor (BDNF).^{9,20} Neurotrophins are regulating compounds that support brain structure and function. Lower levels of BDNF are seen in patients with Alzheimer's and mild cognitive impairment.^{9,21}



 Anti-inflammatory activity. Amyloid brain deposits in Alzheimer's are widely believed to be contributors to cognitive decline. Amyloid may also cause inflammation and oxidative stress. Compounds in sage possess potent antioxidant and anti-inflammatory properties.⁹ Both neuroinflammation and oxidative stress may occur in the early stages of Alzheimer's disease and cause damage to brain cells.²²

Other Brain-Supporting Compounds

In addition to sage, other nutrients have been shown to support brain health, including:

PHOSPHATIDYLSERINE

Phosphatidylserine is a phospholipid component of **nerve cell membranes**, which carry nerve impulses in the brain. It is also a vital part of the **myelin sheath** that insulates nerve fibers, making their conduction more efficient and rapid.²³

Supplementing with phosphatidylserine can help maintain optimal cognitive function. A meta-analysis of human studies concluded that phosphatidylserine intake ranging from **100** to **300 mg** daily improved **memory** in older adults with cognitive decline.²

ASHWAGANDHA

Used in traditional Indian medicine for centuries, the herb **ashwagandha**²⁴ is best known for improving **mood** and reducing **stress**.^{4,24,25} Preclinical as well as some clinical research shows that ashwagandha extract protects neurons from neurodegenerative processes associated with Alzheimer's, Parkinson's, and Huntington's diseases.²⁶

In human studies, ashwagandha extract has also been shown to improve memory and cognitive function.²⁷⁻²⁹ In a study of older adults with mild cognitive impairment, ashwagandha intake improved **memory**, **attention**, and **executive function**, our reasoning and decision-making ability.²⁸

BLUEBERRY EXTRACT

Anthocyanins, polyphenols with wide-ranging health benefits, are concentrated in dark-colored fruits like blueberries.

Human trials have found that **blueberry** intake leads to improved cognitive performance in older adults,^{3,30-33} including enhanced **memory**, and faster **processing speeds**. Blueberry juice intake has been shown to significantly improve **mood** in children and younger adults.³⁴

VINPOCETINE

Vinpocetine, a compound derived from the periwinkle plant, shows benefits for the nervous system in animal and cell studies, including improving blood flow in the brain.³⁵

In a clinical trial of patients with ischemic stroke, 12-week oral supplementation with vinpocetine improved the cerebrovascular reserve capacity and improved cognitive status and general condition of patients with chronic hypoperfusion.³⁶

URIDINE 5'-MONOPHOSPHATE

Loss of **synapses** occurs with age and neurodegeneration. Synapses are the structures where brain cells communicate with another part of our neural network.

Uridine 5'-monophosphate is a compound that supports the formation of synapses, the structures where brain cells communicate. Loss of synapses occurs with age and neurodegeneration.^{37,38}

Studies show that patients with **Alzheimer's disease** may have low levels of uridine 5'-monophosphate.^{39,40} Supplemental intake of uridine has been shown to be beneficial for patients with Alzheimer's disease.³⁸

PREGNENOLONE

Pregnenolone is a hormone that helps modulate nervous system function.

In preclinical studies, pregnenolone demonstrates **neuroprotectant** activity with benefits to **mood**, **memory**, and other cognitive functions. In human trials it has shown significant improvements in well-being, psychomotor activities (cognition and motor performance), and learning.⁴¹

Taking these compounds together with **sage** may help maximize brain health benefits and improve memory and cognition.

Summary

Millions of older adults suffer from cognitive decline, Alzheimer's disease, and other forms of dementia.

A standardized **sage extract** has been shown to improve **cognitive function** in a clinical trial.

Combining this extract with other ingredients shown to support **brain health** may boost cognitive function and help protect against degenerative decline. •

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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Mushrooms

STERNE S

Maitake Shiitake Chaga
Effects of MUSHROOMS on Immune Functions

BY HEATHER L. MAKAR

Mushrooms have been used in traditional **medicine** for thousands of years.^{1,2}

Fungi, including mushrooms and yeast, are rich in compounds called **beta glucans**, which have **antiviral** and **immune-supporting** effects.^{3,4}

In human studies, taking beta glucans was shown to boost immune response,⁵ reduce the number, severity, and duration of **upper respiratory infections**⁶⁻⁸ (such as colds and flu), and ease symptoms of **seasonal allergies**.⁹

Researchers have identified <u>three</u> mushrooms with particularly strong immune benefits: **shiitake**,¹⁰ **maitake**,¹¹ and **chaga**.¹²

Combining isolated **beta glucans** with **mushroom extracts** may offer well-rounded immune support benefits.

Beta Glucans Boost Immunity

Beta glucans are polysaccharides bound within the walls of fungi, bacteria, and some whole grains like oats. They are found in particularly high amounts in **mushrooms** and can be isolated from **yeast**.

They can help support **immune** health and boost defenses against **viruses** and other pathogens.¹³⁻¹⁵

They have also been shown in preclinical studies to reduce the effects of **endotoxins**, harmful byproducts of bacterial infections that cause inflammation.^{16,17}

There are two types of immune responses: **innate** and **adaptive**.^{18,19}

Innate immunity is the body's first line of defense. **Macrophages** engulf and neutralize viruses and other pathogens, while **natural killer (NK) cells** target and destroy unhealthy cells that are cancerous or infected by viruses and other pathogens.

Adaptive immunity is a more specific, targeted response that develops after exposure to a particular pathogen and provides long-term protection. This response is driven by **T-cells** and **B-cells**.

Beta glucans activate and stimulate <u>both</u> innate and adaptive immunity.^{10,20,21}

As we age, our immune system weakens and loses its ability to fight off infections and cancer, a condition known as **immunosenescence**.



Animal studies indicate that **beta glucan** intake can prevent or even reverse immunosenescence.^{20,22}

Renewing these immune responses is particularly important to older individuals.

Mushrooms With Maximum Benefits

Mushrooms contain health-promoting compounds, including **indoles**, **polyphenols**, and **carotenoids**.

