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MAGAZINE Resveratrol in the Prevention of Aging

Obtaining resveratrol's full benefits has been challenging. Combining resveratrol with galactomannan increases bioavailability up to 10 times.

By **William Faloon**.

In **2003**, a plant compound called **resveratrol** emerged as the hottest topic in anti-aging medicine.

The sizzling enthusiasm came from a **Harvard** study showing an astounding **70%** increase in the **lifespans** of yeast given **resveratrol**.¹

Several follow-up studies supported **lifespan** benefits in **resveratrol**-supplemented model organisms.²

What got scientists fired up are **mechanisms** behind resveratrol's **age-delaying** effects.

It turned out that **resveratrol** induced some of the favorable **gene expression** changes seen with **calorie restriction**.¹

This has led to **resveratrol** appearing in thousands of published papers about the multiple disorders that it might protect against.

For example, a PubMed® search for "**resveratrol**" yields **16,000** citations over the past four decades, including **260 clinical trials** since year 2002.

A review article published in **2021** concluded:

"Resveratrol could be an effective and safe compound for the prevention and treatment of aging and age-related diseases."³

We at **Life Extension** funded costly laboratory studies aimed at identifying what dose of **resveratrol** might enable **humans** to live *longer* and healthier lives.

The challenge, however, was finding a way to make resveratrol **bioavailable** to the **human** body.

Resveratrol is rapidly metabolized in the liver, kidneys, and other tissues despite relatively good intestinal absorption.^{4,5}

This helps explain the **longevity-enhancing** effects of **resveratrol** found in flies, fish, worms, and yeast, but inconsistent benefits when tested in mammals.²

Intensive research has uncovered a way to protect **resveratrol** from rapid metabolic degradation.

It is now possible to better explore the potential of **resveratrol** to combat degenerative disorders and assist in the **prevention and treatment of aging**.

In **1997**, a paper was published describing the biological effects of **resveratrol** as it relates to the prevention of **cancer** and other illnesses.⁶

This led to intensive investigations, thousands of published papers, resveratrol-focused conferences, and patents on resveratrol analogs.



William Faloon

The public reacted to the media blitz by ingesting **resveratrol** supplements and increasing their consumption of **red wine**, despite there being little resveratrol in red wine (and other foods).

Longevity Impact of Resveratrol

Published studies document the ability of **resveratrol** to **extend lifespans** in laboratory models.

A meta-analysis of 19 published papers indicated that resveratrol acts as a **life-extending** agent.⁷ The species studied were yeast, roundworms, mice, fruit flies, and turquoise killifish.



Resveratrol has been shown to induce **autophagy** in **human** cells in test tubes (*in vitro*) and in the bodies of roundworms (*in vivo*).³

Autophagy is a cleansing process that promotes the clearance of internal cellular debris.

The induction of **autophagy** by **resveratrol** is thought to be a longevity-enhancing mechanism.

Bees fed with **resveratrol syrup** live longer than controls.⁸ Depending on **resveratrol concentration**, mean and maximum lifespan of these bees increased by **33%** to **38%** respectively.

Short-lived **flies** fed with different resveratrol concentrations had mean lifespan extension of **10%** to **29%**, while other models found **resveratrol** also conveyed **neuroprotective** benefits.^{2,9,10}

Resveratrol-fed **fish** lived **longer** and demonstrated better cognitive ability and locomotor function than the control fish group.¹¹ The fish fed **resveratrol** showed reduced markers of **senescent cells** and less buildup of a wear-and-tear residue called **lipofuscin**.

In a genetically altered strain of **mice** predisposed to neurodegenerative disease and accelerated aging, oral administration of **resveratrol** increased the median survival of these mice from 32 days to 42 days.¹² Resveratrol additionally helped preserve motor function and protect against degenerative changes in the brain.

