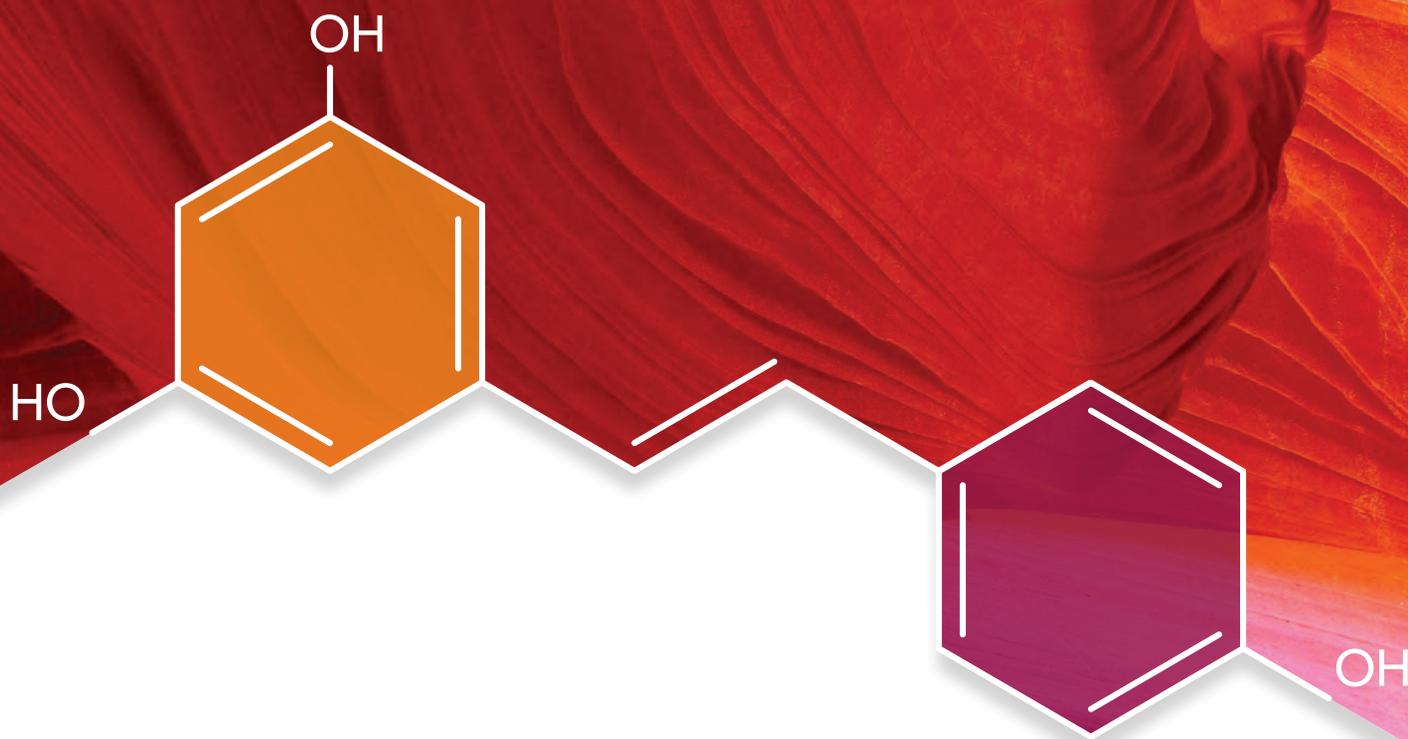


Pure, high quality resveratrol that you can trust.

resveratrol re-imagined™



Veri-te™
RESVERATROL

EVOLVΛ

Resveratrol has many potential benefits:



Bone Health

- Supports bone mineralization and formation
- Complements other bone supporting supplements



Cognitive Function

- Improves mood, well-being and pain perception
- Enhances ability to maintain memory, alertness and concentration



Cardiovascular Health

- Supports blood circulation and healthy blood pressure
- Improves vascular system and maintains healthy cholesterol and lipid levels



Oral Health

- Promotes gum and oral health due to anti-inflammation properties
- Prevents chronic bad breath based on selective anti-bacterial activity



Skin Health

- Protects skin from oxidative stress and inflammation
- Improves skin elasticity and hydration, reduces the appearance of age spots and wrinkles



Healthy Gut Microbiota

- Preserves healthy gut bacteria with selective anti-bacterial activity
- Helps soothe inflammation of the intestine



Eye Health

- Promotes normal blood flow and oxygen delivery
- Helps protect retinal cells from the aging processes and environmental stressors like UV-light



Blood Glucose Support

- Triggers cellular blood glucose (energy) uptake
- Supports healthy fasting and post-meal blood glucose level

How does resveratrol work?

As our body combats daily stress or age, mitochondrial function can become slowly compromised leading to impairment in many bodily functions including blood pressure, attention and concentration, skin health, bone and joint health, and other areas. The latest research highlights that not only does resveratrol act as a very effective antioxidant, but it also exhibits a number of complementary functions on cellular and systemic levels, leading to a plethora of beneficial health effects. Ultimately, resveratrol can potentially help rejuvenate the mitochondria and counteract the negative effects of stress and aging.