Beta glucans are among these biologically active immune-supporting compounds found in mushrooms.²³

There are thousands of species of mushrooms that have health benefits.²⁴ Three mushrooms that have been found to provide especially strong immune effects are: **shiitake**, **maitake**, and **chaga**.

SHIITAKE

Shiitake mushrooms have long been used in traditional Chinese medicine.

In an animal model of severe bacterial **lung infection**, beta glucans from **shiitake mushrooms** significantly reduced the bacterial load in the lungs and improved health.²⁵

Cell studies show that shiitake mushrooms inactivate viruses and downregulate viral replication.^{26,27}

As demonstrated in a clinical study, these immuneboosting effects are likely due to shiitake's ability to increase the number of **immune system cells**, including T-cells and NK cells.¹⁰

Shiitake mushrooms also decrease markers of harmful **chronic inflammation** and stimulate secretion of **antibodies** that protect the gut.¹⁰

MAITAKE

Maitake mushrooms, often used in Asian cuisine, also provide powerful immune benefits.

In animal studies, **maitake extract** significantly increased **NK cells** and **bacterial elimination**.^{28,29} This effect was even more pronounced when blended with shiitake extract.²⁹

Maitake extract also promoted secretion of **interferon gamma (IFN-γ)**, a protein that blocks viral replication.²⁹

CHAGA

Chaga mushrooms are native to colder climates and often grow on birch trees. They are immunomodulators, and in preclinical studies chaga extract has shown antiviral activity.³⁰

WHAT

YOU

NEED

TO KNOW

Shiitake

Mushrooms

In a study of immune-compromised mice, chaga extract **restored immune cells** to nearly normal levels and regulated the levels of **tumor necrosis factor alpha (TNF-a)**, a marker of inflammation, indicating that chaga extract prevented excess inflammation.³¹

In preclinical studies, chaga extract has also exhibited beneficial **activity** against a wide range of **viruses**.^{12,30,32}

Defense Against Infectious Diseases

Beta glucans have been shown to help protect against and treat infections from bacteria, viruses, and parasites.³³⁻³⁵

In various placebo-controlled **human trials**, participants were randomized to receive **beta glucans** or **placebo**. These trials used at least **250 mg** of **beta glucans** daily.

Participants who were part of the beta-glucan group had: $^{\text{5-8,36,37}}$

- Reduced **upper respiratory infections**, including colds and flu,
- Shortened duration of symptoms,
- Fewer lost workdays,
- Increased circulating interferon, and
- Higher levels of salivary **antibodies**, which protect against respiratory and digestive pathogens.

Another study investigated beta glucans' effect on adults who suffer from moderate **seasonal ragweed allergies**.

Compared to a placebo, those who took **250 mg** of beta glucans daily had a reduction in the **duration** and **intensity** of **allergy** symptoms, along with improvements in sleep, quality of life, energy, and mood.⁹

Better Gut Health

There are a variety of microorganisms in the digestive tract. A balanced **microbiome** is critical to fighting infection and maintaining immune health.³⁸

One way beta glucans and mushrooms support immunity is by promoting the growth of healthy microorganisms in the **gut**. Mushrooms' Benefits for the Immune System

- Mushrooms have been used in traditional medicine for thousands of years.
- Fungi, including mushrooms and yeast, are rich in many active compounds responsible for immune-supporting benefits, including **beta glucans**.
- In human trials, taking beta glucans reduced the number and duration of upper respiratory infections, including colds and flu, and relieved seasonal allergy symptoms.
- In a meta-analysis of observational studies, those who consumed the most mushrooms had a 34% lower risk of cancer than those who ate none.
- Combining beta glucans with extracts of the immune-supporting mushrooms shiitake, maitake, and chaga may optimize the immune system's ability to ward off infections and other illnesses.

Three Types of Mushrooms with Strong Immune Benefits



Beta glucans serve as a **prebiotic fiber** that nourishes beneficial bacteria.^{13,39}

Preclinical and clinical studies have shown a healthy microbiome contributes to a robust **immune** response, supports a healthy gut lining and digestive health, and inhibits growth of disease-causing bacteria and inflammation.^{13,40-42}

In addition, beta glucans promote the production of **short-chain fatty acids**, which are vital for gut health and maintaining the integrity of the gut barrier.^{13,40,42}

Fighting Cancer

In September 2021, scientists with the College of Medicine at **Pennsylvania State University** published results from a cohort study of over **30,000 people**. They also included their data in a meta-analysis of prospective studies that had over **600,000** participants, on the relationship between **mushroom intake** and **mortality**.⁴³

They found that *higher* mushroom consumption correlated with a *lower* risk of **death** from *any* **cause**.

This study had several major strengths, including the fact that it analyzed a nationally representative sample of the American adult population, and involved a very comprehensive meta-analysis of cohort studies around the world.

When operating properly, the immune system can identify and neutralize **cancerous cells**. By supporting immunity, mushrooms may improve this ability.

One meta-analysis of observational studies that included over 615,000 people, nearly **20,000** of whom were cancer patients between 1966 and 2020, found that those who consumed the *greatest* amount of **mushrooms** had a **34%** <u>decreased</u> risk of cancer compared to those who ate the least.⁴⁴

Beta glucans and other compounds in **shiitake**, **maitake**, and **chaga** mushrooms increase the activity of protective signaling proteins that can inhibit tumor cell growth.^{30,45}

A <u>combination</u> of beta glucans and extracts of these mushrooms can provide a wide range of immune-supportive compounds.

Summary

Mushrooms have been used medicinally for thousands of years. Research shows that they contain compounds called **beta glucans**, which support immunity and gut health and help protect against viruses and cancer.

