

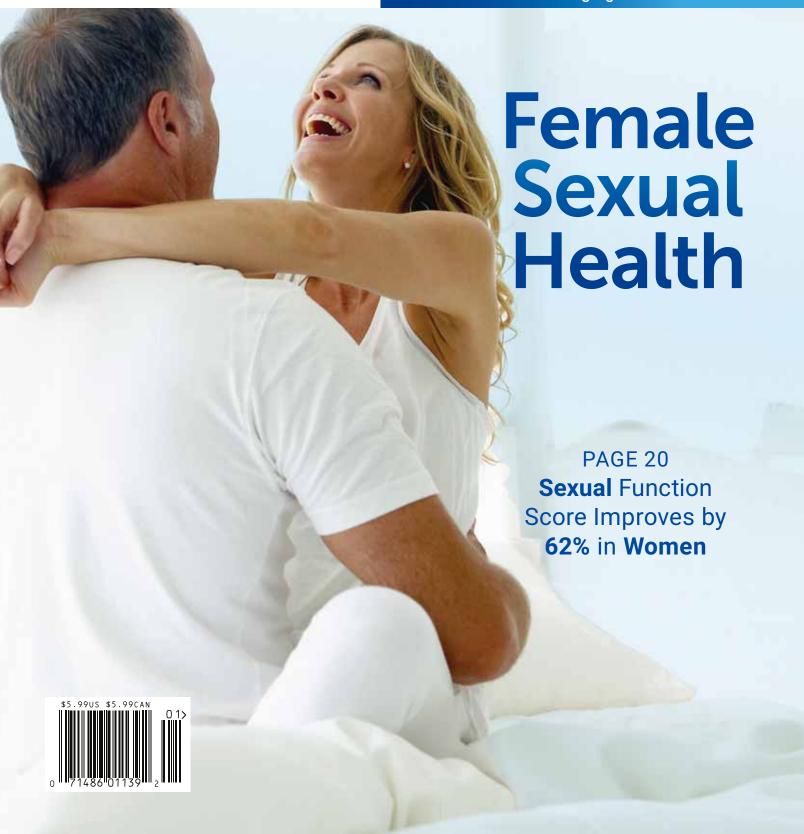
The Science of a Healthier Life®

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January 2025

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January 2025



Female Sexual Health

Studies show that **fenugreek** seed extract enhanced female sexual function and libido. while **saffron** extract *promoted* desire and satisfaction.

REPORTS

30 TAURINE UPDATE

Published studies show that taurine is associated with healthier human lifespans. A 2024 meta-analysis of 25 clinical trials helps corroborate this.

42 NAD+CLINICAL TRIALS

Found in every living cell, **NAD**⁺ levels sharply decline with age. In clinical trials, restoring NAD+ reduced inflammation, reduced fatigue and improved mitochondrial function.

54 CALMING EFFECTS OF L-THEANINE

A recent study found that taking **L-theanine** daily *improved* sleep quality, enhanced cognitive attention, and reduced stress by 18%, without causing drowsiness.

67 WHAT IS REISHI?

Modern research shows Reishi mushrooms boost immune protection and prolong lifespan in mice.

74 PROSPECT OF HUMAN AGE REVERSAL

Research findings published over the last 14 months show multiple indices of age reversal utilizing exosome-rich young plasma and in vivo delivery of cell-restoring transcription factors.

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AWSI: A KITTY HAWK EVENT?

A 2024 published study using OSK gene therapy regenerated old mice, improving overall health and extending remaining lifespans over 100%!

As scientists identify interventions that effectively target degenerative aging, humanity will experience a Kitty Hawk-like transformative era of discoveries and limitless biomedical advances.

13 IN THE NEWS

Poor lung function associated with low vitamin K levels: vitamin E improves liver function in liver disease patients; oral krill oil boosts skin health; lower mortality linked to higher adherence to Mediterranean diet.

71 SUPERFOODS: BEETS

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January 2025

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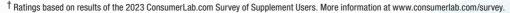
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A Kitty Hawk Event?



WILLIAM FALOON



Words cannot describe the **exhilaration** we feel in response to **rapid** developments in the age-reversal research arena.

A study published in **2024** corroborates prior reports of systemic regeneration in old mice using a gene therapy to improve overall health and extend remaining lifespans.¹

What makes extending the **remaining** lifespan so critical?

Because if a therapy given to young people increases healthy longevity, but does not reverse aging in old persons, then many readers of Life Extension Magazine® will miss out on the upcoming biomedical renaissance.

I'm often asked, "When will humans start enjoying these benefits?"

To put the timeframe in historic context, Wilbur Wright wrote in 1900:

"For some years I have been afflicted with the belief that flight is possible to man."2

But, Wilbur's "belief" contradicted conventional wisdom.

In 1895, Lord Kelvin stated that

"Heavier-than-air flying machines are impossible".3

In October 1903, the Washington Post published:

"It is a fact that man can't fly." 4

None of this pessimism deterred the Wright Brothers. They had no formal technical training, no financial backers, no government subsidies, and little money of their own. They nonetheless persisted until:

INTERNATIONAL HEADLINE NEWS

December 17, 1903

When the World **Changed Forever**

Kitty Hawk, North Carolina



Regenerative Medicine is Further Advanced than the Wright Brothers in 1900

I am privileged to network with scientists who, unlike the **Wright Brothers**, have advanced technical training, and robust interactions with many of the world's foremost interventive gerontology experts.

They are supported by donors like our **Life Extension** group who are determined to <u>reverse</u> human **aging** in our lifetime. And there is growing consensus today about genuine advances occurring in the superlongevity biomedical fields.

Our group funded a record amount of research in **2024** with the goal of enabling significant human **rejuvenation** in the next two to three years...which would perhaps be our **Kitty Hawk** moment (analogous to December 17, 1903).

On page 74 of this month's issue, I describe some of today's **age-reversal** projects, many of which are funded from proceeds of **blood tests** and **supplements** you purchase from **Life Extension**.

Stated succinctly, more progress has been made in the fields of *in vivo* biological **age reversal** over the past 18 months than perhaps in the entirety of human history.

You should enjoy reading in this month's issue about what you can do today to **delay** the **aging** process and how close scientists are to **reversing** it.

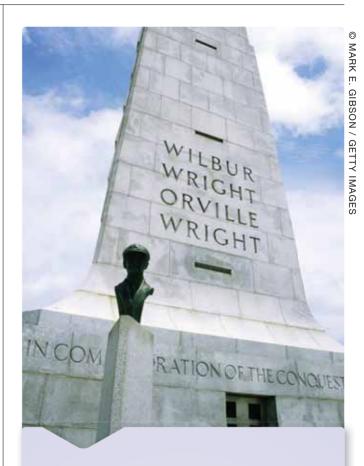
For longer life,

William Faloon, Co-Founder

Life Extension

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Relentless Perseverance

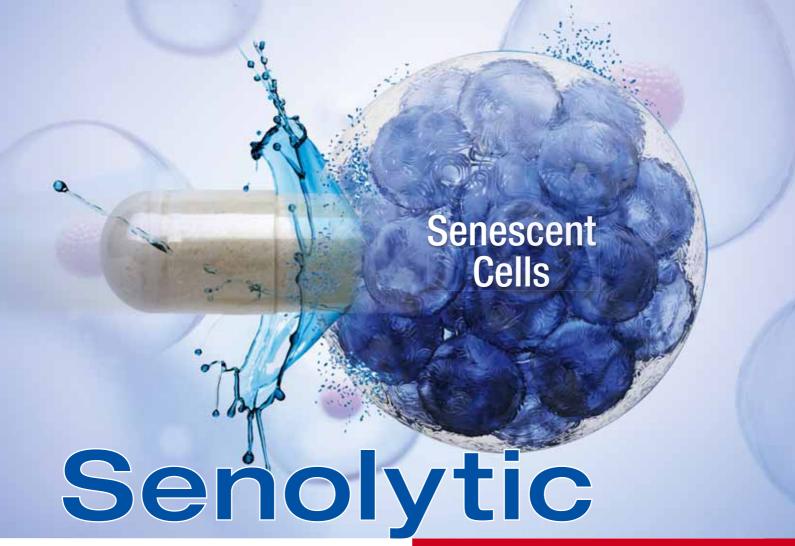
Kitty Hawk is a sparse stretch of barrier islands in North Carolina.

As told in a review in the *Wall Street Journal*, the **Wright Brothers** slept in a tent, cooked food on an open fire, survived hurricanes, scorching heat, and plagues of mosquitoes.

They had frequent mishaps/crashes, forcing them to stop and rebuild. The Wrights made several trips to Kitty Hawk, staying for months at a time...funded from their bicycle business.⁵

On **December 17, 1903**, Orville flew in a powered machine...proving for the first time the feasibility of heavier-than-air flight.^{5,6}

Scientists today are **relentlessly** investigating multiple methods of <u>reversing</u> pathological aging.



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References: 1. Neuropharmacology. 2016 2016/09/01/;108:426-39. 2. Journal of Cellular Physiology. 2016;231(9):1903-12. 3. J Alzheimers Dis. 2016;49(4):971-90.

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In recent years, three nutrients have emerged as having healthy lifespanenhancing potential:

Taurine

Functions via a range of anti-aging mechanisms1-5

Lithium

In epidemiological studies higher dietary intake of lithium (drinking water) is associated with lower risk of mortality.6-8

Spermidine

In epidemiological studies, higher intake correlates with longer healthspan.9-11 A one-year study showed that a diet enhanced with spermidine daily supports healthy memory scores. 12

Consumers have used some of these nutrients for decades, albeit at lower dosages than what may be optimal for healthy aging.

New Healthy Aging Powder provides the following in one scoop:

Taurine

5,000 mg

Lithium

2,000 mcg

 Spermidine 3.000 mca

(0.2% standardization from 1,500 mg Wheat germ extract)

These nutrients may promote healthy aging by supporting cardiovascular health, exercise performance, and cognitive function.

SUPER SALE PRICE

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The full dose is one scoop daily mixed with water or juice.

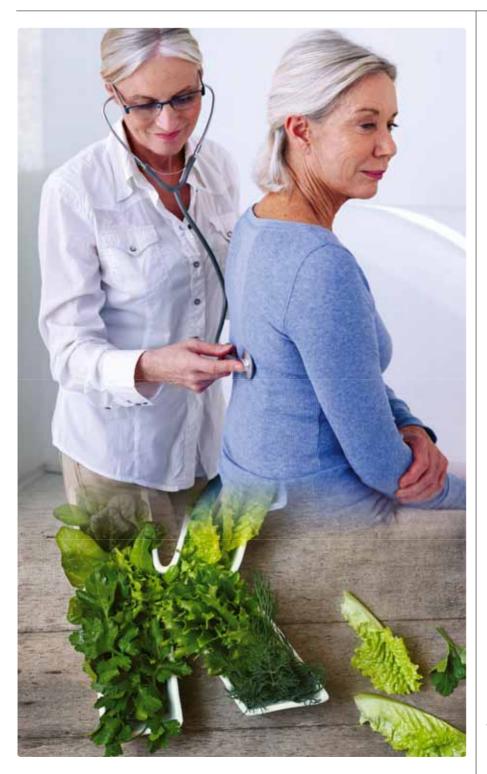


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In the News



Low Vitamin K Linked to **Reduced Lung Function**

People with poor lung function or lung disease were found to have low levels of vitamin K, a recent study showed.*

Questionnaires were completed by 4,066 participants, aged 24-77, providing information about general health, chronic diseases, and lifestyle factors such as smoking, alcohol consumption, physical activity, and diet.