Complementary functions on cellular and systemic level

1 Antioxidant capacity

Scavenges reactive oxygen species¹

2 Activating AMPK

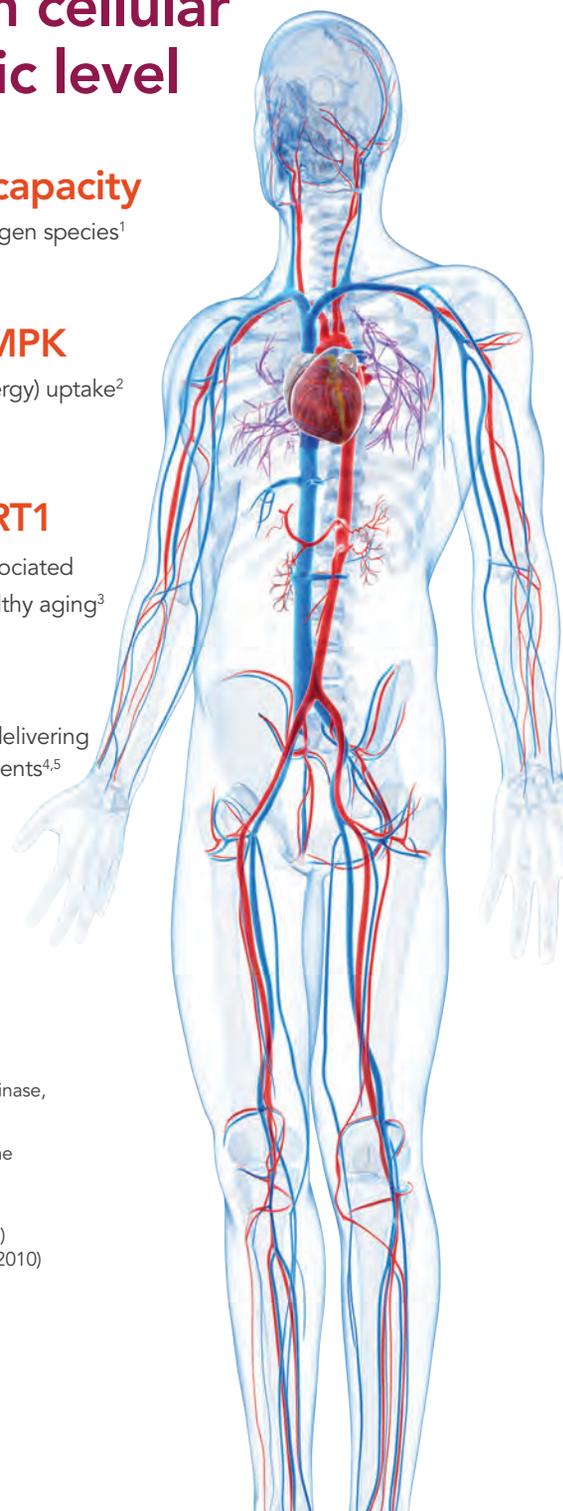
Regulates glucose (energy) uptake²

3 Activating SIRT1

Regulates stressors associated with longevity and healthy aging³

4 Vasoactive

Increases blood flow, delivering more oxygen and nutrients^{4,5}



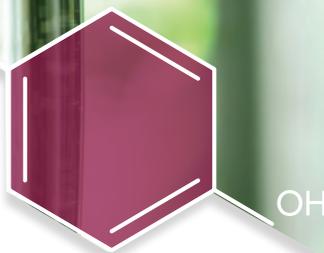
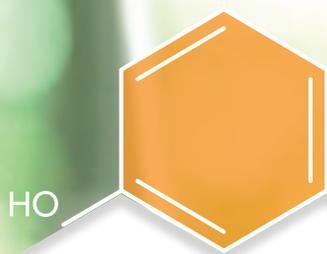
AMPK: Adenylate Monophosphate Kinase, activates proteins

SIRT1: Transcription factor, turns on the expression of genes

¹Gulcin et al., (2010) ²Lan et al., (2017)

³Borra et al., (2005) ⁴Kennedy et al., (2010)

⁵Wong et al., (2011)



A key ingredient for healthy living

Resveratrol is a polyphenol that is naturally produced by grapes, blueberries and other plants as a defense mechanism against harsh growth conditions and pathogens. With more than 12,000 published studies and over 200 human clinical trials, resveratrol is considered one of the most well-investigated compounds applied in dietary supplements, food and beverages, cosmetics and animal health. This published research and clinical data suggests that resveratrol can be a key ingredient for healthy living.

Re-imagine product development with pure, high quality resveratrol.

Veri-te™ resveratrol is produced using an innovative yeast fermentation process. This means our resveratrol is:

- PURE:** >98% pure *trans*-resveratrol
- SAFE:** free of contaminants (e.g. pesticides, emodin & PAHs)
- RELIABLE:** consistent batch to batch
- VERSATILE:** off-white, odorless and neutral taste
- SCALABLE:** large cGMP production capacity

How can Veri-te resveratrol be used?

Our resveratrol can be formulated into multiple applications including:

- | | |
|--------------------------|----------------------|
| Capsules | Film Strips |
| Tablets | Chocolates |
| Liquid Shots | Chewing Gum |
| SoftGels | Effervescent Tablets |
| Instant Powder Beverages | Creams |
| Functional Beverages | Serums |
| Gel Sachets | Make-up |

Tips for sourcing resveratrol:



Innovative Technology: from Switzerland and manufactured in Europe



Sustainable: made by fermentation, a natural process with good customer perception



Reliable: consistent quality & purity >98% *trans*-resveratrol



Approvals: self-affirmed GRAS. EFSA novel food approval daily dose 500 mg - not restricted to 150 mg



Customer Focus: Evolva is solution driven and customer focused



Research: Evolva supports clinical trials



Certified: Halal & Kosher



cGMP and HACCP: food safety conditions



- Safe:** Free from contaminants
- No emodin
 - No harmful polycyclic aromatic hydrocarbons (PAHs)
 - No pesticides, no herbicides
 - No polychlorinated biphenyls (PCBs)
 - No aflatoxins
 - No dioxins nor furans
 - No unwanted organic solvents (e.g. toluene, methanol, diisopropylamine (DIPA))
 - No toxic heavy metals (e.g. Cadmium)
 - Allergen free

EVOLVA

About Evolva:

Evolva is a Swiss biotech company focused on the research, development and commercialization of products based on nature. We have leading businesses in Flavors and Fragrances, Health Ingredients and Health Protection. Evolva's employees, half of which are women, are dedicated to make the best products that can contribute to health, wellbeing and sensory enjoyment. Find out more at www.evolva.com.

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“Our clinical trials with Resveratrol indicate that this bioactive polyphenol can be considered one of the most potent vasoactive nutrients that we have ever studied. The RESHAW study results point to multiple positive impacts of Resveratrol for counteracting the development and progression of chronic diseases afflicting our aging Western population.”

-Professor Peter Howe

Dr. Rachel Wong and Emeritus Professor Peter Howe from the University of Newcastle, Australia are the principal investigators of RESHAW.

Resveratrol Supporting Healthy Aging in Women (RESHAW)

As a result of reduced estrogen production, menopause heightens a woman's risk of osteoporosis, cognitive decline as well as mental and physical discomfort.¹ Postmenopausal women can benefit from resveratrol supplementation, which has been shown to have phytoestrogen activity and combats the cellular aging processes. Since resveratrol can be easily incorporated into a daily diet, it is a well known strategy to support healthy living.²



A brief introduction to RESHAW

RESHAW is the largest and longest clinical trial of its kind, designed to investigate the impact of Veri-te™ Resveratrol supplementation in postmenopausal women. Investigations by Professor Howe, Dr. Wong and PhD student Jay Jay Thaug Zaw at the University of Newcastle, Australia were conducted in 125 post-menopausal women over two years to determine the impact of 75 mg Veri-te™ Resveratrol twice daily on cardio-metabolic, brain and bone health parameters as well as cognitive task performance. A National Health and Medical Research Council funded initiative, RESHAW additionally investigated a wide range of secondary outcomes including body composition and perception of wellbeing, physical function and pain in the subjects. In 2020, RESHAW won the NutraIngredients Asia Award, in the category “Nutrition Research Project”.

RESHAW results support the use of Veri-te™ Resveratrol for healthy living in postmenopausal women



Peak brain health supported by:³

- Enhancing cognitive performance and slowing cognitive decline.
- Increasing healthy blood flow and reducing arterial stiffness in the brain.



Quality of life significantly impacted by:⁴

- Improving mental performance, especially mood and pain perception.
- Reducing menopausal symptoms and sleep disturbance, while improving general wellbeing.