A blend of beta glucans isolated from **yeast**, with extracts of **shiitake**, **maitake**, and **chaga** mushrooms may offer well-rounded immune support benefits. •

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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01727	Bone Restore Calcium Supplement with Vitamin K2 120 capsules Skeletal-strengthening nutrients in one highly absorbable formula.	1 unit 4+ units	\$ 18.00 —	^{\$} 16.20 ^{\$} 14.85 ea.	10% 18%
02414	Bio-Fisetin® • 30 vegetarian capsules A bioavailable form of the plant flavonoid fisetin supports cell health in multiple ways.	1 unit 4+ units	\$ 11.25 _	^{\$} 10.13 ^{\$} 9.00 ea.	10% 20%
02301	Senolytic Activator [®] • 36 vegetarian capsules (3-month supply) Highly <i>absorbable</i> forms of fisetin, quercetin, plus apigenin and theaflavins designed to help manage senescent cells.	1 unit 4+ units	\$ 19.50 —	^{\$} 17.55 ^{\$} 16.20 ea.	10% 17%
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02029	Ultra Prostate Formula • 60 softgels Comprehensive support utilizing extracts from pygeum, nettle, flower pollen, and saw palmetto, plus boron, beta-sitosterol, and lycopene.	1 unit 4+ units 10+ units	\$ 29.25 — —	^{\$} 26.33 ^{\$} 24.30 ea. ^{\$} 22.50 ea.	10% 17% 23%
00335	DHEA • 25 mg • 100 capsules Promotes optimal hormone balance and overall health.	1 unit 4+ units	\$ 11.25 —	^{\$} 10.13 ^{\$} 9.23 ea.	10% 18%
02534	Estrogen Balance Elite • 60 vegetarian tablets Encourages healthy estrogen production and helps relieve hormone-related discomforts with clinically studied fenugreek. This product is intended to promote estrogen but does not contain estrogen.	1 unit 4+ units	\$ 15.75 —	^{\$} 14.18 ^{\$} 12.83 ea.	10% 19%

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Astaxanthin FOR FULL-BODY HEALTH

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BY RICHARD REEVES

Astaxanthin is a **carotenoid** with impressive anti-inflammatory/antioxidant properties.^{1,2}

Research shows that astaxanthin has the potential to provide benefits throughout the body and can be a valuable component of anyone's health program.

While best known for its **eye health** benefits, astaxanthin has also been shown to hold promise for improvement in skin, liver, neuro-logical functions, and more.³

What Is Astaxanthin?

Astaxanthin (pronounced "asta-zanthin") is a red pigment in the **carotenoid** family, which also includes lycopene, lutein, and zeaxanthin.¹

It is formed in **microalgae** and **phytoplankton** in the sea.^{4,5} When eaten by some animals, the pigment concentrates in their tissues, leading to the reddish-pink colors of lobsters, crabs, shrimp, and salmon.^{2,6}

Astaxanthin is best known for its benefits to **eye health**. Its consumption can **protect vision** and help reduce the risk for and progression of chronic diseases of the eyes.^{2,7,8}

But astaxanthin can do <u>much</u> more.^{1,3,9} One recent review analyzes **dozens** of disorders that it has the potential to benefit, including Alzheimer's, cardiovascular disease, diabetes, fatty liver disease, and others.³

How It Works

Scientists have studied how this carotenoid could provide a variety of health benefits. One likely explanation for astaxanthin's biological power is its remarkable antioxidant activity, which is greater than many carotenoids,¹ as well as vitamins C and E.¹⁰

By helping cells scavenge free radicals, astaxanthin neutralizes these cellular toxins *before* they can damage tissues.^{1,11}



Astaxanthin's chemical structure allows it to insert itself into cellular membranes, which are susceptible to oxidative damage. There, astaxanthin acts as an **internal shield**, helping eliminate the threat of oxidative stress and mitochondrial damage¹⁰ that contribute to rapid aging and risk for chronic disease.^{10,12}

Astaxanthin is a superior free radical scavenger for preventing **oxidative damage** to cell membranes. And this property makes it beneficial for cardiovascular and immune health support.¹⁰

Astaxanthin is also a potent **anti-inflammatory**, reducing activity of **NF-kB** (**nuclear factor-kappa B**), a signaling protein that contributes to production of pro-inflammatory compounds.^{3,12}

This powerful pigment may also protect against many different conditions of aging that are associated with chronic inflammation. In one recent study, astaxanthin extended the **median lifespan** of male mice by **12%**.¹³

It also has the potential to improve **metabolic** health through its effects on two proteins, **AMPK** and **mTOR**, that regulate cellular metabolism. By *stimulating* **AMPK** and *inhibiting* **mTOR**, astaxanthin may reduce the risk for metabolic disease and insulin resistance.^{14,15}

In a **clinical trial** of diabetic patients, a **10 mg** daily dose of astaxanthin for 12 weeks resulted in reduction of **inflammatory** markers and **mTOR** activity.¹⁴

This suggests astaxanthin supplementation is a potentially effective strategy for improving cellular defenses, augmenting cellular housekeeping, and promoting autophagy.

Additional preclinical studies support these mechanisms of action related to inflammatory response, mitochondrial function, and autophagy, and suggest that astaxanthin could provide benefits in age-related chronic conditions including atherosclerosis, osteoarthritis, and neurodegenerative disorders.⁹

Eye and Skin Health

Preclinical and clinical studies have shown that astaxanthin is protective against a range of chronic eye conditions, including **cataracts** and age-related **macu-lar degeneration**.^{2,4,8}

In **human studies**, astaxanthin intake improves **visual acuity** (sharpness of vision) in healthy adults⁴ and protects against **eye strain**, even in people whose work involves looking at digital displays all day.^{2,16}



In two separate clinical studies of healthy volunteers, a **6-12 mg** daily dose of astaxanthin for two to four weeks resulted in improved **ocular blood flow**. One of the two trials even reported improvement of visual acuity.⁴ In another trial of patients with cataracts in both eyes, participants underwent surgery in one eye before receiving astaxanthin. The other eye was operated on after intake of the supplement for two weeks. At the end of the study, it was noted that intake of astaxanthin reduced markers of oxidative stress that can cause damage to the eyes.¹⁷

The skin serves as a primary barrier from the external environment. With advancing age, skin structure and integrity deteriorate, in part due to exposure to ultraviolet (UV) radiation.¹⁸ Oxidative stress and UV damage lead to accelerated skin aging, also known as "photoaging."^{18,19}