Exams were conducted from 2017-2020 to evaluate individuals' lung function using spirometry (a common test that measures how much air a person breathes in and out). Urine and blood values were measured to assess vitamin K status.

Individuals with lower vitamin K levels had poorer lung function (as indicated by diminished forced expiratory volume and forced vital capacity) compared to those with higher vitamin K levels.

Those with lower vitamin K had greater odds of having COPD, wheezing, and asthma compared to those with *higher* vitamin K status.

Editor's Note: Participants were enrolled in the Danish study of Functional Disorders.

* ERJ Open Res. 2023 Sep; 9(5):00208-2023.

Vitamin E Benefits People with Liver Disease

A systematic review and metaanalysis of randomized, controlled trials found significant improvement in markers of liver inflammation and microscopic structure and function of liver tissue in people who received the antioxidant vitamin E.*

The study subjects had metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH).

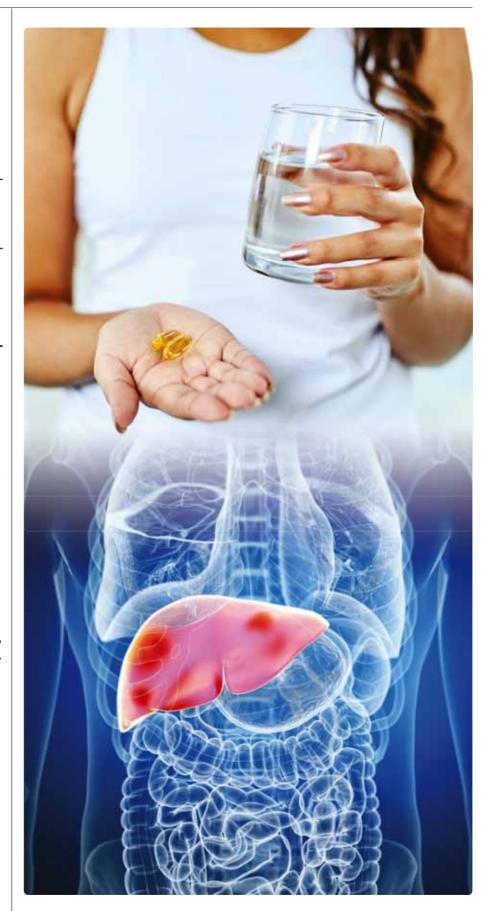
The meta-analysis included seven trials that compared the effects of vitamin E to another nutrient or drug or a placebo among a total of 853 men and women with MASLD or MASH.

Vitamin E significantly <u>reduced</u> serum levels of the liver enzymes ALT and AST, which are elevated in liver disease.

Vitamin E lowered steatosis (the buildup of liver fat) and inflammatory cells within the lobules of the liver, and reduced ballooning of liver cells.

Editor's Note: "Our meta-analysis of RCTs found that vitamin E significantly reduced serum ALT and AST levels. This is consistent with the results of other published meta-analyses," the authors concluded.

* J Gastroenterol Hepatol. 2024 Aug 16; 16723.





Krill Oil Boosts Skin Health

Two randomized, double-blind, placebo-controlled, dose-finding pilot studies found improvements with orally administered krill oil in the skin of healthy adults.*

In the first study, 26 adults were given 1,000 mg krill oil per day and 25 participants received a daily placebo for 12 weeks. The second 12-week study included 29 participants who received 2,000 mg krill oil per day and 21 participants who received a placebo.

Blood omega-3 levels, water loss across skin layers, hydration and elasticity were measured at the beginning of the study and at six and 12 weeks.

"The results from these two studies in healthy volunteers suggest that krill oil supplementation may improve the skin's capability to retain water, in addition to improving its hydration and elasticity," the authors concluded.

Editor's Note: Krill oil is a source of the omega-3 fatty acids EPA and DHA. As essential membrane components, omega-3 fatty acids modulate cell membrane and support skin barrier function.

* J Cosmet Dermatol. 2024 Aug 21; 16513.

Lower Mortality Risk with Greater Adherence to a Mediterranean Diet

In a study reported in *JAMA Network* Open, women with high adherence to a Mediterranean diet had a <u>lower</u> relative risk of mortality compared to women with low adherence to the diet.*

Researchers analyzed data from 25,315 participants in the Women's Health Study who enrolled from 1993-1996. Participant responses to questionnaires completed at the beginning of the study were scored for adherence to a **Mediterranean diet** and categorized as having low, intermediate or high adherence.

Those whose adherence was high had a 23% <u>lower</u> relative risk of dying during the 25 years of follow-up and an 11% lower relative risk after adjustment for lifestyle factors, compared to women whose adherence was low.

Editor's Note: "Participants with higher adherence to the Mediterranean diet generally exhibited healthier lifestyles, including lower BMI and higher intake of fruits, nuts, whole grains, legumes, and fish, while consuming less red and processed meat," the authors stated.

* JAMA Network Open. 2024 May 31; 1533.



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1. Rev Urol. 2004;6 Suppl 6(Suppl 6):S9-S15.
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3. Laila Nutraceutical Internal Study. Data on file. 2019.









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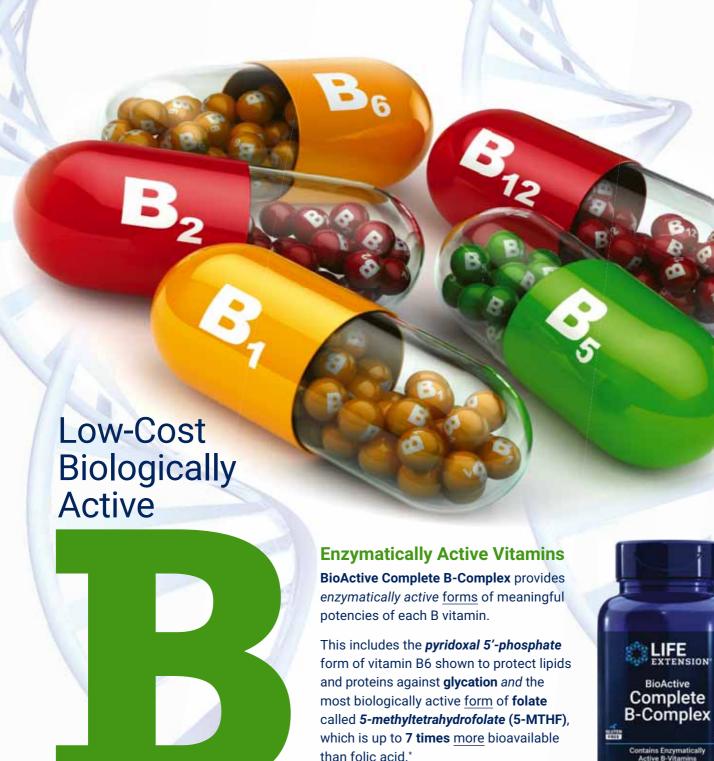
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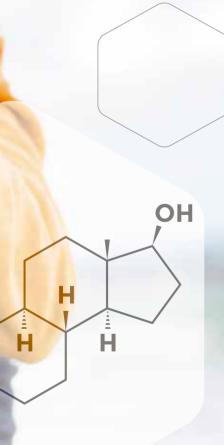
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> Caution: Temporary flushing, itching, rash, or gastric disturbances may occur. * Br J Pharmacol. 2004 Mar;141(5):825-30.



Improving SEXUAL HEALTH for WOMEN of All Ages

BY HEATHER L. MAKAR



In a large population-based survey in the United States, over **40**% of females reported sexual concerns and **12**% reported distressing symptoms.¹

These data reflect sexual problems many women struggle with, including low desire, reduced enjoyment, and other sexual health issues.

Researchers have identified <u>two</u> plant-derived ingredients that can improve multiple aspects of women's sexual function, including supporting **libido**.

In clinical trials:

- Fenugreek seed extract improved sexual drive, arousal, and orgasm, and more than doubled the frequency of sexual activity,² and
- Saffron extract improved sexual function score by 62%, boosting desire, lubrication, and satisfaction.³

This article describes potential solutions to improving female sexual health.

Women's Sexual Health Challenges

In 2008, a large population-based survey of more than **31,000 women** aged 18 and older, showed that nearly half the respondents reported sexual concerns, with low **sexual desire** being the most common.¹

Decline in estrogen during menopause causes thinning of vaginal lining, loss of elasticity and lubrication leading to discomfort, and lack of interest in sexual activities.⁴

However, **sexual dysfunction** is not limited to menopausal and post-menopausal women. **Younger women** also commonly experience issues with desire, arousal, and orgasm difficulties.¹

These issues impact women's **quality of life** and place significant **strain on relationships**.^{5,6}

Women's desire, enjoyment, and satisfaction can be impacted from:⁴

- Medication use, such as mood-altering prescriptions^{7,8} and birth control,^{1,8}
- Mood (stress,^{7,8} anxiety, and depression^{8,9}),
- Hormonal changes (in women of all ages),^{1,7} including pregnancy, hormonal birth control, perimenopause or menopause,⁸ and
- Health issues limiting blood flow to those areas where it is crucial for lubrication.⁴

The Role Hormones Play

Hormone balance modulates female sexual function in multiple ways. ^{7,10} The receptors for estrogen, progesterone, and testosterone are present in vaginal tissues. ¹⁰

- Testosterone, the primary male sex hormone, has important effects in females on ovarian function and sexual behavior.^{7,11} In post-menopausal women it may enhance the effects of low-dose estrogen therapy.^{7,12}
- Estradiol, the main form of estrogen, enhances arousal and lubrication while facilitating the production of neurotransmitters involved in sexual excitement. Decreased estrogen can precede thinning of vaginal tissue and dryness.^{4,7,10}
- Progesterone is commonly associated with a dampening effect on libido, countering the desire-promoting effects of testosterone and estradiol.⁷

While menopause can change the balance of these hormones, they can shift at *any point* in a woman's life, during and after pregnancy, by use of hormonal birth control, and by being perimenopausal, limiting interest in and satisfaction from sex.⁸

Fortunately, there are ways to support hormonal health and promote healthy female **sexual function**.

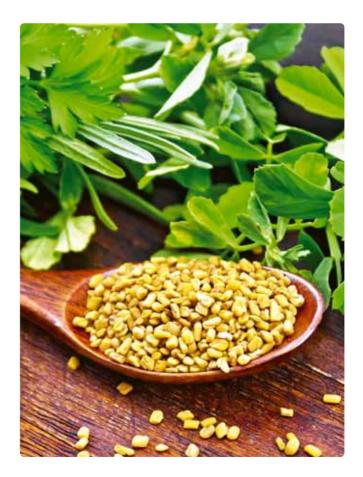
Plant-Derived Solutions for Sexual Function Support and Satisfaction

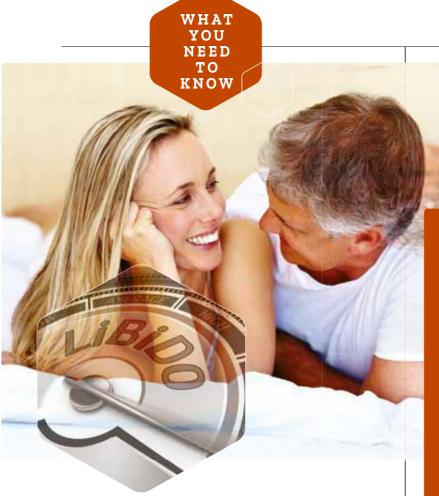
Optimal sexual function generally includes healthy **desire** (libido), **arousal** (physical preparation for sex), and **satisfaction** (pleasure and orgasm).¹³

Researchers have identified two **plant**-derived **extracts** that promote \underline{all} these areas of female sexual enjoyment.