Bone health increased by:⁵

- Improving the bone mineral density measured in the lumbar spine and neck of femur.
- Reducing the risk of bone fracture particularly when combined with calcium and Vitamin D.



Overall health improved by:⁶

- Supporting healthy blood glucose levels and insulin sensitivity.

With over 200 human clinical studies, Resveratrol has continued to gain attention as one of the most active natural activators of SIRT1, a protein which directs the cell cycle and longevity.⁷ This vast amount of research proves that Veri-te™ Resveratrol can be a key strategy for the design and delivery of effective supplements that support healthy aging.⁸

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Evolve is committed to supporting clinical trials and research studies to further understand the important benefits of resveratrol on healthy living and aging.

About Professor Peter Howe

Professor of Clinical Nutrition at the University of Southern Queensland and Emeritus Professor at the University of Newcastle Australia, Peter Howe chairs the TGA's advisory committee for complementary medicines and is a fellow of the nutrition society of Australia. With almost 300 publications, his research has underpinned health claims for functional foods and nutraceuticals. Professor Howe cites resveratrol as the most potent vasoactive nutrient that he has studied and suggests that regular supplementation improves the health of blood vessels throughout the brain and body.

About Dr. Rachel Wong

Dr Rachel Wong is a NHMRC-ARC Dementia Research Fellow who leads research at the University of Newcastle's Clinical Nutrition Research Centre. Using non-invasive transcranial Doppler ultrasonography to assess the cerebral circulation, she is exploring nutritional approaches to enhance cerebral perfusion and improve cognitive function and well-being in populations at risk of premature cognitive decline, e.g. type 2 diabetes, hypertension, postmenopausal women.

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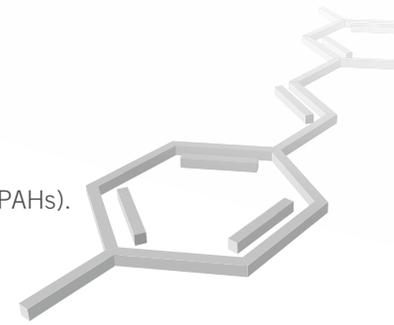
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Veri-Sperse™ CWD

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Blood Glucose

In 2018,
34.2 million
Americans lived
with imbalanced
blood glucose
levels, with
a total of
26.8% of the
population aged
65 or older
impacted.¹

Resveratrol supports
maintaining a healthy blood
glucose level and helps
protect tissues sensitive to
the effects of imbalanced
blood glucose levels.

Glucose homeostasis, a tightly regulated balance

The levels of blood sugar must be kept within a narrow range. Insulin and glucagon are the hormones allowing this regulation. Aging and other factors can cause the body to stop using insulin properly, leading to the increase of blood glucose levels. Prolonged unchecked glucose levels can dramatically reduce one's quality of life. Resveratrol can be key to supporting healthy blood glucose levels.



Resveratrol supports maintaining healthy blood glucose, blood pressure and insulin levels

Three meta-analyses²⁻⁴ individually highlighted the beneficial effects of resveratrol in people with imbalanced blood glucose levels. Subgroup analysis indicated that doses equal to or higher than 100 mg of resveratrol per day resulted in positive outcomes. Furthermore, resveratrol appears not to affect blood glucose levels in healthy individuals. Main conclusions from the meta-analyses were that resveratrol may:

- Significantly lower fasting glucose, insulin levels and insulin resistance
- Improve cardiovascular parameters and maintain healthy systolic and diastolic blood pressure

9 studies, 283 individuals, 4 weeks – 12 months (median 45 d.), median 250 mg resveratrol daily
11 studies, 388 individuals, 2 weeks – 6 months (median 12 w.), median 100 mg resveratrol daily
17 studies, 681 individuals, 4 weeks – 6 months (median 12 w.), median 300 mg resveratrol daily

Resveratrol can improve glycemic control and energy metabolism

A clinical trial⁵ investigated resveratrol's calorie-restriction mimicking effect and documented that resveratrol can activate AMPK, the main cellular regulator of energy and glucose uptake, and also SIRT1 which is known as a regulator protein for stressors associated with longevity as well as healthy aging. The study documented that resveratrol may:

- Lead to balanced glucose, lipid and triglyceride levels
- Reduce oxidative stress biomarkers and improve insulin sensitivity
- Improve muscle mitochondrial activity, and balanced basal and after-meal energy expenditure
- Stimulate metabolic changes mimicking the effects of calorie restriction

11 healthy overweight men, 4 weeks, 150 mg resveratrol daily, biochemical measurements as molecular and protein expression, micro-array data, muscle biopsy, analysis of muscle fibers

Resveratrol supports lipid breakdown by autophagy and may thereby improve insulin sensitivity

Adipose tissue dysfunction may play a prominent role in the development of insulin resistance,⁶ similar to reduced buffering capacity for lipid storage. A clinical trial⁷ investigated the adipose tissue morphology and gene expression using micro-array analysis and revealed resveratrol supplementation may:

- Reduce the overall size of fat cells, from large and very-large to small adipocytes
- Support pathways involved in cell cycle regulation, glucose uptake and lipid breakdown by autophagy

11 healthy overweight participants, 150 mg resveratrol daily, investigations of adipose tissue morphology and underlying processes

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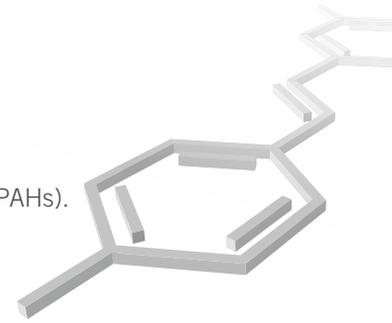
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Bone Health

One in three consumers are concerned about bone health and are looking for ways to support their bones.*

Besides supporting and stabilizing healthy joints,⁴ resveratrol has been shown to have beneficial effects on bone density.⁶⁻⁸ It supports bone health in a way that synergistically complements the actions of vitamin D and calcium⁵ making it a key addition to bone health products.

*Source: 2015 Canadian Report, Global and Regional Mega-Trends: Understanding Consumer Attitudes and Behaviours in Health and Wellness.

Bone health, a matter of balance

The delicate balance between bone formation and bone resorption is lost with aging, when resorption overtakes formation. This process is further exacerbated by obesity-related low-grade inflammation and hormonal changes characteristic of menopause.¹⁻³



Resveratrol supports the balance between bone resorption and bone formation

Besides being known for supporting healthy joints⁴, resveratrol, unlike many supplements targeting bone health, promotes the creation of new bone-forming cells.⁵ Moreover, in a recent randomized, placebo-controlled study⁶, supplementation with Veri-te™ Resveratrol led to a significant increase in bone-specific alkaline phosphatase (BAP), an important biomarker of bone formation.