In preclinical studies, astaxanthin acts as an internal sunscreen, absorbing potentially harmful wavelengths of light²⁰ that cause **wrinkles**, dry skin, pigmentation, inflammation, and reduced skin elasticity.¹⁸

In a clinical trial, participants were randomized to receive **4 mg** daily astaxanthin or placebo for nine weeks. At the end of the study, they were exposed to controlled levels of UV rays. Upon exposure, participants in the treatment group had increased time before burning (sunburn), and reduced loss of skin moisture in areas exposed to UV light. Non-irradiated areas in the **astaxanthin** group showed significant improvement in skin texture and roughness.²¹

In addition, a 2021 **meta-analysis** of studies concluded that **astaxanthin** improves skin moisture content and elasticity and reduces **wrinkles**.²²

WHAT YOU NEED TO KNOW

A Powerful Pigment

- Astaxanthin is a carotenoid pigment responsible for the pinkish-red color of many fish and crustaceans. It is one of the most potent antioxidants and has many other health-promoting properties.
- Astaxanthin has long been known for its eye health benefits. It has been shown to improve visual sharpness and protect against common eye diseases.
- Human studies show that astaxanthin also helps protect against skin aging, reduces risk factors for metabolic and cardiovascular disease, improves liver health, and boosts measures of cognitive function.

Metabolic and Cardiovascular Disease

Beyond its proven antioxidant abilities, many studies have demonstrated astaxanthin's protective effects on inflammation and lipid and glucose metabolism, which offer potential to improve **arterial health**.

In preclinical studies astaxanthin has been shown to support healthy **glucose** metabolism and reduce the risk of **arterial blockage**. In clinical studies astaxanthin has shown an ability to inhibit **LDL** oxidation and increase **HDL** ("good") cholesterol, thereby helping protect against risk factors for heart disease.²³

In one pilot study of **heart failure** patients, a threemonth intake of astaxanthin not only *suppressed* **oxidative stress** and improved **cardiac contractility**, but it also *improved* their **exercise tolerance**.²⁴ Astaxanthin also improves several markers and risk factors for cardiovascular disease. In a study of healthy adults, astaxanthin intake reduced **triglycerides** and increased **HDL** ("good") cholesterol.²⁵ Similar results were seen in a trial of prediabetic adults with high cholesterol: **12 mg** astaxanthin daily for 24 weeks resulted in reduced levels of **fibrinogen** (a marker of CVD risk).²⁶

In another clinical study, participants, who were obese men, were randomized either to:

- · Receive 20 mg astaxanthin or a placebo, or
- Undergo high-intensity exercise training, or
- Receive astaxanthin along with undergoing high-intensity training.

After 12 weeks the exercise group had decreased body weight and had an improved lipid and metabolic profile. These changes were more pronounced in the group that received astaxanthin along with the training.²⁷

In postmenopausal women, taking **12 mg** of astaxanthin daily for eight weeks reduced **blood pressure**, improved markers of blood vessel health, and reduced signs of oxidative stress.²⁸



In a study of prediabetic individuals, taking **12 mg** of astaxanthin daily for 12 weeks resulted in improved glucose tolerance and heart function and reduced **hemoglobin A1c** levels (a measure of average glucose levels over time) and cholesterol.²⁹

Astaxanthin can even boost **physical performance**. In studies of younger athletes³ and older adults,^{3,30} astaxanthin intake increased endurance, improved walking distance and speed, and enhanced other measures of exercise performance.

Brain and Liver Function

As seen in preclinical studies, astaxanthin may help support neurologic functions and reduce risk for **dementia** in several ways, including:³

- Protecting brain cells from cell death,
- Preventing glutamate toxicity (which can kill neurons),
- Reducing buildup of the proteins associated with Alzheimer's disease and other neurodegenerative conditions, and
- Reducing neuroinflammation.

Human studies in both younger and older adults have shown that taking astaxanthin improves measures of cognitive function, including **memory** and **brain processing speed**.³

A trial in healthy middle-aged and elderly individuals who reported age-related decline in memory showed that supplementation with astaxanthin at a dose of **12 mg** daily for 12 weeks improved cognitive function.³¹

In animal models and preliminary human studies, astaxanthin can also help defend the liver from common threats. These include prevention and even reversal of fatty liver changes, liver fibrosis (scarring), and alcohol-induced liver damage.³

In a trial of **humans** with existing **fatty liver**, subjects were randomized to receive either **12 mg** of **astaxan-thin** per day for 24 weeks or a **placebo**. Compared to the placebo, astaxanthin was able to reduce liver fat and **slow the progression** of fatty liver.³²

Even in a study of healthy older women, astaxanthin reduced liver *enzymes* in the blood, which can be markers of **liver damage**.³³ This provides evidence that astaxanthin intake may protect the liver in people *with or without* any obvious signs of liver damage.

Summary

The carotenoid pigment **astaxanthin** has long been recognized for its protective effects in the **eyes**.

Preclinical and clinical studies show that astaxanthin intake has benefits for **skin** and **liver** while also supporting the health of the **cardiovascular**, **metabolic**, and **neurological systems**.