Fenugreek seed¹⁴⁻¹⁶ and **saffron**¹⁷⁻²⁰ both have a long history of use in **traditional medicine** to safely support female gynecological function and health.

Clinical evidence supports that they promote healthy sexual function, including **arousal**, **lubrication**, and **fulfillment**.





Fenugreek Supports Desire and Function

Fenugreek, an herb native to Western Asia and the Mediterranean, has been extensively used in Ayurvedic medicine for enhancing libido and balancing female hormones.14,15

Fenugreek is rich in saponins, a compound that is believed to be responsible for these effects.^{21,22}

In a placebo-controlled clinical trial of 80 healthy women aged 20-49 with low libido, those taking 600 mg of standardized fenugreek seed extract daily for eight weeks had:2

- Improved sexual arousal and orgasm based on the Female Sexual Function Index questionnaire, a commonly used scale for assessing sexual health,
- Increased the frequency of sexual activity from one or two times per month to once per week, and
- Elevated free testosterone levels by 24% and estradiol levels by 66%, promoting female sexual response while leaving other hormones unaffected.

Boost Female Libido and Satisfaction

- Women of all ages can suffer from declining **sexual desire** or an inability to experience sexual pleasure.
- In a clinical trial, **fenugreek** seed extract boosted sexual desire, arousal, and orgasm.
- **Saffron** extract improved total sexual function index scores by 62%, increasing arousal, lubrication, and satisfaction, in another clinical study.
- A **blend** of these extracts may offer a comprehensive approach to improving women's libido and sexual satisfaction.

Saffron Enhances Arousal and Satisfaction

In South Asia, the Mediterranean, and ancient Persia, saffron was celebrated for its aphrodisiac properties and commonly used as an ingredient in formulas to enhance libido and promote women's sexual desire and satisfaction. 17,20

In a clinical trial, women (ages 18-55) with low sexual function who took 30 mg of saffron extract daily for six weeks had a:3

- 62% improvement in total Female Sexual Function Index scores compared to baseline, and
- · Significant improvements in arousal, lubrication, and satisfaction.

A Combination for Women's Sexual Health

Fenugreek and saffron extracts work in different ways to promote female sexual function.^{2,3}

Fenugreek helps balance hormones essential for a healthy female sex drive, boosting free testosterone to promote sexual desire and increasing estradiol to support arousal.2

Saffron promotes sexual enjoyment,3 enhancing desire. lubrication, and satisfaction while supporting a pleasurable intimate experience.3

Combining these plant extracts may help support healthy sexual desire and satisfaction in women of all ages.

Summary

Women of any age can face sexual issues like low desire and decreased satisfaction.

Research has identified two plant-based ingredients that support women's sexual health.

Fenugreek seed extract enhances arousal and hormone balance, while saffron extract promotes desire and sexual satisfaction.

Combined, these ingredients can offer a comprehensive way to support healthy female libido and support women's sexual health.

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



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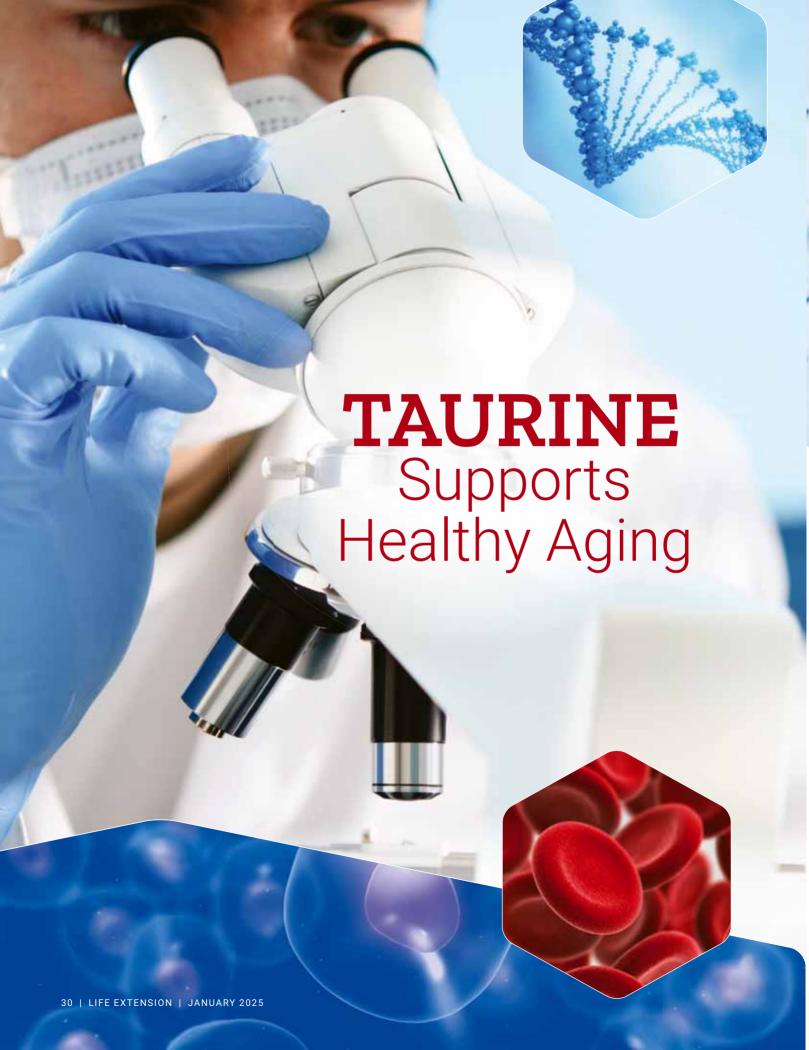
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Taurine is the most abundant amino acid found in nearly all tissues.¹ It facilitates multiple biological functions.¹⁻⁴

But levels drop by about **80%** in **older** adults.⁵

That decline puts our health at risk. A **2023** study even named **taurine** <u>deficiency</u> a "driver of aging."⁵

In animal models, inadequate taurine results in <u>accelerated</u> **aging** and *higher* risk for disease.⁶⁻⁸ Oral intake to maintain *higher* levels has demonstrated beneficial effects.^{5,7}

In **human** studies, **taurine** intake ranging from **500-6000 mg** daily has shown:

- Lowered blood pressure⁹⁻¹¹ and cholesterol,¹⁰⁻¹³
- Reduced markers of inflammation, 14-16
- Reduced complications in people with metabolic dysfunction,^{11,18}
- Improved blood sugar and insulin levels in adults with type II diabetes,¹²
- Improved cognitive function in elderly women with dementia.¹⁹

These and other findings indicate the role taurine plays in supporting **healthy aging**.

Taurine's Role in Aging and Disease

Most animals, including humans, synthesize some amount of **taurine** internally.

Additional taurine is obtained in our diets, with seafood being the richest source, and some coming from meat and dairy.^{2,7}

Similar to aging humans, cats and some dogs do not produce enough taurine internally. They must get ample taurine in their diet or via supplementation to avoid a **taurine deficiency**.⁷

Taurine deficiency in animals affects a wide range of their organ systems, leading to visual, cardiovascular, neurological and reproductive defects^{6,7} along with a weakened immune system.⁷

The situation also occurs in **humans**. With age, body levels of taurine tend to drop precipitously. Older adults, on average, have **80**% <u>less</u> taurine than young, healthy adults.⁵

These <u>lower</u> levels of **taurine** are associated with age-related disorders.

A 2023 study in a large cohort of European adults performed an association analysis. Levels of taurine, its precursor, and its metabolites were measured. Higher blood taurine and related compounds were associated with <u>lower</u> body mass index (BMI) and <u>less</u> **abdominal obesity**, as well as <u>lower</u> levels of the inflammatory marker **C-reactive protein** (CRP). Higher taurine metabolite levels were associated with <u>less</u> chance of **type** II **diabetes** as well as with lower **glucose** levels.⁵

Taurine is so vital that our cells contain **transporters** specific to taurine.^{6,7} When taurine is consumed orally, these transporters shuttle it into cells to maintain an adequate supply.⁴ Experimental animals that are missing taurine transporters develop significant health problems and have a **shortened lifespan**.⁷

In numerous animal and cell studies, taurine has been found to:

- Support mitochondrial health^{7,20} and improve cellular energy metabolism,^{7,8}
- Regulate healthy gene expression,⁷
- Improve neurotransmitter function in the nervous system,²¹
- Boost cellular quality control and housekeeping,²⁰
- Protect against oxidative stress⁷ and chronic inflammation,^{7,20} and
- Protect DNA from damage and shortening of telomeres.^{5,20}

These and other beneficial effects may have a favorable impact on healthy aging.

In a recent study elderly mice supplemented daily with taurine increased **life expectancy** up to **25%**, compared to a placebo.^{5,20}

These supplemented mice suffered from less agerelated deterioration and disease. Similar results were seen in rhesus **monkeys** given taurine.



An observational study found low levels of taurine within the brain are associated with major depressive disorder in young women.²²

In an observational survey in 25 countries, with more than 14,000 people, scientists measured urinary excretion of taurine and used that to estimate dietary taurine intake. They found that Japanese people had the highest intake of seafood and thus of taurine, and they also had the lowest rate of **heart disease** and the *longest* average lifespan.23

Wide-Ranging Benefits

Clinical studies of taurine intake have shown a huge range of benefits that can promote healthy aging.

In Japan, taurine has been used to help improve the heart function and exercise capacity of heart failure patients.24-27

This improvement in energy metabolism and exercise capacity has been observed in other subjects as well.

In a crossover trial of healthy young elite athletes. participants were randomized to receive 6,000 mg of taurine or placebo in the first session. After a 72-hour washout period the groups were reversed, with the firstsession placebo group receiving supplementation and the supplemented group getting placebo. Participants were tested with a series of physical and blood tests for lactate levels (an indirect marker for fatigue in exercising muscle).

It was found that taurine intake enhanced their peak, average, and minimum power output, and their functional response to the training, as compared to a placebo.28

Several other studies have found that taurine supports heart and metabolic health:

 In adults with type II diabetes, taking 3000 mg of taurine per day for eight weeks significantly reduced insulin resistance, blood sugar, hemoglobin A1c, and cholesterol levels. The markers of glycation damage caused by high blood sugar were also reduced.¹² Two other trials in diabetics have shown improvements in glycemic markers and lipid profile at the same dose.13 These results suggest that taurine supplementation may have potential to help with diabetic complications by improving glycemic control.



Healthier Aging with Taurine

- Taurine is an amino acid available mostly from seafood but also meats and dairy; it is also produced by the body. Its levels drop dramatically with advancing age.
- Lower levels of taurine have been tied to accelerated aging and increased risk for age-related chronic disease.
- In elderly mice, taurine intake increased lifespan up to 25%.
- **Human studies** show that taurine intake can improve many aspects of health, including reducing elevated blood sugar and blood pressure, lowering cholesterol, improving cognitive function, and reducing risk for metabolic syndrome.