Not all studies demonstrate these kinds of elongated lifespans. One study found that **resveratrol** delayed **vascular aging** in **rats** but had no effect on overall survival.¹³

Another study found that in **mice** fed a standard diet, resveratrol did not enhance lifespan.¹⁴ In mice eating a **high-calorie** diet, however, resveratrol reduced the **risk of death** by **31%** and improved **insulin sensitivity**, suggesting it helps protect against diet-related metabolic diseases.¹⁵

Effect on Neurodegenerative Disorders



The aging brain is afflicted with neuroinflammation, autophagy defects, mitochondrial dysfunction, cell loss, and elevated oxidative status. This all contributes to memory loss and motor impairments.^{16,17}

A large body of data shows how **resveratrol** protects against **neurodegenerative** disorders in rodents.³

Resveratrol-supplemented animals demonstrate improved **memory** performance, enhanced secretion of **neurotransmitters**, and increased production of new brain cells with beneficial decreases in **inflammation** and **oxidative stress**.¹⁸⁻²¹

A **human** trial using **200 mg** a day of **resveratrol** showed enhanced **memory performance** accompanied with improved glucose metabolism and hippocampal functional connectivity.²²

Effect on Cardiovascular Disorders

Aging is associated with **endothelial dysfunction** that leads to arterial blockages and increased risks of cardiovascular diseases.²³

In animal models, resveratrol was shown to exert a cardioprotective effect mainly through enhancing the production of endothelial **nitric oxide**, improving blood vessel **dilation**, reducing **blood pressure**, and ameliorating **oxidative stress**.²⁴⁻²⁶

Effect on other Disorders

Research findings show how resveratrol may help protect against **cancer, osteoporosis, sarcopenia** and possibly even **infertility**.²⁷⁻³⁰

What impresses scientists are the many **pathological** mechanisms of **aging** that resveratrol has been shown to thwart.

The challenge up to now has been how to deliver enough **bioavailable resveratrol** to the bloodstream to induce systemic (whole-body) effects.

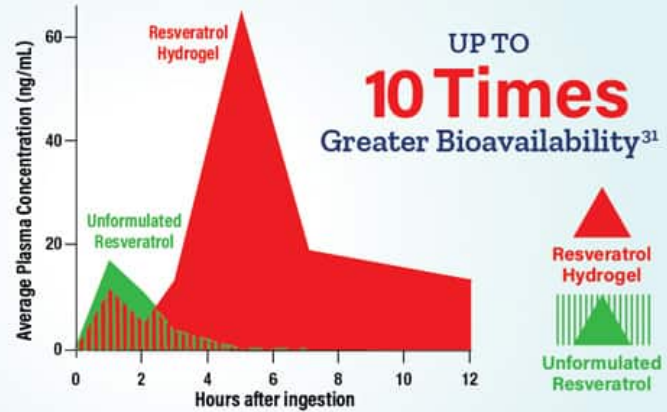
After oral administration in humans, a resveratrol hydrogel formula boosted plasma concentration (ng/mL) about 10-fold higher than unformulated resveratrol.

530 mg of Resveratrol Hydrogel providing 80 mg of trans-resveratrol (red)

380 mg of unformulated resveratrol providing 80 mg of trans-resveratrol (green)

Adapted from: Joseph A, Balakrishnan A, Shanmughan P, et al. Micelle/Hydrogel Composite as a "Natural Self-Emulsifying Reversible Hybrid Hydrogel (N'SERH)"

Enhances the Oral Bioavailability of Free (Unconjugated) Resveratrol. ACS Omega. 2022 Apr 19;7(15):12835-45.



Up to 10 Times Greater Bioavailability

Orally ingested resveratrol is rapidly metabolized and transformed primarily in the digestive tract and the liver.^{4,5} This leaves very little *free* resveratrol in circulation.

Scientists found a solution to this by combining **resveratrol** with **galactomannan** fibers from **fenugreek seed**. This creates a **hydrogel** coating that allows greater resveratrol bioavailability.

Compared to unformulated resveratrol, this **resveratrol-galactomannan** hydrogel showed **up to 10 times greater bioavailability**.³¹

The graph on this page shows the magnitude of **resveratrol** increase and the longer period this proprietary **hydrogel** formulation of **resveratrol** remained in the blood compared to unformulated resveratrol.

It's Time for More Clinical Research!



Resveratrol is a widely studied **plant extract** in the health and longevity fields.

Physician-scientists have been frustrated with **resveratrol research** because most of what is **orally** ingested is quickly degraded in the **human** body.

With the advent of a new **bioavailable resveratrol**, far better dosing schedules can be tested, and consistently **higher** blood levels achieved.

The good news for consumers is lower cost, as fewer milligrams of resveratrol need to be ingested to achieve *higher* circulatory levels.

I look forward to this new **bioavailable resveratrol** being used in upcoming clinical trials that seek to extend healthy human longevity.

Your ongoing support enables us to fund many of these **human** studies.

For longer life,

William Faloon

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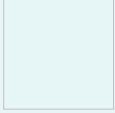
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