More benefits of astaxanthin are being uncovered, making this pigment a vital part of a health maintenance program. •

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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Vitamin A (as beta-carotene, acetate) 1,500 mcg^	5,000 IU
Thiamine (vitamin B1) (as thiamine HCI)	125 mg
Riboflavin (vitamin B2) (as riboflavin, riboflavin 5'-phosphate)	50 mg
Niacin (as 61% niacinamide, 38% niacin, 1% niacinamide ascorbate)	190 mg•
Vitamin B6 [as pyridoxal 5'-phosphate (100 mg), pyridoxine HCI (5 mg)]	105 mg
Folate (as L-5-methyltetrahydrofolate calcium salt)	680 mcg°
Vitamin B12 (as methylcobalamin)	600 mcg
Biotin	3,000 mcg
Pantothenic acid (as D-calcium pantothenate with 5 mg pantethine)	600 mg
Vitamin E (as D-alpha tocopheryl succinate, D-alpha tocopherol)	67 mg
Magnesium (as magnesium oxide, citrate, arginate, glycinate, taurinate, ascorbate)	420 mg
Selenium [as sodium selenite, SelenoExcell ^{®4} high selenium yeast, Se-methyl L-selenocysteine]	200 mcg
Zinc (as zinc citrate, L-OptiZinc®3 zinc mono-L-methionine sulfate)	35 mg
Calcium (as Ca ascorbate, D-calcium pantothenate, dicalcium phosphate)	140 mg
lodine (as potassium iodide)	150 mcg
Copper [as copper bisglycinate chelate]	1 mg
Manganese (as manganese citrate, gluconate)	1 mg
Chromium [as Crominex®5 3+ chromium stabilized with Capros® amla extract (fruit), PrimaVie® Shilajit]	500 mcg
Molybdenum (as molybdenum amino acid chelate)	125 mcg
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N-acetyl-L-cysteine (NAC)	600 mg
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Acerola extract 4:1 (berry)	300 mg
Inositol	250 mg
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Fruit/berry proprietary blend [European elder, blackberry, blueberry, sweet cherry, cranberry, plum, persimmon (Diospyros kaki) po	wders] 200 mg
Wild blueberry anthocyanin extract (fruit)	150 mg
Sensoril®11 Ashwagandha extract (root, leaf) [std. to 32% oligosaccharides, 10% glycoside conjugates]	125 mg
Silymarin [from milk thistle extract (seed)]	100 mg
Trimethylglycine (TMG) (as betaine anhydrous)	100 mg
CherryPure®1 sour cherry (tart cherry) proanthocyanidin powder (skin)	85 mg
POMELLA® pomegranate extract (fruit) [std. to 30% punicalagins]	85 mg
Natural mixed tocopherols (providing gamma, delta, alpha, beta tocopherols)	60 mg
MirtoSelect®11 bilberry extract (fruit)	30 mg
BioVin®7 grape proanthocyanidin extract (whole grape)	25 mg
Leucoselect ⁸⁶ grape seed proanthocyanidin extract	25 mg
Bio-Quercetin® Proprietary Blend providing 35% quercetin (5 mg) [from Japanese	
sophora concentrate (flower bud)], 30% galactomannans (4 mg) [from fenugreek (seed)	14 mg
Bromelain [from pineapple (stem)] (2400 gelatin digestive units/gram)	15 mg
Lutein [from marigold extract (Tagetes erecta) (flower)] (providing 465 mcg trans-zeaxanthin)	15 mg
Olive extract (fruit) (providing polyphenols, hydroxytyrosol, tyrosol, oleuropein)	12.5 mg
Sesame seed lignan extract	10 mg
Luteolin [from Japanese sophora (flower bud)]	8 mg
Apigenin	5 mg
Boron (as boron amino acid chelate)	3 mg
Lycopene [from LycoBeads®® natural tomato extract (fruit)]	3 mg
Delphinidins [from Delphinol ^{®2} maqui berry (Aristotelia chilensis) extract (fruit)]	2 mg
Cyanidin-3-glucoside (C3G) [from black currant extract (fruit)]	1.25 mg

itching, rash, or gastric disturbances may occur. Liver function testing is recommended when niacin is taken in excess of 500 mg daily. Consult with your doctor before using this product if you are taking anticoagulant medications. Individuals consuming more than 50 mcg (2,000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Vitamin D supplementation is not recommended for individuals with high blood calcium levels. Individuals with in-born errors of copper metabolism (e.g. Wilson's disease) should avoid daily, chronic use of this product

Caution: Temporary flushing,



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Other ingredients: maltodextrin, natural orange flavor, stevia extract, silica, food starch-modified, luo han guo extract, sunflower lecithin, sunflower oil.

^RAE (retinol activity equivalents). °DFE (dietary folate equivalents). •NE (niacin equivalents). Contains sesame.

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References 1. *Mol Nutr Food Res.* 2012 Sep;56(9):1385-97. 2. *Eur J Pharm Sci.* 2003 Jul;19(4):299-304.

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A Healthy Diet Supports BRAIN HEALTH

BY RYAN STARKE

They say, "You are what you eat." It turns out this is particularly true for your **brain**.

A poor diet can contribute to increased risk of **neurodegeneration.**^{1,2} A healthy diet can help maintain peak mental performance and shield against **cognitive decline** and **dementia**.

For example, one study found that older adults who closely adhered to a **Mediterranean diet** had a whopping **72%** <u>lower</u> risk of developing **dementia** than those who did not follow this diet.³

The Link Between Diet and Brain Function

A **healthy diet** provides a wide array of vital nutrients, including healthy fats like omega-3 fatty acids, minerals like magnesium, plant compounds like polyphenols/ carotenoids, and more.⁴

Poor diets, including the standard American diet, are often lacking in these nutrients. They provide excess calories and an overabundance of unhealthy fats, carbohydrates, and processed sugars.⁴

The brain can be critically impacted by diet.

A large population study that followed over **10,000** Brazilian participants for **eight years** found that consuming even modest amounts of **ultra-processed** food is associated with a **28%** <u>faster</u> rate of **cognitive decline** as compared to those who don't eat it.⁵

Epidemiological studies and reviews of clinical trials support the theory that certain modifiable lifestyle factors, including diet, are linked to **cognitive function** and risk of its deterioration in older age.⁶⁻⁸

Generally, the most <u>protective</u> diets (including Mediterranean, MIND, and DASH) include:

- Ample amounts of **fruits**, **vegetables**, **nuts**, and **legumes** (beans, peas, and lentils),
- Moderate consumption of fish, and
- Low to moderate intake of dairy and meat products.⁹

Multiple reviews and analyses of human studies suggest that the more people adhere to diets that follow these patterns, the <u>better</u> their **cognitive function** and the <u>lower</u> their risk of **cognitive decline** and **dementia**, including **Alzheimer's**.^{6,7,9}

Healthy eating patterns are particularly supportive of cognitive function, *lowering* the risk of neurodegenerative disease and age-associated cognitive decline.^{10,11} For instance, *greater* legume and nut intake correlates with *better* performance in cognitive functioning.⁷

On the other hand, typical Western diets are associated with overall **cognitive function decline**,¹² dementia, increased risk of Alzheimer's,² and diminished **executive function**.⁷

The Best Brain Diets

Two of the beneficial dietary patterns are the **Mediterranean diet**^{11,13-16} and the **MIND diet**.^{17,18}

Both emphasize eating large amounts of vegetables, fruits, whole grains, olive oil, legumes, nuts, and fish. They limit red meat intake, contain little or no highly processed foods, and include small amounts of wine.