- In preclinical studies taurine has shown an ability to protect against common diabetic complications, including diabetic kidney disease, eye disease, and neuropathy.^{29,30}
- A review of clinical studies found that taking from 1000-6000 mg of taurine daily significantly reduced both systolic (top number) and diastolic blood pressure.¹⁰ This effect has also been documented in adults with pre-hypertension or hypertension.³¹
- A meta-analysis affirmed taurine's ability to reduce blood pressure while also lowering cholesterol and triglycerides in patients with liver or metabolic dysregulation at a dose of 500-6000 mg for a period of 15 days to six months.¹¹
- In a study of obese females, a combination of 3000 mg taurine intake and nutritional counselling for eight weeks reduced C-reactive protein (CRP) levels—a marker of systemic inflammation.¹⁵ A meta-analysis of trials has shown similar results for CRP and biomarkers of oxidative stress.¹⁶
- A 2024 meta-analysis of 25 human trials including a total of over one thousand participants determined that taurine (in doses ranging from 500-6000 mg per day) for a follow-up period of 5–365 days was capable of reducing blood pressure, fasting blood glucose and triglycerides. These markers are associated with risk for metabolic syndrome, a cluster of conditions that increases risk for cardiovascular disease and type II diabetes.¹⁸

Other studies show benefits beyond heart and metabolic health.

For example, in hospitalized elderly women with dementia, taking **3000 mg** of taurine daily led to improvements in **cognitive function** after just four weeks.¹⁹

In a clinical trial of patients with chronic liver disease, **2000 mg** per day of oral supplementation with taurine resulted in a clinically significant reduction in the frequency, duration, and intensity of muscle cramps (which are commonly seen in patients with chronic liver diseases).³²

And in patients recovering from a traumatic **brain injury**, taurine reduced the marker of inflammation and improved clinical outcomes.¹⁴

Dozens of studies are currently testing taurine's benefits for everything from diabetes to mental health disorders.³³ The existing evidence clearly shows how vital it is for **healthy aging**.

Strikingly Low Taurine Levels in Food

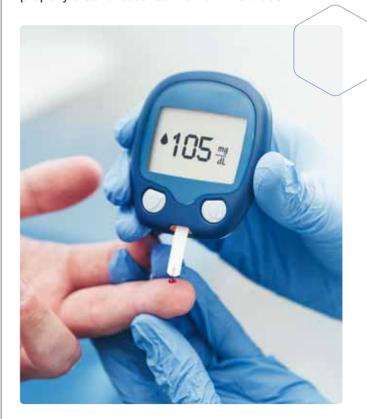
In youth, **taurine** is synthesized in our body from the amino acid **cysteine** by an enzyme called **cysteine sulfinate decarboxylase**.³⁴

With age, levels of this enzyme plummet. The result is <u>lower</u> body taurine. Studies indicate elderly people have about **80**% less taurine compared to their youth.⁵

Published studies use thousands of milligrams a day to achieve clinical results. Yet the typical dietary intake of taurine is only **100-180 mg** a day. (Strict vegetarians/ vegans may only obtain **17 mg** of taurine from their plant based diet (no seafood or meat).³⁴

Based on accumulating published clinical data, people today are supplementing with **3,000** to **6,000 mg** daily of **taurine**.

The only caveat about these higher doses is people with end stage **kidney failure** who may not be able to properly clear excess taurine from the blood.



Summary

Taurine is an amino acid available mostly from seafood but also meats and dairy. It is also made in the human body. Its levels tend to plummet with age, and lower levels are associated with increased risk for numerous diseases.

Taurine intake increases lifespan in animal models. In human studies, it has reduced high blood sugar, cholesterol, hypertension, oxidative stress, and chronic inflammation, helping to promote healthy aging. •

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

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3. Food Sci Biotechnol. 2019 Dec;28(6):1779-84. 4. J Clin Med. 2023;12(20).

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What Is Nicotinamide Riboside?

Nicotinamide riboside is an activated form of vitamin B3 that functions as a *precursor* to one of the most important compounds found in all living cells, **NAD**⁺.¹¹

NAD⁺ plays multiple roles in cells, many that are critical to **healthy aging**.^{3,4,8,14}

Preclinical studies have shown that boosting **NAD**⁺ levels reduces **chronic inflammation**, 11,15-17 a driver of most age-related chronic diseases. 15-17

The Importance of NAD+

NAD⁺ is a coenzyme required for **cellular respiration** and **metabolism**. Without an ample supply of NAD⁺, cells can't properly convert nutrients into energy.

Some tissues, including those in the **brain**, **heart**, and other **muscles**, have particularly high metabolic rates. That means they require *more* cellular respiration and *more* **NAD*** to power them.

NAD⁺ is critical for metabolism and energy supply to the cells and is also required for the normal function of over **300** enzymes and proteins, including many which help protect and maintain the integrity of a cell's **DNA**.³

For example, **sirtuins** are protective proteins that shore up a cell's health in multiple ways, including by preventing DNA damage, improving DNA structure and maintaining cellular health.^{18,19}

In animal models ranging from worms to mammals, *increased* sirtuin activity is associated with *increased* **lifespan**. ^{18,19}



Sirtuins require **NAD**⁺ to function.^{4,20} But in older adults, **NAD**⁺ levels and sirtuin function tend to drop. In preclinical research, this *declining* sirtuin function has been associated with **accelerated aging** and increased risk for age-related disease.²¹

As a **NAD**⁺ precursor, **NR** can readily replenish NAD⁺ levels in cells, ²²⁻²⁵ allowing sirtuins and other enzymes to continue working effectively.

Wide-Ranging Benefits

Raising **NAD**⁺ levels with **NR** has been shown to improve various aspects of health in preclinical studies. For example, in rodents, nicotinamide riboside:

- Improves memory in models of Alzheimer's disease,²⁶
- Helps prevent heart failure,²⁷ and
- Improves metabolism and helps prevent weight gain.²⁶

Giving animals **NR** also resulted in an **extension** of **lifespan**.²⁸⁻³¹

In worms, for instance, lifespan was extended by at least 10%. In mice the human equivalent of 70 years old,³¹ nicotinamide riboside extended their life by about 5%, the human equivalent of *four additional years of life* based on today's average U.S. human life expectancy of 76 years.³²

Human Studies

Nicotinamide riboside is a relatively newly studied nutrient. The first human study of its use was only published in **2016**.²³

In early clinical studies, **NR** has been shown to be **safe** and well tolerated.^{23,33}

Taking various doses has been shown to increase body levels of **NAD**⁺²²⁻²⁵ as much as **five-fold**.²² The increase in **NAD**⁺ levels correlates with an increase in cellular **metabolic adaptations**.^{23,34}

In a randomized controlled trial of adults with **Parkinson's disease**, taking **1,000 mg** of nicotinamide riboside daily for 30 days significantly increased brain levels of NAD+ (measured via magnetic resonance imaging). Supplementation was associated with decreases in markers of inflammation and *mild clinical improvement* in symptoms of Parkinson's disease.³⁵



In a randomized controlled crossover trial, a 1,000 mg daily dose of nicotinamide riboside in mildly overweight, healthy, elderly men for 21 days resulted in elevated levels of NAD+ in muscles of participants in the intervention group. Nicotinamide riboside also reduced levels of circulating inflammatory cytokines.³⁶

In another study, four patients hospitalized with advanced heart failure were given escalating doses of NR (500 mg to 2,000 mg) for five to nine days. Blood samples were collected before and after the intervention.

In this human study, whole-blood NAD+ levels and respiration of peripheral white blood cells were increased. The researchers demonstrated that increasing NAD+ levels through NR treatment can improve mitochondrial function and lower inflammatory cytokines in heart failure patients.¹³

Mitochondrial dysfunction in heart failure patients is associated with reduced NAD+ levels. In a trial of clinically stable heart failure patients with reduced ejection fraction (a measurement of the heart's ability to pump blood) 1,000 mg of NR twice daily for 12 weeks resulted in increased blood levels of NAD+ and improved mitochondrial respiration. It also reduced the proinflammatory marker in circulating immune cells, evidence that boosting NAD+ with NR may help reduce systemic inflammation.37

The Emerging Benefits of Nicotinamide Riboside

- Nicotinamide adenine dinucleotide (NAD+) is critical to many cellular processes, including energy metabolism and DNA repair, and to proper function of protective sirtuin proteins.
- NAD* levels tend to wane with older age. Nicotinamide riboside (NR), a precursor to NAD+, has been shown in human studies to restore NAD+ levels in cells.
- In preclinical studies, nicotinamide riboside has reduced risk for disease. improved health, and extended lifespan.
- In human trials, nicotinamide riboside reduced inflammation and oxidative stress, boosted physical performance, and led to improvements in Parkinson's disease.

Nicotinamide Riboside and Resveratrol: A Powerful Combination

Resveratrol is a polyphenol found in red wine, grapes, and various other plants. It has been shown in preclinical settings to activate sirtuins, proteins linked to healthy aging.20,39

Sirtuins require NAD+ to function, and the possible lifespan extension benefits of calorie restriction may be associated with the role of sirtuins.40

A combination of nicotinamide riboside to boost levels of NAD+ and resveratrol to increase sirtuin function can maximize sirtuins' ability to protect cells.



In a randomized controlled, crossover trial, 12 young and 12 aged men were given nicotinamide riboside or placebo. Muscle fatigue and strength were assessed two hours before and after exercise along with the collection of blood and urine samples. At rest, older individuals had lower red blood cell antioxidants and NAD+ reserves. NR supplementation increased NAD+ reserves and lowered oxidative stress in both groups. and increased antioxidant reserves in the elderly participants. In **elderly** subjects who were supplemented with NAD+, there was an improvement in the **fatigue** index and in one measure of isometric strength.38

Research into nicotinamide riboside is exploding, with about 100 ongoing clinical trials listed in the National Institutes of Health's directory.³⁹ But already there is evidence for its potential to improve many aspects of health.

Summary

Maintaining optimal NAD+ levels can help support cellular metabolism and DNA repair.

Levels of NAD+ decline with age, but **nicotinamide riboside** is capable of helping to restore them.

In human trials, nicotinamide riboside reduced markers of inflammation, reduced oxidative stress, led to clinical improvements in Parkinson's disease, and improved exercise performance in older adults.

Many clinical trials for other conditions are underway. •

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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02530	Aged Black Garlic • 500 mg • 30 vegetarian capsules A clinically studied dose of aged black garlic extract to support cardiovascular health.	1 unit 4+ units	\$ 18.00 —	^{\$} 16.20 ^{\$} 15.30 ea.	10% 15%
02334	Super K • 90 softgels (3-month supply) Two forms of vitamin K2 (MK4 + MK7) and K1 to support bone/arterial health.	1 unit 4+ units	^{\$} 22.50 —	^{\$} 20.25 ^{\$} 18.23 ea.	10% 19%
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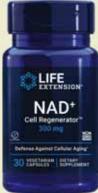
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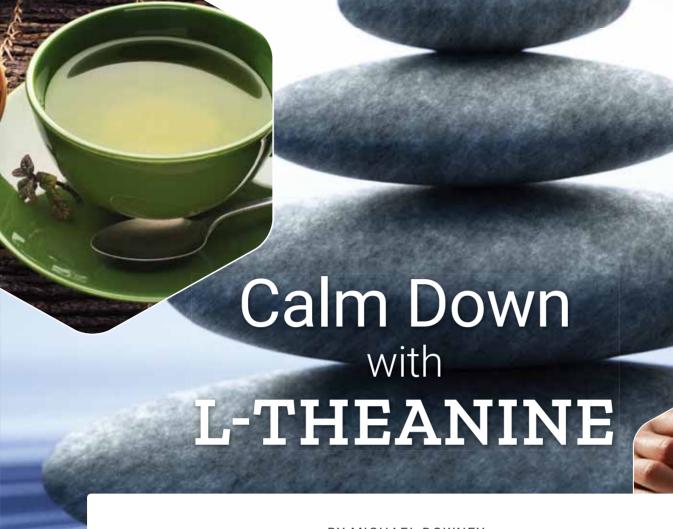






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BY MICHAEL DOWNEY

In today's hectic world, many of us need to find safe ways to reduce stress and calm down.