24 healthy overweight men, 4 weeks, 500 mg Veri-te resveratrol daily, BAP

Resveratrol is shown to increase spinal bone density

In a follow up to the above study⁷, conducted with Veri-te™ Resveratrol, the results show:

- A significant increase in BAP
- A dose-dependent increase in spinal bone mineral density (BMD), with a significant effect observed for the 1,000 mg dose
- That resveratrol supplementation may affect bone primarily by stimulating formation or mineralization

66 overweight men with unbalanced blood pressure, blood glucose and blood lipid levels, 16 weeks, 150 or 1,000 mg Veri-te™ Resveratrol daily, BAP and lumbar spine bone mineral density

Resveratrol supports bone health in people with unbalanced blood glucose levels

A double-blind, randomized placebo-controlled trial⁸ investigated the effect of resveratrol on bone fracture risk and documented:

- Supplementation with 500 mg resveratrol prevented bone density loss, particularly in people with underlying health concerns prior to supplementation

192 people with unbalanced blood glucose levels, 6 months, 40 or 500 mg Resveratrol daily, bone mineral density, BAP, serum calcium, phosphorus and vitamin D

Veri-te™ Resveratrol reduces risk of bone fracture in menopausal women

Evolve co-funds RESHAW (Resveratrol Supporting Healthy Aging in Women), the largest and longest resveratrol study ever conducted in post-menopausal women.⁹ With a focus on bone health, the interim evaluation after 12 months of this double blind, placebo-controlled crossover study revealed:

- Improvement in the BMD measured in the lumbar spine and in the neck of the femur
- 36% reduction in hip fracture risk and a 9% reduction in the 10 year risk of a major osteoporotic fracture

125 post-menopausal women, 24 months, 75 mg Veri-te™ Resveratrol twice daily, cardio-metabolic, brain and bone health parameters as well as cognitive task performance

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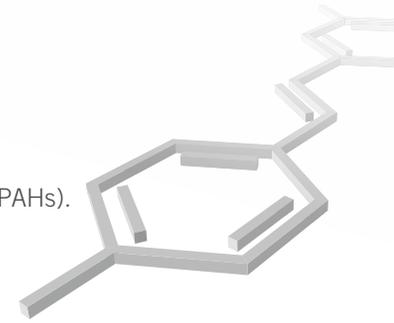
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Globally, it is estimated that approximately 1.3 billion people live with some form of vision impairment. However, 80% of all vision impairment is considered preventable.¹

Resveratrol has been shown in studies to have beneficial effects in supporting eye health.

Eye health, a vision for change

Poor eye health may in-part be caused by impaired blood-flow, inflammation, cell degradation, oxidative stress.¹⁻⁴ Resveratrol can be a key ingredient to supporting healthy vision and eye function by improving blood flow and counteracting the deleterious effects of oxidative stress.⁵



Resveratrol may improve blood flow and support eye health

Impaired blood flow and subsequent ischemic changes can lead to blurred or no vision in the center of the visual field. Resveratrol supplementation has been suggested to lead to anatomical restoration of retinal structure, improvement of blood flow and the suppression of pathological changes induced by low oxygen levels.⁶ A clinical study⁷ showed the benefits of resveratrol supplementation for eye health when compared to a placebo after only 1 hour of administration by:

- Increasing the choroidal thickness and thereby improving blood flow in the eye

34 healthy individuals (23-29 yrs), supplement with 100 mg resveratrol, single dose, choroidal thickness measured using optical coherence tomography (OTC) imaging

Resveratrol may protect retinal cells and reduce retinal degeneration

Resveratrol has been shown to lessen the gradual retinal cell degeneration caused by unbalanced blood sugar levels and associated inflammation.⁸ Resveratrol has also been reported to affect mitochondrial biogenesis and protect retinal cells against oxidative stress, light damage,^{9,10} and pathological changes such as increased vessel leakage.¹¹ A three year clinical trial with resveratrol¹² confirmed:

- Broad bilateral recovery in the ocular structure and function by improving contrast sensitivity and glare recovery

3 elderly individuals, supplement with 100 mg resveratrol daily, 2 - 3 years, clinical measurement of ocular structure, visual function

Resveratrol can reduce oxidative stress for improved eye health

Oxidative stress is thought to be a leading cause in poor eye health. Resveratrol has been shown to increase the levels of glutathione, which serves to protect against oxidative damage and also to play a role in preventing trabecular meshwork tissue abnormalities.¹³ An additional cell-culture study documented¹⁴ resveratrol:

- Prevents increased production of intracellular reactive oxygen species and affected inflammatory markers (IL1, IL6, IL8, and ELAM-1), all biomarkers of oxidative stress
- Reduces cell death and supports normal cell proliferation

Cell-culture preclinical study, trabecular meshwork cells, 15 days, 25 µM (5.7 mg/L) resveratrol, markers for inflammation, oxidative damage, and cellular aging (e.g. carbonylated proteins)

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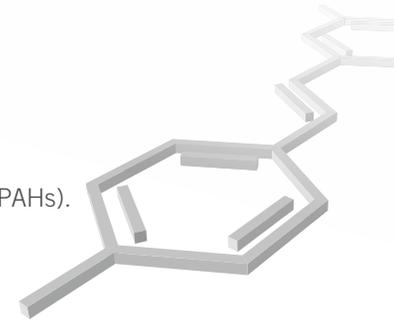
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SAFE: free of contaminants (e.g. pesticides, emodin & PAHs).

RELIABLE: consistent batch to batch.

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- Water dispersible Veri-te™ Resveratrol, made with LipiSpense® technology from Pharmako Biotechnologies.
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Veri-te™ API

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Veri-te™ Aqua

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In the anti-aging market where proven effectiveness really matters, resveratrol is a powerful and scientifically-backed ingredient that can help rejuvenate and energize skin.

Veri-te™ Resveratrol is an ideal ingredient for use in Cosmetics and Dermatology, in topical creams, serums and “*beauty-from-within*” applications.

Skin health, a matter of protection

Pollution as well as unhealthy habits (e.g. poor nutrition, sun-bathing and smoking) can contribute to the development of oxidative stress and damage our skin. This can cause age spots, wrinkles, and further forms of irritation, giving skin a prematurely aged look.¹ Resveratrol's anti-oxidative and rejuvenating properties can contribute to the maintenance of healthier and younger looking skin.²



Resveratrol helps protect skin cells from UV light-induced oxidative stress

Resveratrol has several intracellular targets that mediate its beneficial biological effects.³ Among these targets, resveratrol binds to and inhibits the activity of tyrosinase, a key enzyme involved in melanin synthesis and skin pigmentation.⁴ Literature documents how resveratrol can help protect human skin cells from UV-induced oxidative stress and damage.⁵ This work highlights that resveratrol can:

- Protect the health of skin cells
- Enhance the skin's natural protection mechanisms and the activity of antioxidant enzymes

Topically applied Resveratrol helps rejuvenate the skin

A single-blind study⁶ investigated resveratrol's effect on visible skin health by applying a cream with 0.1 mg resveratrol/g cream, daily. The clinical evaluation was monitored before and after 30 days of treatment and revealed:

- Resveratrol treatment showed visible improvement with a remarkable decrease in signs of aging
- Improved skin hydration by 21%, elasticity by 50%, and color uniformity by about 6%

8 healthy women with signs of aging skin (45-70 yrs), 30 days, 2 x 0.1 mg resveratrol cream daily, corneometry, colorimetry and elastometry measurements

Topically applied Resveratrol can improve overall skin appearance

The effect of resveratrol on skin health was investigated in a clinical trial⁷ that compared skin quality prior to treatment versus week 8 and week 12 intervals of topical use of 1% resveratrol blend. This clinical evaluation on skin quality improvement documented that resveratrol:

- Improved fine lines, wrinkles, firmness, elasticity, skin laxity, skin tone, unbalanced pigmentation, radiance, tactile roughness and overall skin appearance
- Is well absorbed and supports skin's cellular regeneration by stabilizing dermal thickness by 19%

55 healthy women (40-60 yrs), 12 weeks, 1% resveratrol blend daily, visual and clinical evaluations on skin quality

Resveratrol blend supports ‘beauty-from-within’

The oral intake of resveratrol was studied in a placebo controlled, double-blind clinical trial⁸ and showed that the resveratrol blend:

- Significantly decreased systemic oxidative stress and increased plasmatic antioxidant capacity, and skin antioxidant power
- Improved skin hydration and elasticity, appearance of skin roughness and depth of wrinkles
- Significantly decreased intensity of age spots

50 healthy women (35-65 yrs), 60 days, blend containing 8 mg resveratrol, clinical measurements and skin oxidative stress levels

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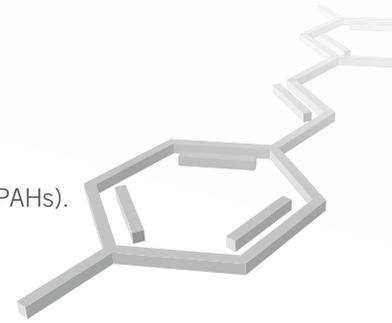
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Heart Health

Heart health is one of the top concerns among the 65+ age group* and this population segment is set to double in the next 30 years.**

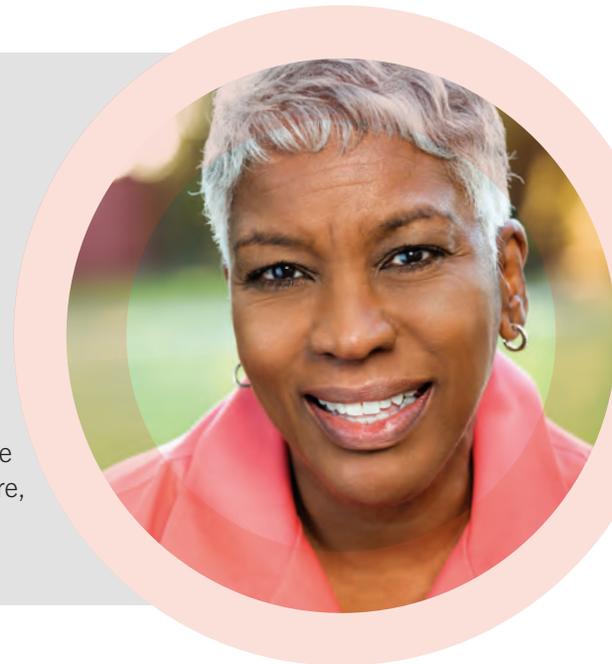
Resveratrol is an ingredient found in nature with a range of potential cardiovascular benefits.

*Source: Innova Insights 2016

**Source: United Nations, World Population Ageing 2015

Heart health, a matter of flexibility

The cardiovascular system becomes less capable of adapting to normal fluctuations with age and stress on the body caused by diet, physical activity and environmental factors in our daily routine. Keeping the cardiovascular system (heart, arteries, capillaries and veins) flexible helps maintain normal blood pressure, blood flow, blood glucose levels and overall health and wellness.



Resveratrol may manage cardiovascular health in overweight individuals

Twenty one studies on the cardiovascular effects of resveratrol in overweight subjects were pooled in a recent meta-analysis.¹ Resveratrol was found to:

- Help maintain healthy levels of cholesterol, systolic blood pressure and fasting glucose⁵
- Doses equal to or greater than 300 mg/day were seen to significantly help maintain normal blood pressure and insulin levels⁵

21 studies, 681 overweight individuals, 2 weeks – 6 months (median 3 mo.), 8 – 3000 mg resveratrol daily (median 300 mg), lipid profiles, blood pressure and glucose control

Resveratrol supports healthy blood pressure

Systolic blood pressure (SBP) increases progressively with age and is therefore considered a more important risk factor for cardiovascular disease than diastolic blood pressure.² Several studies have shown that resveratrol can:

- Help support healthy blood pressure³⁻⁵
- A meta-analysis of six studies found that resveratrol at doses of equal to or greater than 150 mg/day significantly help improve arterial function.

6 studies, 247 overweight individuals, 30 days – 1 year, 16 – 1000 mg resveratrol daily, blood pressure.

Resveratrol promotes healthy blood flow

Studies have shown that resveratrol may support healthy blood flow (vascular function) by dilating blood vessels (vasodilation), which in turn helps to maintain healthy blood circulation.⁶ Flow-mediated dilatation (FMD) measures how effectively an artery relaxes in response to increases in blood flow rate⁷; healthy FMD is an important factor in supporting heart health.⁸ According to clinical study results, resveratrol may:

- Improve vascular function by increasing FMD with evidence linking this to the ingredient's ability to increase nitric oxide concentrations.⁸

19 individuals with unbalanced blood pressure, 4 weeks (weekly intervals), placebo, 30, 90, 270 mg resveratrol daily, FMD of the brachial artery.

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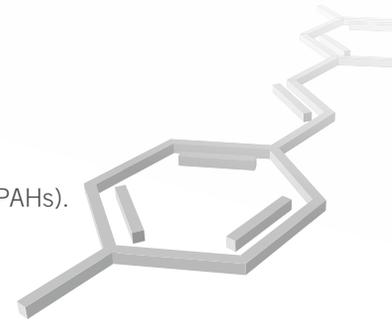
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As the aging population continues to increase there is an unprecedented need for safe, dietary-based interventions to help support and preserve optimal cognitive function.

Research shows Resveratrol is an effective ingredient in supporting many key neurological functions.