The **MIND** (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet emphasizes consuming **green leafy vegetables** like spinach and kale and prioritizes **berries** over other fruit.⁹

Numerous studies show that following the Mediterranean^{14,15} or MIND diet^{17,18} correlates with



better cognitive function, a significant reduction in risk for **cognitive dysfunction**, and lower risk of **Alzheimer's** and other forms of **dementia**.

In one study, older adults who most closely followed a **Mediterranean diet** had a massive **72%** <u>lower</u> risk of developing **dementia** compared to those who did not adhere to this diet.³

Key Nutrients Tied to Cognitive Function

Brain-health diets include large amounts of **specific nutrients** that may be particularly beneficial. They include:

- POLYPHENOLS AND CAROTENOIDS. These health-promoting plant compounds have potent antioxidant and anti-inflammatory properties. Examples found in many fruits and vegetables include lutein, zeaxanthin, resveratrol, and more.¹⁹
- OLIVE OIL. Olive oil is a rich source of polyphenols such as oleuropein that have been found to be neuroprotective.²⁰ Diets that include olive oil have been tied to better cognitive function and reduced risk of dementia.²¹
- VITAMIN C. Various studies have linked vitamin C status to cognitive function.^{22,23} Low levels of vitamin C have been tied to reduced mental vitality. Oral intake of 500 mg vitamin C two times a day for four weeks has been shown to improve levels of attention in healthy young adults in a clinical trial.²⁴ Citrus fruits, tomatoes, broccoli, and spinach are important sources of vitamin C.²⁵
- B VITAMINS. Vitamins B6, B12, thiamine (B1), and folate (B9) all may support short-term memory in aging individuals and are found in various fruits and vegetables.²⁶ Deficiencies of any of these can cause depression, confusion, fatigue, brain fog, and irritability.²⁷
- MAGNESIUM. In observational studies, those with the *highest* magnesium levels perform better on cognitive tests, have lower risk of developing dementia, and maintain larger brain volumes.²⁸⁻³⁰ Seeds and nuts, spinach, beans, some fruits, and soybeans are good sources.³¹



Brain-Supporting Diets

- Studies show that largely plant-based diets low in processed foods are associated with better cognitive function and reduced rates of cognitive decline and dementia.
- The Mediterranean and MIND diets, which emphasize vegetables, fruits, whole grains, olive oil, legumes, nuts, and fish, shield against brain aging and risk for cognitive impairment while boosting mental function.



How Diet Supports the Brain

There are numerous ways that **diet** impacts the brain. Here are just some of the most important:

NEUROINFLAMMATION: Cognitive decline and neurodegenerative diseases such as Alzheimer's and Parkinson's disease are all driven, in part, by inflammation in the brain. A healthy diet can prevent or reduce neuroinflammation.³²

 OXIDATIVE STRESS: A largely plant-based diet provides antioxidants that help counter oxidative stress, including vitamin C, vitamin E, polyphenols, and carotenoids.³²

 OBESITY AND METABOLIC DISEASE: Excess body weight and metabolic abnormalities are associated with impaired cognitive function and accelerated development of cognitive dysfunction. A healthy diet can help prevent or reverse these body changes.¹¹

GUT DYSBIOSIS: The close link between gut health and brain health is known as the "gut-brain axis."³³ Poor diet is the top cause of dysbiosis, an abnormal mix of gut microorganisms that encourages inflammation and metabolic problems.

Improving the gut microbiome through better diet can boost brain health.³⁴ Research has suggested that adherence to a Mediterranean diet may reduce the risk of neurodegenerative diseases by maintaining a balanced microbiome.³⁵ INHIBITION OF NF-KB: Excess calorie intake increases activity of the protein complex nuclear factorkappa B (NF-kB), which contributes to chronic inflammation and metabolic disease. A healthy diet can inhibit NF-kB, reducing these contributors to brain deterioration.³²

A mostly **plant-based** diet can provide these and other benefits to support optimal brain health, as shown in **human** studies.³⁶

Summary

Consistent findings document that ingesting more <u>un</u>processed and plant foods, such as those found in the **Mediterranean** and **MIND** diets, is significantly associated with improved **brain health** and lower rates of **dementia**.

Some specific foods and nutrients found in these diets, including olive oil, fish-derived omega-3 fatty acids, polyphenols, carotenoids, vitamins and minerals, have been shown to provide cognitive benefits.

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



Comprehensive Nutrition and Brain Aging Study

The results of a fascinating new study were published in the medical journal *NPJ Aging*, associated with the prestigious *Nature* journal.³⁷ It represents one of the largest and most comprehensive studies that have assessed links between diet and nutrition and brain health.

This study stands out from many others that have evaluated the links between diet and brain health in a number of notable ways. For one, many prior studies used only one marker of brain health or a small set of markers. For example, they may have used a single standardized test to evaluate cognitive function.

The design of the study by Zwilling *et al.* was much more comprehensive. Not only did the authors assess cognitive function, but they also used brain imaging and other testing to evaluate brain structure and metabolism. As there are structural and metabolic changes that can accompany brain aging and progression of cognitive decline, looking at these results gives a much broader assessment of brain health status and allowed the researchers to estimate each subject's "brain age."

The other way this study differentiates itself is in the way it assessed diet and nutrition. Many other studies assess dietary intake of nutrients based on detailed surveys, questionnaires, or journals completed by the subjects. These methods are, of course, prone to inaccuracy and subjectivity.