Stress can severely harm quality of life. Chronic stress boosts risk of physical and mental problems,1 and can impact an individual's immune function ²

L-theanine is an amino acid found in green tea. It has been recognized for its ability to safely reduce anxiety, calm the mind and produce a state of relaxation³ without drowsiness.³⁻⁵

Clinical studies confirm that L-theanine has relaxing properties that have stress-relieving effects on the body.6-9

One study published in 2024 showed that I -theanine lowered perceived stress by nearly 18%, enhanced sleep quality, and provided a sustained improvement in cognitive attention.7

A Serious Health Risk

Stress is the body's way of helping you deal with occasional, serious risks to life and health. After a perceived danger has passed, your stress hormones, heart rate, and blood pressure levels are supposed to return to normal.¹⁰

But when life throws constant stressors at you, that **fight-or-flight reaction** can stay turned on.¹⁰

Excessive exposure to stress hormones such as **cortisol** and the *long-term* activation of the stress response system can put your health in danger. This **chronic stress** increases the risk of: 1,10

- Heart disease, heart attack, high blood pressure, and stroke,¹⁰
- Musculoskeletal problems,¹⁰
- Depression,¹⁰
- Digestive issues,¹⁰
- Headaches, muscle tension, and pain,¹⁰
- Chronic fatigue, ¹⁰
- Hormonal imbalance/menstrual irregularities,¹⁰
- Dysregulation of the immune system,^{1,10}
- Weight gain,¹⁰ and
- Memory and cognition problems.¹



Researchers have looked for healthy ways to promote non-sedative alert relaxation.

Despite containing caffeine, **green tea** has traditionally been associated with producing a *calming* effect.¹¹

In **1949**, scientists identified the specific compound in green tea leaves associated with these relaxing, **anti-stress** effects: **L-theanine**.¹¹

How L-Theanine Blocks Stress

L-theanine is a water-soluble amino acid⁷ that has the ability to cross the blood-brain barrier.⁵

L-theanine works to **reduce stress** by the following mechanisms:

- Preclinical evidence suggests that it modulates activity of the excitatory neurotransmitter glutamate.¹²
- In preclinical studies L-theanine is found to be associated with stimulating the production of the relaxing neurotransmitter GABA (our main inhibitory neurotransmitter) as well as enhancing dopamine release.⁵ Levels of GABA are associated with sleep, and reduced feelings of stress and anxiety. Dopamine is associated with learning and mood.¹³
- In human studies L-theanine has been shown to increase alpha wave activity in the brain, especially in individuals with moderate to high anxiety levels.^{6,7,14} Alpha waves are associated with a relaxed but alert mental state.¹⁵

In **1964**, after Japanese researchers conducted numerous clinical trials demonstrating that **L-theanine** is both safe and effective, Japanese authorities declared it to be completely safe and approved adding it to foods. ¹⁶

Since then, multiple **clinical studies** have shown that L-theanine effectively reduces **stress**.^{3,17-19}

Clinically Validated

In one unpublished study, scientists enlisted healthy subjects, aged 21 to 47, who were considered *not* particularly stressed. The study involved initial screening and an experimental visit lasting two hours.⁹

During this experimental visit one group took a **placebo**, and the other took **200 mg** of **L-theanine**.



Prior to taking the doses participants were tested for alpha brain waves (by electroencephalography, or EEG) seven times over a 120-minute period and received a stress test. Ninety minutes after receiving the dose, two further stress tests were administered, and heart rate was measured three times.9

The L-theanine group had:9

- Increased alpha brain wave activity, indicating increased relaxed wakefulness (while the placebo group's activity was unchanged),
- Significantly less fatigue than the placebo group,
- Decreased tension and anxiety, and
- Lower **heart rates**, a further sign of stress reduction.

This shows L-theanine is effective in helping to reduce heart rate and increase relaxation, and has the potential to relieve stress.9

In a triple blind, placebo-controlled, crossover study, individuals aged 19 to 60 were evaluated who were moderately stressed.6

Decrease Stress Without Drowsiness

- Chronic stress affects millions of American adults. It can contribute to low-quality sleep, poor general health, and increased risk for anxiety, depression, and heart disease, and can also impact immune function.
- In clinical studies, **L-theanine**, an amino acid found in green tea, has been shown to reduce stress and promote relaxation while maintaining alertness-unlike sedating medications.
- Results of a clinical trial published in 2024 found that taking 400 mg of L-theanine daily significantly reduced feelings of stress, improved sleep quality, and enhanced cognitive attention.

At screening, participants were randomized to the L-theanine or placebo group and were given instructions and kits to collect salivary cortisol levels. Subjects were given either a **placebo** or **200 mg** of **L-theanine**, as well as an arithmetic test to induce mental stress before and after they received the dose.

Alpha brain wave activity, salivary cortisol levels, and vital signs were recorded before and after participants took the arithmetic test. There was a seven-day washout period between the L-theanine test and placebo test. Participants returned for the crossover period and all assessments from the first study period were repeated.

All participants experienced stress <u>during</u> the test, as evidenced by increases in heart rate, blood pressure, and self-reported stress and anxiety. But **three hours** later, those who had taken **L-theanine** had greater **alpha wave** activity compared to the placebo, showing a higher level of alert relaxation without drowsiness.

L-theanine also resulted in greater decreases in salivary **cortisol** levels, compared to placebo, further indicating increased relaxation and calm.⁶

These studies show how L-theanine can reduce the nervous system's stress reaction, which can yield benefits for body and mind.

Recent Human Trial

A clinical study published in **2024** enrolled healthy but *moderately stressed* subjects. But this time, treatments continued over a **28-day** period.⁷

Subjects ranging from 18 to 65 years were randomly given either a placebo or **400 mg** of **L-theanine** daily, taken as **200 mg** in the morning and at night.

Participants were asked to maintain their normal lifestyle, avoid high caffeine consumption (no more than two cups of coffee a day), and refrain from vigorous exercise within 24 hours of testing days.

Tests and other evaluations were done at baseline, day 14, and day 28. On day 28, the **L-theanine** group had:⁷

- About 18% lower levels of perceived stress,
- Improved sleep quality, and
- Greater cognitive attention.

The significantly lower levels of self-perceived stress corresponded with a decrease in morning salivary cortisol.



This shows that **L-theanine** can reduce general stress over an extended period in people who experience stress on a regular basis, and this may improve the quality of life.7

Green tea has only about 8 mg of L-theanine per cup.20 Studies on L-theanine's anti-stress effects usually use a 200 mg dose, taken once or twice daily.6,7

Summary

Stress contributes to reduced quality of life and greater risk for chronic disorders and impaired immune system function.

L-theanine, an amino acid found in green tea, has been clinically shown to reduce stress and enhance relaxation while maintaining alertness.

In **human** trials, **L-theanine** reduced signs of stress after just a single 200 mg dose. It also improved sleep, relaxation, and cognitive attention after 28 days of daily use without serious adverse effects. •

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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What is Reishi?



Reishi mushrooms (Ganoderma lucidum) have been utilized in Chinese folk medicine to promote health and longevity.¹

They are so revered in traditional Chinese medicine for their health benefits that they have been referred to as the "mushroom of immortality."¹

More recently, modern research has validated that reishi contains key health-promoting components that boost immune function, reduce inflammation, and stop the growth of cancer cells.¹

And animal research has shown its potential to increase **lifespan**.^{2,3}

Immune-Boosting Properties

A strong immune system is a key factor necessary for a longer, healthier life. Unfortunately, immune systems decline with age.⁴

Preclinical⁵⁻⁷ and clinical⁸⁻¹¹ research has validated reishi's ability to modulate immune function.

Animal research has shown that **reishi** promotes the maturation and activation of immune cells that are part of both the innate and adaptive immune systems.¹²

The **innate immune system** is the body's first line of defense against harmful invaders like viruses, bacteria, and cancer cells.¹³

Adaptive immunity targets the specific pathogens causing a problem.¹³

In preclinical studies the bioactive compounds from reishi have shown an ability to activate immune cells including T cells, natural killer cells, dendritic cells, and macrophages.^{5,14}

Activating **natural killer cells** is crucial for protection against viruses, which is especially critical for older adults who often suffer from diminished natural killer cell activity. This is one crucial reason why, with increasing age, people are susceptible to high rates of infection with viruses ranging from influenza to various herpes viruses. 15,16

Lab studies show that reishi also helps combat inflammation by increasing protective **IL-10** levels and lowering pro-inflammatory **IL-6** levels. 17,18

In a clinical trial, 30 older women received either **2000 mg** daily reishi extract or placebo. After eight weeks, reishi extract consumption was shown to regulate T-lymphocyte function and IL expression, leading to significant anti-inflammatory action as compared to a placebo group.⁸

Infection-Fighting Power

With its ability to boost components of both innate and adaptive immunity, reishi could protect the aging body from infections.

Lab studies demonstrate activity against many common viruses, including:

- Herpes simplex viruses (the causes of oral and genital herpes),¹⁹
- Influenza viruses (cause of the flu),^{19,20}
- Epstein-Barr virus (causes mononucleosis and can contribute to the formation of cancer),¹⁹
- Hepatitis B virus (a common cause of liver disease that can lead to cirrhosis, liver cancer, and liver failure),^{21,22}
- Human immunodeficiency virus (the virus that causes HIV/AIDS).^{22,23}

Anti-Cancer Properties

Reishi's ability to boost the function of immune cells gives it potential anti-tumor and anti-cancer properties.²⁴

In preclinical studies, reishi was shown to target tumor cells by activating anti-tumor activity of natural killer (NK) cells and by cytokine release from T-lymphocytes and macrophages.⁵

Reishi may also <u>directly</u> combat tumors through many mechanisms, including the following:¹⁹

- Stopping tumor cells from growing,
- Preventing tumor blood vessels from developing,
- Starving abnormal cells, and
- Directly killing cancer cells.^{25,26}

A meta-analysis of five clinical trials of cancer patients found that patients who were given reishi in combination with their standard chemotherapy/radiation therapy had greater tumor regression with treatment than those treated with standard therapy alone. Treatment groups were also found to have improved quality of life.²⁷

However, further analyses and trials on survival benefits are needed.