Cognitive performance, a matter of flow and preservation

As we age, decreased blood flow to the brain and biological processes such as inflammation, normal neurobiological changes, and diet and lifestyle play a role in the cognitive performance.¹

In addition to physical and mental exercise helping to preserve cognitive function², many individuals are seeking specialized nutritional strategies to support memory, cognition, and overall mental health.^{3,4}



Resveratrol helps improve memory performance in older adults

A randomized, double-blind human study showed that a daily dose of 200 mg/day of resveratrol:⁵

- Helps improve memory performance and hippocampal functional connectivity in healthy 50-75 year olds

46 individuals, 26 wks, 200 mg daily, memory performance and hippocampal functional connectivity

Resveratrol helps improve healthy blood flow in the brain

Three separate double-blind, placebo-controlled, crossover clinical studies have investigated the role of resveratrol (250-500 mg) in modulating cerebral blood flow. The studies⁶⁻⁸ agree that resveratrol:

- Alone or in combination with piperine, is able to increase cerebral blood flow parameters (i.e. concentrations of total hemoglobin and deoxyhemoglobin)

22 healthy adults, 45 minutes after intake, 250 or 500 mg, cerebral blood flow after cognitive tasks

23 healthy adults, 28 days, 250 mg resveratrol ± 20 mg piperine, cerebral blood flow

60 young adults, 28 days, 500 mg, cerebral blood flow after cognitive tasks

Resveratrol supports cognitive performance in postmenopausal women

In a randomized, double-blind, placebo-controlled clinical study⁹ indicates that resveratrol:

- Elicited a 17% increase in cerebrovascular responsiveness (CVR)
- Increased cognitive performance (e.g. memory)
- Tended to reduce anxiety and other parameters in the Profile of Mood States (POMS)

80 post-menopausal women, 14 weeks, 75 mg twice daily, neuropsychological test battery & others

Resveratrol positively effects cognitive function biomarkers

In a randomized, double-blind, placebo-controlled clinical study^{10,11} the authors showed that resveratrol:

- And its metabolites were well tolerated and crossed the blood-brain barrier
- Reduced the decline in memory and task performance
- Slowed the decline in the levels of Aβ40 and Aβ42
- Regulated the levels of neuro-inflammation while inducing adaptive immunity markers

119 individuals with mild to moderate cognitive decline, 52 weeks, 500 to 2000 mg daily, memory performance, MRI and clinical outcomes

On-going research

Evolve co-funds the largest and longest resveratrol study ever conducted in post-menopausal women. A double blind, placebo-controlled and cross-over study which investigates brain and bone health, pain perception and cognitive task performance.¹² The 12 month interim data presents that Veri-te™ resveratrol:

- Improved cerebrovascular function and cognitive performance
- Reduced risk of bone fracture
- Reduced perception of pain and improved overall wellbeing

125 post-menopausal women, 24 months, 75 mg Veri-te™ Resveratrol daily, neuropsychological test battery and others

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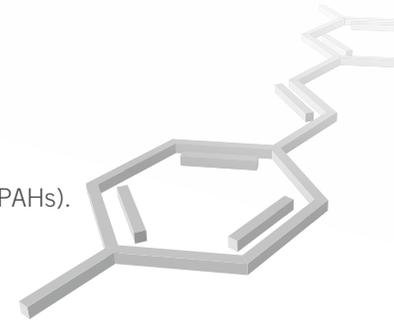
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- Allows the highest loading of resveratrol for your products.

Veri-Sperse™ CWD

- Water dispersible Veri-te™ Resveratrol, made with LipiSpense® technology from Pharmako Biotechnologies.
- Appropriate for instant powder beverages, liquid shots, oral dispersible, and effervescent tablets.
- With a neutral taste, the system is easy to flavor in a variety of formulations.

Veri-te™ API

- API grade Resveratrol manufactured under Pharma GMP. DMF available, compliant with regulatory requirements for pharmaceutical products.

Veri-te™ Aqua

- Completely water and fat soluble, made with NovaSOL® technology from Aquanova.
- Suitable for crystal clear liquid applications such as soft-gel capsules, liquid shots or functional beverages, liquid cosmetics and gel sachets.

Regulatory & Quality Status:

- EU Novel Foods approved, US self-affirmed GRAS, and other country approvals.*
- Made under cGMP and HACCP based food safety conditions.
- Halal and Kosher certified resveratrol available.

*Contact Evolva for a full list of countries where approved by regulation.

About us

Evolva is a Swiss biotech company focused on the research, development and commercialization of products based on nature. We have leading businesses in Flavours and Fragrances, Health Ingredients and Health Protection. Evolva's employees, half of which are women, are dedicated to make the best products that can contribute to health, wellbeing and sensory enjoyment. Find out more at www.evolva.com.

For more information:

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Blood Glucose

In 2018, 34.2 million Americans lived with imbalanced blood glucose levels, with a total of 26.8% of the population aged 65 or older impacted.¹

Resveratrol supports maintaining a healthy blood glucose level and helps protect tissues sensitive to the effects of imbalanced blood glucose levels.

Glucose homeostasis, a tightly regulated balance

The levels of blood sugar must be kept within a narrow range. Insulin and glucagon are the hormones allowing this regulation. Aging and other factors can cause the body to stop using insulin properly, leading to the increase of blood glucose levels. Prolonged unchecked glucose levels can dramatically reduce one's quality of life. Resveratrol can be key to supporting healthy blood glucose levels.



Resveratrol supports maintaining healthy blood glucose, blood pressure and insulin levels

Three meta-analyses²⁻⁴ individually highlighted the beneficial effects of resveratrol in people with imbalanced blood glucose levels. Subgroup analysis indicated that doses equal to or higher than 100 mg of resveratrol per day resulted in positive outcomes. Furthermore, resveratrol appears not to affect blood glucose levels in healthy individuals. Main conclusions from the meta-analyses were that resveratrol may:

- Significantly lower fasting glucose, insulin levels and insulin resistance
- Improve cardiovascular parameters and maintain healthy systolic and diastolic blood pressure

9 studies, 283 individuals, 4 weeks – 12 months (median 45 d.), median 250 mg resveratrol daily
11 studies, 388 individuals, 2 weeks – 6 months (median 12 w.), median 100 mg resveratrol daily
17 studies, 681 individuals, 4 weeks – 6 months (median 12 w.), median 300 mg resveratrol daily

Resveratrol can improve glycemic control and energy metabolism

A clinical trial⁵ investigated resveratrol's calorie-restriction mimicking effect and documented that resveratrol can activate AMPK, the main cellular regulator of energy and glucose uptake, and also SIRT1 which is known as a regulator protein for stressors associated with longevity as well as healthy aging. The study documented that resveratrol may:

- Lead to balanced glucose, lipid and triglyceride levels
- Reduce oxidative stress biomarkers and improve insulin sensitivity
- Improve muscle mitochondrial activity, and balanced basal and after-meal energy expenditure
- Stimulate metabolic changes mimicking the effects of calorie restriction

11 healthy overweight men, 4 weeks, 150 mg resveratrol daily, biochemical measurements as molecular and protein expression, micro-array data, muscle biopsy, analysis of muscle fibers

Resveratrol supports lipid breakdown by autophagy and may thereby improve insulin sensitivity