The Zwilling study instead used blood-based biomarkers of diet and nutrition to objectively measure the levels of nutrients found in each subject's body. Unlike a survey or questionnaire, a blood test is not something that a subject could "fake" or misremember.



What did the researchers find? They discovered that the subjects generally fell into two major groups defined by their brain aging and dietary/ nutrient patterns. The scientists called the first group the "accelerated aging" group because their brain aging markers were significantly more advanced compared to the other group. The second group was called the "delayed aging" group because their brain structure and function were superior to the first group and testing revealed "slower-than-expected" brain aging.

They found that demographics (age, gender) and anthropometrics (body weight, BMI, etc.) could not account for the differences between these two groups. Instead, they found that the delayed aging group was associated with a greater body content of several key nutrients. For one, they had higher levels of some important healthy fats, including some monounsaturated fatty acids and omega-3 polyunsaturated fatty acids.

In addition to healthy fats, they found elevated levels of the carotenoids lutein and zeaxanthin as well as vitamin E and choline. Lutein and zeaxanthin have long been recognized in maintaining eye health, but recent studies show their levels also correlate with healthier brain function and reduced risk of dementia.³⁸⁻⁴² Choline is an essential nutrient that is also important for healthy brain function.⁴³

This compelling study adds to the growing knowledge of dietary patterns and specific nutrients that are most important to optimal brain health and reducing risk of accelerated brain aging and cognitive decline.



New Study Data: Diet, Inflammation, and Brain Health

It is recognized that chronic inflammation is a major contributor to rapid aging and risk for many age-related diseases—including cognitive decline and dementia.^{44,45} And diet is a major determinant of body-wide inflammation. While some foods have an anti-inflammatory effect, many foods consumed in modern Western diets are *pro*-inflammatory, meaning they contribute to and worsen inflammation.⁴⁶

Some diets—such as the Mediterranean diet discussed in this article—are considered antiinflammatory, including a greater intake of anti-inflammatory foods and nutrients and less pro-inflammatory ones.

A study published this year looked at data from the famous and robust research cohort, the UK Biobank, to evaluate the impact of anti-inflammatory diets on risk for dementia. The subjects included in this analysis had a history of cardiometabolic disease—including type II diabetes and/or a history of heart disease or stroke.⁴⁷

Cardiometabolic disease is an important risk factor for accelerated brain aging for at least two reasons. First, poor diet and inflammation are underlying causes of *both* cardiometabolic health and brain health. Furthermore, poorly controlled metabolic disease is an additional contributor to risk for cognitive decline and dementia. In other words, this group of UK Biobank subjects with cardiometabolic disease would normally be at high risk of progressing to dementia.

The researchers in this study used a detailed dietary questionnaire to estimate the intake of over 30 key nutrients known to be either antiinflammatory or pro-inflammatory. Using this information, they were able to calculate dietary inflammatory index scores for each subject.

With over 12 years of follow-up, they were able to determine that people with cardiometabolic disease who followed an anti-inflammatory diet, compared to those who did not, were **31%** less likely to develop dementia. While all patients with cardiometabolic disease have some increased risk for cognitive decline, an anti-inflammatory diet can have an important impact and can significantly reduce the risk.

In addition, the study evaluated brain MRIs of subjects. They found that those with more antiinflammatory diets had larger gray matter brain volumes and less evidence of white matter disease. In other words, an anti-inflammatory diet appears to be protective against the damage and loss of brain volume that is seen in older adults suffering from cognitive deterioration.

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CAUTION: This product breaks down histamine but won't prevent severe allergic or gluten-related (celiac) reactions. Do not knowingly ingest food you are allergic to. 1. Biomolecules. 2020 Aug 14;10(8):1181. 2. Clin Nutr. 2019 Feb;38(1):152-8. 3. Food Sci Biotechnol. 2019 Dec;28(6):1779-84. 4. J Clin Med. 2023;12(20).

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BY BRIAN WILTON

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A natural housekeeping process called autophagy functions as a built-in cleansing service whereby damaged cellular components are identified and

The vital **autophagy** process *declines* with age.^{1,3,4}

Curcumin, a compound found in the spice turmeric, has been shown to boost autophagy.⁵⁻¹¹ Preclinical and clinical studies have shown that it can help combat several key factors involved with

Importance of Autophagy

The body has a natural way to detect, clean and recycle the cellular damage that accumulates over time.¹⁻⁴ This process, called **autophagy**, enables cells to clean up their metabolic waste.

Autophagy literally translates to "self-eating." In this process, cells devour and break down old, worn-out internal components to make room for fresh, new replacements.

This helps enable cells to continue functioning optimally.

Aging and poor diet lower the rate of autophagy. As it slows down, metabolic waste accumulates inside cells and compromises optimal functions.

Cell and animal studies show that when autophagy is **deficient**, organisms suffer premature aging, chronic disease, and shortened lifespan.^{1,4} In several animal studies, when autophagy is **enhanced**, longevity is *increased*.¹²⁻¹⁵

For example, in one study, activating autophagy in mice extended the average **lifespan** by **17.2%**.¹⁵

Ways to Stimulate Autophagy

Research has indicated that physical **exercise**¹⁶ and **intermittent fasting** or **calorie restriction**¹⁷ stimulate **autophagy**.

Metabolic abnormalities contribute to chronic diseases. The enzymes **mTOR** and **AMPK** play a key role in modulating cellular autophagy.^{1,4}



Autophagy. A lysosome (orange) fusing with an autophagosome (large sphere). Autophagy is the natural mechanism that destroys unnecessary or dysfunctional cellular components and recycles their materials. The target components are first isolated from the rest of the cell within the double-membraned autophagosome. This then fuses with a lysosome, the contents of which degrade the target components. When calorie intake is high, **mTOR** is activated and *shuts off* autophagy, whereas <u>inhibiting</u> excess **mTOR** activity can <u>increase</u> **autophagy**.¹⁸

AMPK activates autophagy. Increased cellular **AMPK** activity has been shown to improve metabolic health and longevity.¹

When **AMPK** is *increased* and **mTOR** is *decreased*, autophagy is most active.^{1,4}

As we age, the autophagy process can become impaired or diminished, leading to catastrophic results. Most age-related **chronic diseases**, from cardio-vascular to neurodegenerative disorders and cancer, have been linked to **diminished autophagy**.^{1,4}

A decline in autophagy leads to metabolic conditions, which further impair autophagy, creating a vicious cycle that advances aging.¹

Curcumin Promotes Autophagy

Curcumin is a polyphenol compound found in turmeric root.