Blood Sugar Support

Reishi contains compounds like polysaccharides, proteoglycans, and triterpenoids that have all been shown in preclinical settings to help lower blood sugar levels.²⁸

Animal studies have demonstrated reishi's potential to decrease blood sugar and improve lipids.^{29,30}

In a clinical trial to assess the cardiometabolic benefits of reishi in people with mild hypertension or high lipids, participants received 1.44 grams of reishi extract or placebo for 12 weeks. After 12 weeks the treatment group showed improvements in plasma insulin and insulin resistance along with a reduction in triglycerides and elevation of HDL cholesterol. Overall results indicate its potential to support health in diabetics and improve dyslipidemia. However, further clinical trials are needed to confirm this benefit in humans.31



Lifespan Extension

A mouse study has provided an exciting glimpse into reishi's potential to expand lifespan.32

This study showed that the mice supplemented with reishi lived as much as 148 days longer than the un-supplemented control group.

This represents a dramatic increase in longevity given that the lifespan of a mouse is typically less than two years.

Summary

Reishi mushrooms have earned the nickname "mushroom of immortality" because of their potent health benefits.

Preclinical and clinical research has shown reishi mushroom's potential to improve immune function, reduce inflammation, help regulate blood sugar, and fight against cancer.

Reishi is a low-cost plant extract that helps support health for aging individuals. •

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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Beets



The deep red color of beetroot comes from its high concentration of phytochemicals called betalains.1

These and other active components in beets have been shown to have anti-inflammatory, anti-cancer, anti-diabetic, anti-obesity, blood-pressure-lowering, and lipid-lowering effects.1,2

A systematic review of clinical trials concluded, "Beetroot juice supplementation should be promoted as a key component of a healthy lifestyle to control blood pressure in healthy and hypertensive individuals."3

This beneficial effect is likely due to the vegetable's high concentrations of nitrates. Nitrates support the production of *nitric oxide*, a vasodilator that helps relax and widen blood vessels.3

Compared to other nitrate-rich vegetables, beets were found to be the best non-drug therapy for increasing nitrates and nitrites in the blood.4

BY LAURIE MATHENA

To find out if consuming whole beets would be equally effective on blood pressure as compared to beet juice, researchers conducted a randomized, crossover trial with 15 healthy young adults. (Raw beets provide about 200 mg of nitrate per 100 grams.)5

Both interventions resulted in a significant reduction in systolic and diastolic blood pressure, with no significant difference between the two groups. Nitrite concentration in the blood was increased in both groups, however it was higher in the beetroot juice group as compared to the group that consumed beets and other nitrate-rich vegetables.

Even though beets have 900 grams of sugar per cup,6 research indicates that consuming beets may be beneficial for alucose metabolism.

In one study, when type II diabetics consumed 100 grams of raw beets daily for eight weeks, they experienced decreases in fasting blood sugar levels and in serum levels of HbA1c. Researchers concluded that, "red beetroot could be considered as a part of a healthy diet for diabetic patients."7

In a trial of non-diabetic patients, consuming about a cup of beetroot juice significantly lowered post-meal insulin response as compared to the placebo group that received another form of glucose beverage.8

Beets can be consumed raw, roasted, pickled, or even juiced. However, it's worth noting that cooking reduces the bioavailability of the beneficial nitrates in the beets.

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The Prospect of **Human Age Reversal**

By William Faloon • Slides Designed By Chase Falcon

The leading cause of human suffering is not what vou read in the media.

The culprit is **biological aging**, whereby our body becomes increasingly susceptible to diseases that diminish quality of life, leading to pain, disability, and eventual personal extinction.1

Research that aims to reverse degenerative aging holds immense societal benefits. This includes slashing healthcare costs,2 enhancing productivity, and retaining the cumulative wisdom of millions of humans 3

As scientists identify new aging mechanisms, **interventions** that target degenerative decline are rapidly being investigated.

Successful clinical outcomes will revolutionize humanity in ways analogous to Gutenberg's invention of the movable-type printing press in the 1440-1450 period.

Gutenberg's innovation played a crucial role in the spread of knowledge and the advancement



read and learn from.)

(Before Gutenberg's invention, there were virtually no "books" to

of literacy, leading to

significant cultural

and economic changes,

along with exponential

improvements in living

standards.4

Extending healthy lifespans by enabling older people to grow biologically younger may eliminate age-related ailments, while restoring mobility, cognition, and functional independence.2

With populations rapidly aging across the globe, the need for effective interventions to mitigate degenerative diseases and extend healthy lifespans is urgent.3

This article describes research findings published over the last 14 months...most overlooked by mainstream media.

Young Plasma **Increases** Median Lifespan

Healthy young plasma contains tens of thousands of extracellular vesicles, exosomes, cytokines, growth factors, regulatory proteins and other molecules that may revitalize function and restore organ integrity in elderly individuals.5

Published studies demonstrate systemic effects of young plasma delivered to older organisms,6-14 including preliminary data on humans. 15,16



1520. Printing press.

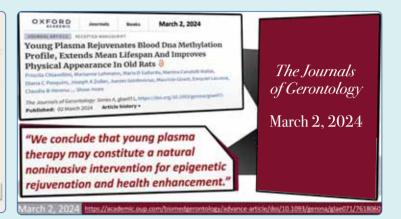
Rejuvenation Studies Published in

2024 17-19



- Exosome-rich young plasma cut old rat epigenetic ages in half and improved overall health...research now advancing to dogs.
- Young plasma reversed epigenetic aging in old rats and increased median lifespan human equivalent of about 7 years.
- OSK transcription factors reversed epigenetic age, improved overall health and extended remaining lifespans >100% in old rats...research advancing to old monkeys.

Next steps: Replicate these findings in murine models while simultaneously initiating OSK and young plasma research in old primates.



Exosome-Rich Young Plasma Fraction Treatment Protocol

Intriguing dosing schedule:

Exosome-rich young plasma fraction infused IV (tail) every other day for 8 days.

↑ 95 days later repeat once

"Cuts old age in half"

This dosing regimen is practical for humans & a primate study is being designed using same exosome-rich young plasma fraction.

February 2024 https://link.springer.com/article/10.1007/s11357-023-00980-6/

Young Plasma Increases Median Lifespan Beginning human equivalent of 60-65 years March 2, 2024 https://pubmed.ncbi.nlm.nih.gov/38430547/ Beginning at age 25.6 months, one rat group given young plasma every other week until death. ■ The same age control group received <u>no</u> treatment. Survival curve of no treatment group began to decline at 26 months. From age 26 to 30 months, none of the young plasma animals died.

Robust Age Reduction measured by DNAmAge in Tissues ent Condition for Rat in Tauting Set, by Tiess Tissue Epigenetic Age of Old Control Rat Tissue Epigenetic Age of Young Control Rat Tissue Epigenetic Age of Old Rat Given Young Plasma February 2024 https://link.springer.com/article/10.1007/s11357-023-00980-6/fi

Remarkable > 100% Extension in Median Remaining Life in Response to OSK Expression Two-part AAV system employed for systemic intracellular OSK delivery. Old mice equivalent to 77-year-old people used to enhance human translatability. Partial OSK reprogramming increased lifespan and improved frailty scores in old mice. Control mice had 8.86 weeks of life remaining vs. 18.5 weeks in OSK-treated group

I helped fund a university study that assessed the effects of *young plasma* on the lifespan, epigenetic age, and healthspan of **old rats**.¹⁷

Beginning at age 25.6 months one group of rats was **infused** every *other* week with **plasma** from **young** rats until their natural death. The same age control group received <u>no</u> treatment. Blood samples were collected every other week. The rats were **human** equivalent of **60-65 years**.

Survival curves showed that <u>none</u> of the **young plasma** animals died from age **26** to **30** months, whereas the survival curve of the <u>no</u> treatment group began to decline at age **26 months**.

The chart on this page shows a **9.1%** improvement in median **lifespan** of the **young plasma** treated group compared with controls. In addition, the **young plasma** treated rats appeared and behaved significantly **younger** than the control group. (See side-by-side photo at bottom of this page.)

DNA methylation testing measures **epigenetic age** and is considered the most <u>accurate</u> method of assessing future morbidity/mortality risk.²⁰

In this study, DNA methylation **age** of **young plasma** treated rats beneficially fell <u>below</u> the control group. In numerical terms, it remained consistently <u>lower</u> in the **young plasma** group until natural death. (We all want lower, *younger*, DNA methylation age measures.)

Analysis of **epigenetic age** in genes revealed favorable **insulin signaling** indicators, better **immune/metabolic** health, and reduced **inflammation**.

The authors of this published study summarized:

"We conclude that young plasma therapy may constitute a natural noninvasive intervention for epigenetic rejuvenation and health enhancement."¹⁷

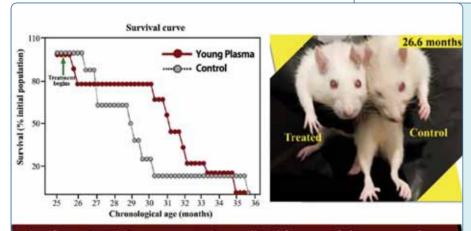
This **2024** published study had an interesting nuance. The *longest*-lived animal was in the **control** (no treatment) group. This indicates that **young plasma** can delay **median age** of death but may not confer **super longevity**. That's where **gene therapy** can come to the rescue as I describe later in this editorial.¹⁷

Plasma Fraction Cuts Old Rat Age in Half

A study I reported on at scientific conferences in **2020** was formally published in **2024** and demonstrated robust **epigenetic age** <u>reversal</u> in response to a **young plasma** fraction rich in **exosomes**.¹⁸

Exosomes are microscopic vesicles secreted by cells. They carry various biological factors, such as RNA and proteins, and are an important part of cell-to-cell communication. Exosomes secreted by stem cells and young cells are being investigated for their potential **rejuvenating** effects.²²

In this study, researchers treated **old rats** with an exosome-fortified **plasma fraction** from the blood of young adult pigs.¹⁸



Significant 9.1% improvement in median lifespan of the young plasma treated group (red) compared with no treated controls (black).

This chart shows a significant 9.1% improvement in the median lifespan of the young plasma treated group compared with no treatment controls. However, the most remarkable effect of the voung plasma treatment is the clear improvement in healthspan of the old rats that the photos reveal. The treated old rats look biologically younger than controls and the clock data (DNA methylation age) confirm that they are epigenetically younger. Although a 9.1% increase in lifespan seems rather modest, this figure is associated with a marked revitalization of the old rats. If applied to healthy humans aged 65, this might increase median lifespan by about 7 years, thus extending the remaining median life expectancy from age 85 to about 92 years.17

What is Epigenetic Age?

Epigenetic age is a biomarker of aging associated with future disease risks and all-cause mortality.²¹

The **epigenetic age** is measured by a composite of cellular **DNA methylation** (DNAm) levels.²¹

Epigenetic age is considered the most <u>accurate</u> way of assessing whether individuals are **aging** biologically <u>faster</u> or <u>slower</u> than their chronological age. (You don't want to "age faster.")



Slower (younger) **epigenetic age** (what you want) occurs among long-lived individuals.²¹

Older (worsening) epigenetic age is associated with <u>lower</u> levels of **physical functioning** and <u>decline</u> in **cognitive functioning** among long-lived individuals. ²¹

The treatment's effect was measured using several tailor-made **epigenetic clocks** which measure **biological age** by analyzing changes in the epigenome.

In plasma-treated old rats, the researchers showed reduced epigenetic ages of blood, liver, and heart by huge margins, i.e., to levels "comparable with young rats."

According to the six epigenetic clocks used, the treatment **rejuvenated**, on average, **liver** tissue by **74.6%**, **blood** by **64.3%**, **heart** tissue by **46.5%**, and the hypothalamus (in the **brain**) by **24.4%**.