Adipose tissue dysfunction may play a prominent role in the development of insulin resistance,⁶ similar to reduced buffering capacity for lipid storage. A clinical trial⁷ investigated the adipose tissue morphology and gene expression using micro-array analysis and revealed resveratrol supplementation may:

- Reduce the overall size of fat cells, from large and very-large to small adipocytes
- Support pathways involved in cell cycle regulation, glucose uptake and lipid breakdown by autophagy

11 healthy overweight participants, 150 mg resveratrol daily, investigations of adipose tissue morphology and underlying processes

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4. Fogacci F. *et al.* Effect of resveratrol on blood pressure: A systematic review and meta-analysis of randomized, controlled, clinical trials. *Crit Rev Food Sci Nutr.* 2018; 0: 1-14.
5. Timmers S *et al.* Calorie restriction-like effects of 30 days of resveratrol supplementation on energy metabolism and metabolic profile in obese humans. *Cell Metab.* 2011; 14(5): 612-22.
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Resveratrol re-imagined

Veri-te™ Resveratrol is sustainably produced using an innovative yeast fermentation process.

This means our Resveratrol is:

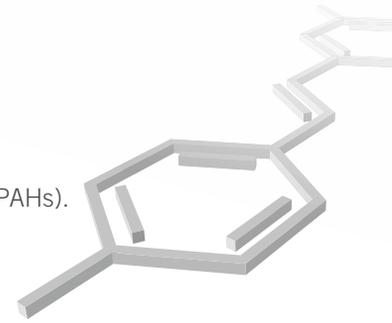
PURE: >98% pure *trans*-Resveratrol.

SAFE: free of contaminants (e.g. pesticides, emodin & PAHs).

RELIABLE: consistent batch to batch.

VERSATILE: off-white, odorless and neutral taste.

SCALABLE: large cGMP production capacity.



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What is the “resveratrol paradox”?

Although it is thought that resveratrol has low bioavailability, the evidence of its bio-activity with more than 170 published clinical studies seems unquestionable. Additionally, numerous systematic reviews and meta-analysis have reported positive associations. Therefore, it is clear that the low levels of resveratrol found in blood plasma are not telling us the whole story, and resveratrol is considered to have high bio-efficacy.^{2,3}

Rethinking bioavailability for resveratrol

Bioavailability is classically defined as “the rate and extent to which the active substance or active moiety is absorbed from a pharmaceutical form and becomes available at the site of action.”¹

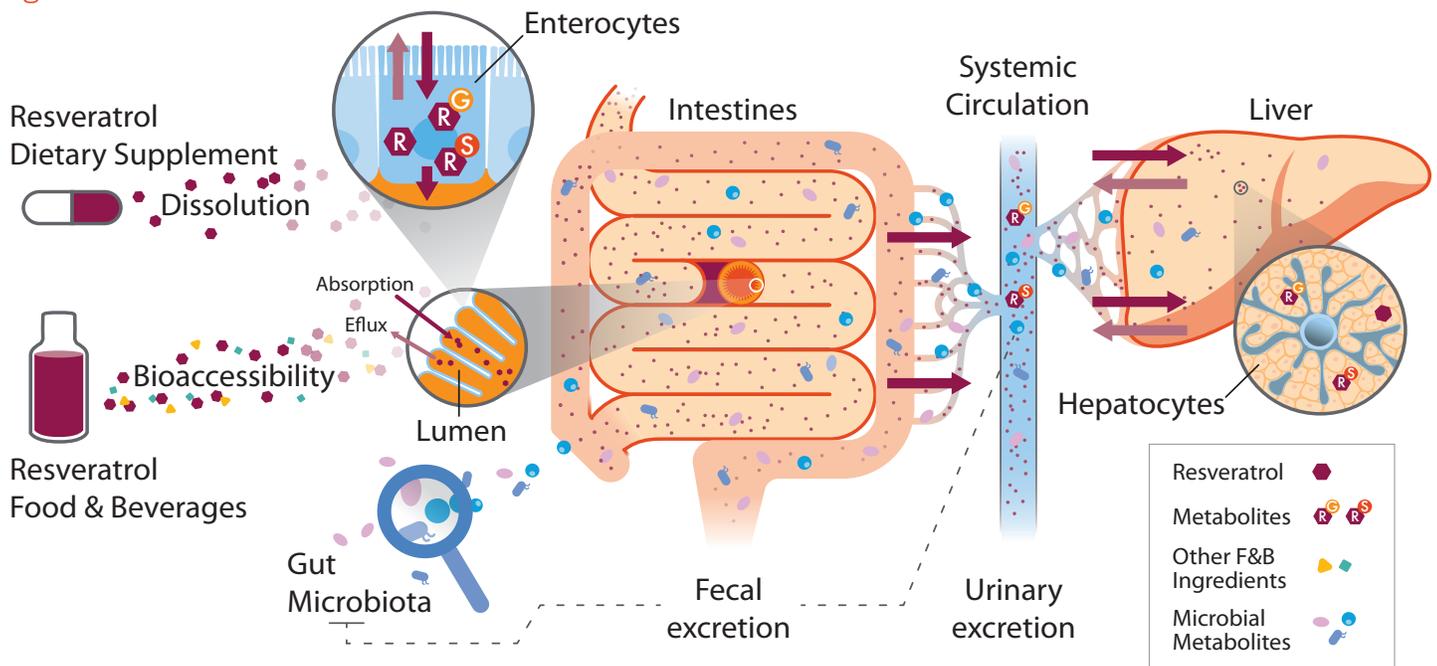
Although monitoring the circulating levels of a compound in the blood may be informative, it is important to consider that many compounds undergo *in situ* activation. Due to this activity, many compounds can be transformed into one or more active metabolites and potentially contribute to the observed clinical response. Another critical point to consider is the definition of “site of action.” The site of action or target can be an organ, tissue, or impact humans and animals on a cellular level; this is a critical factor when considering bio-efficacy.¹ This broadened understanding is key, particularly with dietary supplements containing bio-active compounds such as resveratrol, since resveratrol metabolites should be considered as part of the answer to bio-efficacy.

How bioavailable is resveratrol?

Resveratrol has been reported as being highly absorbed orally (~70%) in humans, yet has low systemic bioavailability (~0.5%), meaning that only low levels are found in the blood plasma.⁴ Figure 1 summarizes the metabolic fate and bio-transformation of resveratrol in the human gastrointestinal tract and metabolism in different organs.

The reason for the referred low systemic bioavailability is that resveratrol undergoes a rapid metabolism into resveratrol sulfate and glucuronide conjugates. In addition, resveratrol can be further metabolized by the gut microbiota. All these metabolites coming from the conjugation with sulfates and glucuronides and from microbial metabolism can be further absorbed into the systemic circulation and therefore reach different organs and have an effect.