In clinical studies, curcumin has long been known as a potent **anti-inflammatory**. By reducing oxidative stress and chronic inflammation, it may support metabolic, cardiovascular, and gastrointestinal health.¹⁹⁻²¹ Maintaining metabolic health slows the progression of damage related to aging and chronic conditions.²²

Preclinical research over the last decade has also identified curcumin as a promoter of **autophagy**.^{5-7,23-25}

It works by *suppressing* **mTOR** activity and *boosting* **AMPK** activity.^{5,6,23,24} It also binds to and activates a key protein in cells called transcription factor **EB**, or **TFEB**, which triggers cellular machinery important for autophagy.²⁵

In cell and animal models, curcumin has been shown to augment autophagy, $^{5\text{-}7,26}$ improve health, $^{5\text{-}7,23\text{-}27}$ and extend life. 28,29

Giving fruit flies **curcumin** led to as much as a **26%** extension of their average **lifespan**.²⁸

Reduced Risk for Chronic Disorders

By promoting autophagy and combating oxidative stress and inflammation, curcumin may lower risk for a wide range of age-related and chronic diseases.

Adequate levels of autophagy help reduce risk for most chronic diseases of aging, which suggests that curcumin's potential benefits extend to other illnesses.^{8,30}


Mild cognitive impairment, Alzheimer's, Parkinson's, and other **neurodegenerative diseases** are associated with the accumulation of abnormal proteins in the nervous system. Autophagy may help clear these proteins.

In animal models of Alzheimer's, curcumin intake induces autophagy and reduces build-up of **amyloid plaques**.^{5,31} In models of Parkinson's, it has been shown to reduce accumulation of an abnormal protein called **alpha-synuclein** and improve disease symptoms.^{6,32}

Being obese and overweight increases the risks of developing chronic conditions like heart disease, stroke, cancer, and diabetes. Inflammation associated with obesity also accelerates the aging process.³³

A meta-analysis of 876 subjects randomized to receive **curcumin** supplementation showed a reduction in **body weight** and body mass index (BMI).³⁴

In preclinical studies curcumin has demonstrated benefits in **cardiovascular disease** in diabetic²³ and non-diabetic models.³⁵ Activating autophagy helps protect blood vessel health and shield the heart from damage.^{23,36}

In a study of diabetic mice on a high-fat diet, curcumin supplementation resulted in increased **AMPK activity** and **autophagy** in heart muscles, resulting in improvement of overall cardiac muscle function.²³

In a **human** study of young, obese men, 12-weeks of a specially formulated curcumin-galactomannan supplement led to a **34%** increase in protective **HDL** ("good") cholesterol and a **29%** reduction in **homocysteine** (an amino acid linked to development of atherosclerosis) compared to **placebo**.³⁷

Curcumin Boosts Autophagy for Better Health

- In autophagy, a cellular housekeeping process, old and faulty cellular components are removed to make room for new parts. This helps rejuvenate each cell and keep it running smoothly.
- Autophagy typically declines with age, allowing damaged and dysfunctional parts to accumulate. Reduced autophagy contributes to most forms of age-related chronic diseases, including neurodegeneration, cardiovascular disease, and cancer.
- In cell and animal models, boosting autophagy supports healthy aging and promotes longer life.
- Curcumin, a compound found in turmeric root, has been shown in cell and animal models to activate autophagy to rejuvenate cells and counter age-related diseases.
- Curcumin extends lifespan in animals and has shown an ability to improve memory, cardiovascular health, and more in human studies.

A large review of 54 meta-analyses of human trials revealed curcumin intake was associated with reduction of **inflammatory** markers like *C-reactive protein*. There were also reductions in markers of metabolic health—fasting blood glucose levels, **A1c** (a long-term marker of blood sugar management), insulin resistance, and cholesterol levels.³⁸

The review suggests the potential of curcumin in prevention and management of chronic metabolic inflammatory diseases.

In cell cultures and animal studies curcumin has shown promising results in reducing growth and inducing **apoptosis** of various types of **cancer cells**.

Autophagy plays a role in combating **cancer**. By boosting autophagy, curcumin has been shown in lab studies to fight cancer cell growth in a wide range of cancer types, including aggressive cancers like **melanoma** and **brain gliomas**.^{26,39-42}

A systematic review and meta-analysis of **21** clinical trials in patients with different types of cancers was conducted. Five trials were associated with relieving side effects of aggressive cancer treatment when curcumin was given as an adjuvant to standard treatment, while 16 of the 21 clinical trials were associated with the effectiveness of curcumin on various types of cancers.

The results from these **clinical trials** highlight curcumin's potential for cancer risk reduction and adjuvant intervention.⁴³

Summary

The process of **autophagy** identifies faulty and deteriorating cellular components and removes them, so they can be replaced with new parts.

This **rejuvenation** effect helps keep our bodies running smoothly and may slow aging and onset of age-related disorders.

Unfortunately, beneficial **autophagy** tends to <u>decrease</u> with age, which has been tied to many chronic conditions. Cell and animal models show that boosting **autophagy** can improve health and extend lifespan.

The compound **curcumin**, along with healthy dietary and physical activity practices, helps to increase **autophagy**. •

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. Phytother Res. 2015;29(8):1123-30. (significant versus placebo) 2. Avicenna J Phytomed. 2022;12(3):257-268. (significant versus baseline)

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Methods to delay and reverse early-stage cognitive deficits are moving into clinical practice.

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In preclinical models, **curcumin** *activated autophagy*, a vital cellular housekeeping process.