According to this published study, the *young plasma* fraction <u>halved</u> the epigenetic (DNAm) age.

To put these findings into clinical perspective, **kidney failure** is often first detected by reduced glomerular filtration rate and an elevation of serum **creatinine**. In response to this **young plasma** fraction, **creatinine** levels in <u>old</u> rats, which were significantly elevated (as expected) dropped to virtually the <u>same</u> healthy level as **young** rats (see chart on this page).

If this translates into improved **renal function** in the tens of millions of Americans

with chronic **kidney disease**, countless numbers of lives will be spared each year.

The same potential exists in those suffering **heart** or **liver** failure, i.e., **exosome-rich young plasma** could restore youthful organ functionality.

Plasma Fraction Reverses Epigenetic Age

February, 2024

Two-year-old rats (circa 60-year-old human age)
treated with "exosome fraction of plasma" from
young adult pigs reduced epigenetic age by:

Liver: 74.6%

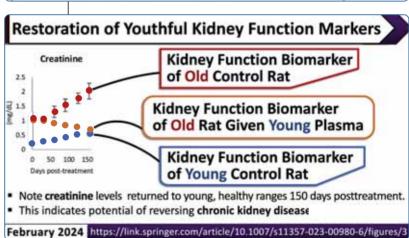
Blood: 64.3%

Heart: 46.5%

Brain: 24.4%
(hypothalamus)

Average DNAm age reduced as much as 67.4%

Horverth, S., Singh, K., Raj, K. et al. Reversal of biological age in multiple rat organs by young porcine plasma fraction. GeroScience 46, 367-394 (2024). https://doi.org/10.1007/s11357-023-00980-6



What intrigued us about this study was the dosing schedule of the exosome-rich *young plasma* fraction. It was infused into the rats every other day for eight days and then repeated 95 days later. If this easy-to complywith administration schedule applies to old humans, it makes compliance practical for most people.

Published Reports Describing Regenerative Potential of Young Plasma

The Stanford Parkinson's Disease Plasma Study²⁵

https://www.clinicaltrials.gov/study/ NCT02968433

A randomized, controlled clinical trial of plasma exchange with albumin replacement for Alzheimer's disease: Primary results of the AMBAR Study²⁶

https://pubmed.ncbi.nlm.nih.

The Plasma for Alzheimer Symptom Amelioration (PLASMA) Study²⁷

https://clinicaltrials.gov/study/ NCT02256306

Preclinical Assessment of Young Blood Plasma for Alzheimer Disease²⁸

https://pubmed.ncbi.nlm.nih.gov/27598869/

Safety, Tolerability, and Feasibility of Young Plasma Infusion in the Plasma for Alzheimer Symptom Amelioration Study: A Randomized Clinical Trial²⁹

https://pubmed.ncbi.nlm.nih.gov/30383097/

Young Blood Plasma Administration to Fight Alzheimer's Disease?³⁰

https://pubmed.ncbi.nlm.nih.gov/28384033/

Platelet factors attenuate inflammation and rescue cognition in ageing³¹

https://pubmed.ncbi.nlm.nih.gov/37587343/

Plasma-Based Strategies for Therapeutic Modulation of Brain Aging²³

https://pubmed.ncbi.nlm.nih. gov/31161489/ Aging and age-related diseases with a focus on therapeutic potentials of young blood/plasma⁷

https://pubmed.ncbi.nlm.nih.aov/37552316/

Circulating plasma factors involved in rejuvenation⁹

https://pubmed.ncbi.nlm.nih.gov/33197235/

Plasma from Young Rats Injected into Old Rats Induce Antiaging Effects⁶

https://pubmed.ncbi.nlm.nih. gov/33161876/

The effect of aging on the bone healing properties of blood plasma³³

https://pubmed.ncbi.nlm.nih.gov/34049703/

Young plasma ameliorates agingrelated acute brain injury after intracerebral hemorrhage³²

https://pmc.ncbi.nlm.nih.gov/articles/PMC6522807/

Undulating changes in human plasma proteome profiles across the lifespan³⁴

https://pubmed.ncbi.nlm.nih.gov/31806903/

Young Plasma Rejuvenates Blood Dna Methylation Profile, Extends Mean Lifespan And Improves Physical Appearance In Old Rats¹⁷

https://pubmed.ncbi.nlm.nih.gov/38430547/

Young blood plasma reduces Alzheimer's disease-like brain pathologies and ameliorates cognitive impairment in 3×Tg-AD mice³⁵

https://pubmed.ncbi.nlm.nih.gov/32513253/

Numerous Young Plasma Research Projects

Over the past nine years, published studies have demonstrated the **rejuvenation** effects of **young plasma**, including the use of young <u>human</u> **plasma** to **regenerate** the brains of **old rats**.^{8,18,23,24}

Projects are being initiated to assess the effects of healthy *young plasma* on <u>older</u> humans to ascertain the impact on degenerated organs such as **hearts** and **kidneys**. Initial emphasis has been on attempting to reverse various forms of **neurodegeneration**, with varying indicators of potential efficacy.

What physician/scientists have learned in clinical studies is that plasma from <u>un</u>healthy young people is <u>not</u> the *healthy* **young plasma** you want infused into your body.

Plasma from healthy young donors (18-24 years) is thought to provide a balanced spectrum of regenerating factors, including **exosomes** secreted by the abundant healthy stem cells in their **young** bodies.

There are several different protocols being studied, including removing senile proteins from old people's blood and replacing the senescent proteins with quality albumin + immunoglobulins or healthy young plasma.

In the listing on this page there are titles and links to *young plasma* research published in recent years. You can find direct links to these studies by visiting:

www.age-reversal.net/plasma



Follistatin Gene Research

Aging is associated with <u>loss</u> of **muscle** mass (sarcopenia) that contributes to frailty, falls, fractures, and premature mortality.³⁶

Follistatin is a protein-coded **gene** that plays several roles in the human body. Young people have <u>high</u> **follistatin** levels that plummet with normal aging.

Older people are traveling to offshore clinics today for **follistatin** gene injections based on the following discoveries:

Year <u>2001</u>: Increased **follistatin** greatly <u>increases</u> **muscle mass** in mice.³⁷

Year <u>2009</u>: Follistatin gene delivery in monkeys increases muscle growth and strength.³⁸

Year 2020: Follistatin gene delivery <u>reduces</u> inflammation, metabolic dysfunction and osteoarthritis in mice.³⁹

Year 2022: Follistatin gene delivery shown to extend median lifespan of mice by 32.5%.⁴⁰

A **human** project published in **2024** shows plasmid*based **follistatin gene** delivery resulted in average:⁴⁰

- Decrease in intrinsic epigenetic age of 6 years,
- Decrease in extrinsic epigenetic age of 8 years,
- Increase in fat-free mass of 1.69 lbs,
- Decrease in body fat of 0.80%, and
- Zero adverse events.

Over 100 people have had plasmid-based **follistatin** gene therapy at an offshore clinic in Central America operated by American scientists.

The cost is high (around \$25,000) but will likely plummet with mass production of **plasmid-based follistatin** delivery vehicles. It is estimated that each injection of plasmid-based follistatin lasts three to six months.

Note that in order for the **gene** that produces **follistatin** to be transported <u>inside</u> cells, it requires a **delivery vehicle**, with plasmids being the current vehicle of choice, usually along with other substances (like lipid nano particles) that help the gene enter the nucleus of the cell.⁴¹

If the findings about follistatin remain consistent, it will likely become a therapy that people over age 40-50 will utilize several times a year to increase fat-free muscle mass and help reverse their **epigenetic age**.

Alpha-Klotho Gene Research

Alpha-klotho is a gene that has prominent ageregulating effects.

It is being investigated in a **plasmid-delivery** vehicle to reverse the effects of age-related **cognitive decline** and **neurodegeneration**.⁴²

Specific brain cell populations, including neural **progenitors** require klotho. Human correlational studies and mouse models show that **klotho** is protective against multiple neurological and psychological disorders.⁴³⁻⁴⁵

Klotho gene <u>over</u>-expression in mice resulted in a **30%** increase in median **lifespan**.⁴⁶

Klotho-<u>deficient</u> mice have **shortened lifespans** that are accompanied by an array of **disorders** normally associated with human aging.⁴⁷

Alpha-klotho has been shown to decrease during middle age in **humans**, which is when short-term **memory loss** is often noticed.^{48,49}

<u>Lower</u> alpha-klotho plasma levels in older adults are associated with **frailty** and all-cause **mortality**.⁵⁰⁻⁵⁴

A 60-year-old man was the first to receive plasmidbased klotho delivery and reported marked cognitive improvements in **2024** that lasted for over 90 days (internal research awaiting publication).⁵⁵

Formal alpha-klotho projects are being planned. If it works in people the way it does in mice, **alpha-klotho** gene therapy injections (perhaps twice per year) may be combined with **follistatin** to provide broad-spectrum rejuvenating effects in older humans.

Those who don't want to wait for formal studies plan to travel to offshore clinics.

Interestingly, healthy *young plasma* may provide some **alpha-klotho**, **follistatin** and other regenerative proteins like **GDF11**.⁵⁶



What Are Plasmids?

*Plasmids are circular DNA strands that contain within them the gene that codes for the protein of interest (such as follistatin). By encoding genes like follistatin, klotho or OSK into a plasmid and injecting them into the body, the plasmids lodge inside the cell nucleus where they act as a time-release gene addition approach, producing a protein that is released into circulation. After several months (usually three to six months), the plasmids are mostly degraded, and a new injection is required.

Most Promising Youth Restoration Project

Transcription factors are proteins that help turn specific **genes** "on" or "off" by binding to DNA.

The **regenerative** power of *transcription* factors lies in their ability to **reprogram** old cells back into **stem cells** or **younger cells** capable of regenerating tissues throughout the body.

Said differently, transcription factors may transform cells in our aging bodies into a limitless youthful state. They do this by turning "on" genes that promote youthful vitality and turning "off" the expression of genes involved in degenerative aging.

Cyclic Induction of OSK Expression in 2-Year-Old Wild Type Mice¹⁹

In March 2022, **Salk Institute** researchers showed for the <u>first</u> time that partial **cell reprogramming** using **Yamanaka** transcription factors <u>reversed</u> systemic aging in **old** mice.

Salk scientists showed that mice receiving these transcription factors "*in many ways resembled younger animals*," including having more youthful epigenetic age of **skin** and **kidneys**.⁵⁷

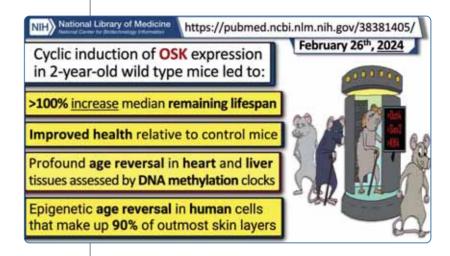
Transcription factor-treated mice had <u>lower</u> **inflammation**, <u>reduced</u> **senescent cell** secretions, and looked **younger** than untreated control mice.

This **Salk Institute** study found <u>no</u> toxicity but did not assess the **lifespans** of transcription factor-treated mice.