Figure 1. biotransformation of resveratrol



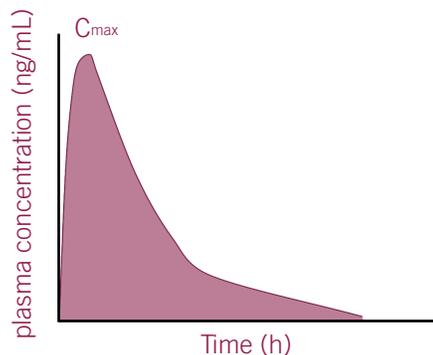
What are the key parameters?

Bioavailability of a compound is basically estimated by two key parameters, maximum plasma concentration (C_{max}) and the area under the concentration-time curve (AUC). See figure 3 below.

C_{max} is related to the fraction of the dose that reaches the circulatory system without being metabolized. The time to reach C_{max} (t_{max}) depends on the rate of absorption, distribution, and elimination.

AUC is the area under the concentration versus time curve and is expressed in (concentration) x (time), which relates to the total amount of the compound that reached the systemic circulation.

Figure 3. C_{max} and AUC



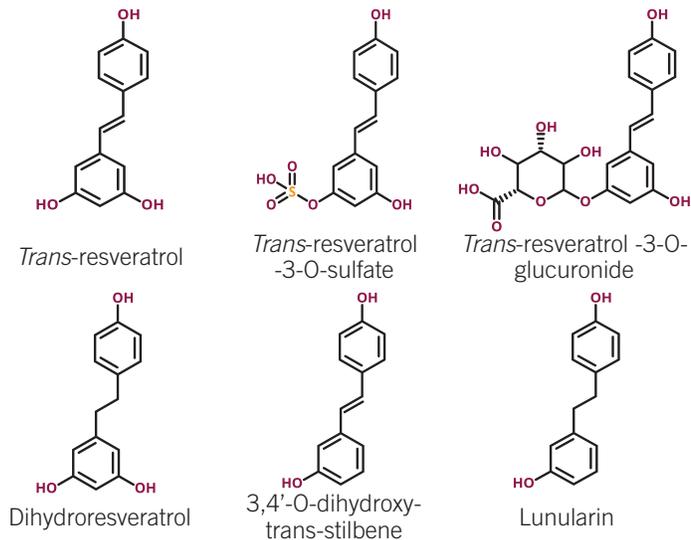
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Resveratrol metabolites play an important role in bioactivity

Figure 2 summarizes the main conjugates and microbial metabolites generated by the metabolization of resveratrol. These conjugates are produced as resveratrol is processed and digested. These conjugates play an important role in resveratrol's bioactivity and can be recirculated through the blood from the liver and bowel.⁴

Figure 2. resveratrol metabolites



About us

Veri-te resveratrol is produced by Evolva, which was founded in 2004. Based on a strong research foundation, we focus on producing high-quality ingredients for use in applications for health, wellness and nutrition. We have a talented R&D team working on cutting edge science and technology to solve the supply chain issues of nature. Evolva is a pioneer and global leader in sustainable, fermentation-based ingredients. Visit www.evolva.com to learn more.

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What are PAHs?

- PAHs are polycyclic aromatic hydrocarbons (PAHs)
- They are a large group of chemical contaminants produced both naturally and by human intervention
- Wood-burning and combustion of other biofuels contribute more than half of annual global PAH emissions, a particular problem in India and China
- Food is the main source of exposure

Why should I be concerned about PAHs?

- A number of PAHs have been shown to be carcinogenic
- The crop burning and the drying techniques used in the extraction process for botanicals can result in high levels of PAHs
- These environmental contaminants are passed naturally *via* the soil
- There is concern about the levels of PAHs in foods, supplements and personal care products

Are there maximum safe levels of PAHs?

- The European Commission has restricted concentrations of 8 carcinogenic PAHs in consumer products that contact the skin or mouth (Commission Regulation (EU) 1272/2013)
- The Commission Regulation (EC) No 1881/2006, amended by Commission Regulation (EU) 2015/1933, sets maximum levels for certain contaminants in foodstuffs
- California's Proposition 65 limits also limits the allowable levels of specific PAHs in foods

Type of PAH	Limits by Region
EU Example	Max. safe level allowed in a finished product*
Benzo(a)pyrene	10 µg/kg
Sum of PAH4**	50 µg/kg
California Prop 65 Example	No Significant Risk Level (NSRL)
Benz(a)anthracene	0.033 µg/day (oral)
Benzo(b)fluoranthene	0.096 µg/day (oral)
Benzo(a)pyrene	0.06 µg/day (oral)

* Max. safe level allowed in finished food supplement products containing botanicals and their extracts

** PAH4 is the sum of benzo(a)pyrene, benz(a)anthracene, benzo(b)fluoranthene and chrysene

Veri-te™ Resveratrol - Trusted Quality and Purity

The problem with PAHs in resveratrol

- A significant quantity of resveratrol sold in the market today is Chinese-sourced resveratrol that is extracted from the Japanese Knotweed plant (aka *Polygonum* sp.)
- Given the origin of polygonum-derived resveratrol, there is a serious risk that these products are contaminated with PAHs
- In-house testing to monitor contaminants can be expensive and complex

Veri-te™ resveratrol eliminates your risk of PAH contamination

- Evolva tested its own fermented Veri-te™ resveratrol and 3 Chinese-sourced resveratrol samples to analyze the levels of PAHs
- Based on this analysis by an independent laboratory, there is a very high risk that polygonum-derived 98% *trans*-resveratrol will contain unacceptable levels of PAHs that exceed limits set in EU and California Prop 65 regulations

PAH (µg/kg)	Polygonum sample A	Polygonum sample B	Polygonum sample C	Veri-te™
Anthracene	14	250	NT	Not detected
Benz(a)anthracene	0.89	300	41.4	Not detected
Benzo(a)pyrene	0.5	350	30.2	Not detected
Benzo(b)fluoranthene	0.74	350	59.6	Not detected
Benzo(g,h,i)perylene	0.52	260	20.2	Not detected
Benzo(k)fluoranthene	<0.5	130	19.7	Not detected
Chrysene	1.2	360	34.7	Not detected
Dibenzo(a,h)anthracene	Not detected	31	5.45	Not detected
Fluoranthene	15	940	NT	Not detected
Indeno(1,2,3-cd)pyrene	Not detected	190	20.6	Not detected
Phenanthrene	67	860	NT	Not detected
Pyrene	13	920	NT	Not detected
Sum of PAH4	3.3	1400	166	Not detected

■ Exceeds maximum safe levels
 ■ Within safe levels
 ■ Not detected
 Not tested

Note that the sum of PAH4 which is defined as benzo(a)pyrene, benz(a)anthracene, benzo(b)fluoranthene and chrysene, has a maximum safe level in the EU; Lowest limit of detection: 0.5 µg/kg; NT: not tested

All samples had a stated purity level of 98% • Testing was conducted by an independent laboratory

Veri-te™ resveratrol delivers peace of mind for those customers with supply chain concerns.