Move forward to **2024** and a published study showing that *transcription factor*-treated <u>old mice reversed</u> **epigenetic age** measures <u>and</u> extended <u>remaining</u> **lifespan** over **100**%!¹⁹

The **human** equivalent age of these **old mice** was about **77 years**, and the *transcription factor*-treated animals had:

- Improved health relative to control mice,
- Profound age-reversal in heart and liver tissues assessed by DNA methylation clocks,
- Improved Frailty Index scores (another measure of aging), and
- Transcription factor treated mice had remaining lifespans of 18.5 weeks versus 8.86 weeks in the control group.



While these findings further corroborate the Salk Institute *transcription factor* results published in **2022**, there are even <u>more</u> reasons to be optimistic than I've revealed so far.

Minimal Transcription Factor Induction = Robust Results

The acronym for the <u>four</u> **Yamanaka transcription factors** discovered in 2006 is **OSKM** (Oct3/4, Sox2, Klf4, c-Myc).

A **Nobel Prize** was awarded to the scientists who showed that delivering **OSKM** to **old cells** in a petri dish turned them back into **young cells**, with greater **age reversal** occurring in response to *longer* OSKM induction.⁵⁸

The initial concern with continuously over-expressing OSKM in live mice was possible side effects. So, the **Salk Institute** scientists only expressed OSKM intermittently in the **2022** published study.

In the **2024** published study showing age reversal, improved health, <u>and</u> *longer* remaining **lifespans**, only **OSK** *transcription factors* were used on an intermittent (one week on, one week off) basis. Using only three Yamanaka factors (**OSK**) is considered safer and likely more effective than **OSKM**.¹⁹

But here is where it gets exciting. Due to a series of typical challenges when studying new technology, only a **small fraction** of the intended **OSK dose** was delivered into the cells of the live mice.

Despite this smaller than intended **OSK delivery**, the results of this study are unprecedented and demonstrate the urgent need to replicate these results using varying doses of **OSK** in mice while at the same time studying the effects of OSK in old **primates**.

Rapid Transition of Age Reversal from Cells to Mice to Monkeys to Humans

- --> Rewriting the Rules of Biology | https://pubmed.ncbi.nlm.nih.gov/33627519
- > 2006: cell reprogramming demonstrates cell rejuvenation.
- > 2011: Rejuvenation induced in very old human cells (in vitro)
- > 2022: Aging partially reversed in live mice (independent studies)
- > 2024-2027: Research to rejuvenate old monkeys & humans.

Prior biology doctrine: Cell rejuvenation not possible.

The unanswered question is whether continuous, or near continuous induction of **OSK expression** in old monkeys and humans might restore their bodies back to a long-lasting, youthful state.

Effect of OSKM Gene Therapy: Injections Directly into Old Rat Brains

In July 2024, another study we helped fund showed that injecting OSKM transcription factors directly into the hippocampus of old rat brains improved learning and memory skills.59

The charts on this page show the degree of cognitive improvements in old rats using this primitive method of embedding **OSKM** into the hippocampal region of the brain, but still achieving significant results.59

This method of delivering OSKM improved memory and learning capability. It showed indices of epigenetic age reversal. But it did not restore cognitive capacity back to the young control group.

That's where enhanced OSKM and OSK delivery methods (such as lipid nanoparticles) might yield more robust results by delivering higher precision doses of OSK or OSKM into brain cells.18

We provided funding for this study to prove a concept, i.e., even crudely delivered viral vector **OSKM** into a small portion of the brain (hippocampus) yielded meaningful results.

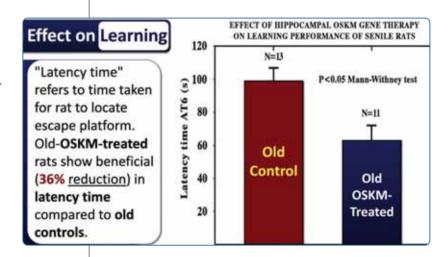
Our focus in recent months has been designing systemic delivery studies using large amounts of OSK in old primates with the objective of enabling whole-body rejuvenation.

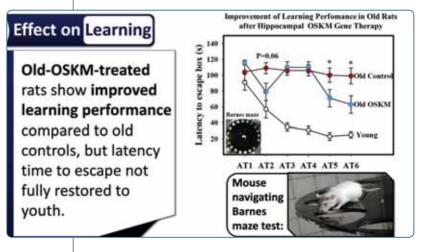
Are You More Motivated to Stay Alive?

There is published scientific evidence that biological aging is reversible and meaningful extensions of remaining lifespans possible.60

A theoretical basis exists to assert that various cell reprogramming techniques (such as OSK induction) might enable our cells to regain youthful functionality for a sustained period. 61,62

This is of little value to those who perish from preventable disorders.





Be it a failure to control blood pressure, ingestion of processed, sugary and over-cooked foods, lack of physical activity, and/or not optimizing **blood test** markers, most people aren't doing enough to stay alive.

With the prospect of **age-reversal** transforming into biological reality, there is more motivation to avoid premature morbidity and mortality than ever before.

There has never been a greater incentive to follow healthy lifestyle patterns to be alive when validated **rejuvenation** therapies become available.

Your Purchases Fund this Research

We are not the only group studying the restorative potential of young plasma, **OSK**, and other geneaddition approaches (like **follistatin** and **klotho**).

This is good news, as we don't care who discovers optimal rejuvenation methods, but we want someone to make the breakthroughs fast, as degenerative aging is by far the leading cause of disease and death in modern cultures.

Our research group is spending **millions** of dollars utilizing differing **OSK** delivery doses/methods to evaluate safety and assess what **rejuvenating** effects are occurring in old mice and monkeys.

If these projects find safe ways to restore youthful health, we are targeting OSK **human** research to initiate in **2026** (or sooner).

Every time you purchase a **Life Extension®** supplement or blood test, you help fund multiple OSK induction, young plasma, and other research projects aimed at reversing our biological age clocks.

Stay Current with Research Findings

For those who want to stay current with advances occurring on the research front, enroll for <u>free</u> as a member of the **Age Reversal Network** at:

www.age-reversal.net

Newsletter updates are sent several times a year about these emerging sciences and super-longevity clinical projects.

There are thousands of dietary supplement brands on the market. I don't know of *any* that dedicates its proceeds to this type of aggressive **age-reversal** research plus has the expertise to design and evaluate multiple simultaneous scientific studies.

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For longer life,

Bill Faloon, Co-founder Life Extension Group Age Reversal Network





Meeting the Experts in Person

Each year, scientists, physicians, and interested lay people gather to learn about what can be done to delay and reverse biological aging.

Clinical findings and laboratory research discoveries are presented onstage followed by robust interactions with the entire group.

This year's 10th annual RAADfest will be in Las Vegas starting Thursday evening, July 10th through Sunday, July 13th, 2025. Special clinic services will be available on the hotel premises throughout the event.

RAADfest is a non-profit event that seeks to unite super-longevity enthusiasts to educate and motivate a revolution against aging and death.

Registration fees, which include two free meals, are a fraction of what commercial conferences charge.

The group meals are designed to keep the entire group together, sharing information and interacting in positive ways to achieve the ultimate super-longevity objectives.

To review the venue and registration fees, log on to www.raadfest.com

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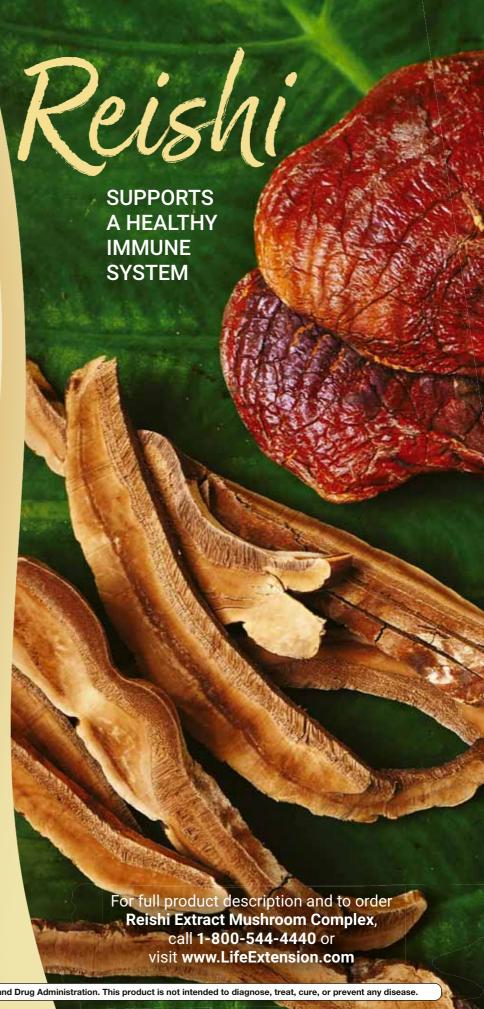
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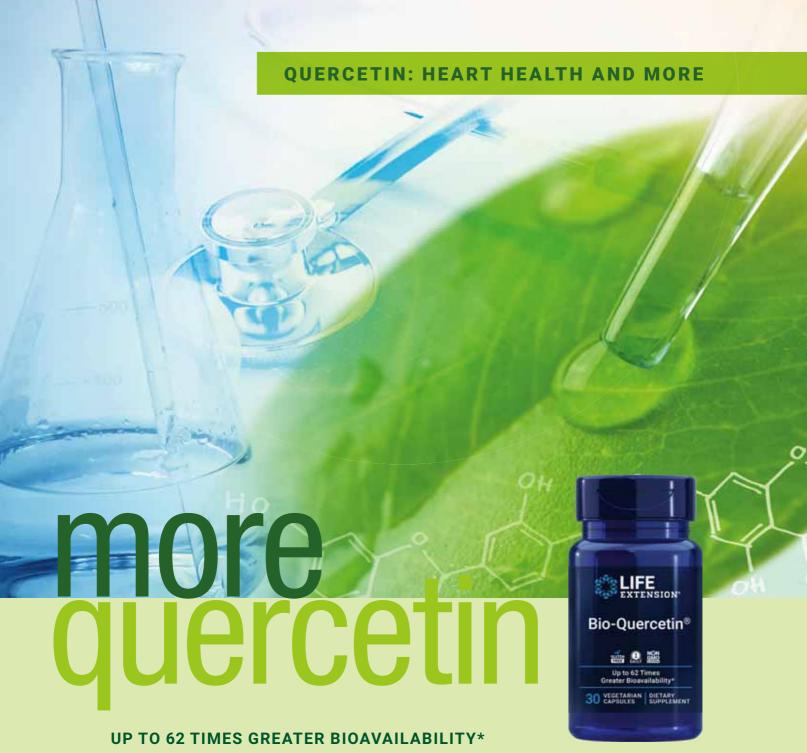
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7 A KITTY HAWK EVENT?

A 2024 published study using OSK gene therapy regenerated old mice, improved overall health and extended remaining lifespans over 100%!

20 FEMALE SEXUAL HEALTH

Studies show that **fenugreek seed extract** *enhanced* female **sexual function**, while **saffron** extract *promoted* **desire**.

30 TAURINE UPDATE

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NAD⁺ levels decline with age. In clinical trials, restoring NAD⁺ reduced inflammation, reduced fatigue, and improved mitochondrial function.

54 CALMING EFFECTS OF L-THEANINE

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74 PROSPECT OF HUMAN AGE REVERSAL

Key research findings show multiple indices of **age reversal** utilizing **exosome-rich** young **plasma** and *in vivo* delivery of cell-restoring *transcription factors*.