

PTEROVITA

The most efficient pterostilbene ingredient available on the market.



PTEROVITA is the most potent pterostilbene ingredient available on the market. This extraordinary potency is due to the solid form in which it crystallized during its isolation. In some infrequent cases, two highly pure products can form a single crystal unlocking its healthy properties.

This is the case of **PTEROVITA**.

Active Ingredient	—————	Pterostilbene
Coformer	—————	Picolinic acid
Purity	—————	>99.4%
Pterostilbene Content	—————	68%

Stilbenoid Natural Products Family

Resveratrol and **Pterostilbene** are both **natural stilbenoid compounds** present in many plants, with a very similar chemical structure. As a consequence, similar pharmacological activity has been described for both of them, including **analgesia, antiaging, antidiabetic, anti-inflammation, anti obesity, antioxidation, cholesterol lowering, neuroprotection**, and so on. Beyond these similarities, pharmacological activity of pterostilbene is usually stronger than that of resveratrol. This has been explained due to the **better bioavailability of pterostilbene and a significantly longer half life** (Wang, 2018).

To exert efficacy, these stilbenoids must be absorbed by the body and remain unaltered. **Resveratrol** is **rapidly metabolized**, rendering very low levels of unaltered resveratrol in blood after its intake. **Pterostilbene** is more resistant to these modifications, but due to its **low solubility**, the body absorbs a low fraction of the ingested product. It improves on resveratrol... but contrary to popular belief, not so much.



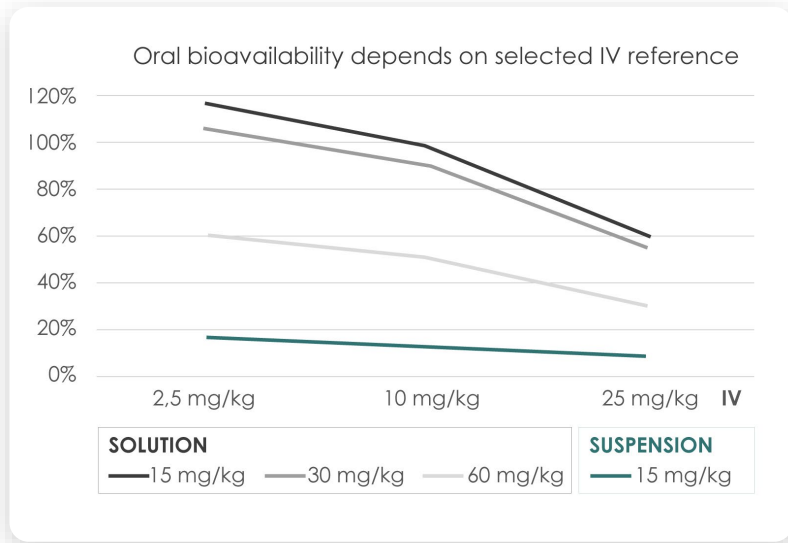
Pterostilbene bioavailability: myths and facts

An accurate calculation of bioavailability of pterostilbene renders less than 15%

It is commonly accepted that resveratrol has a bioavailability of 20% and pterostilbene 80%.

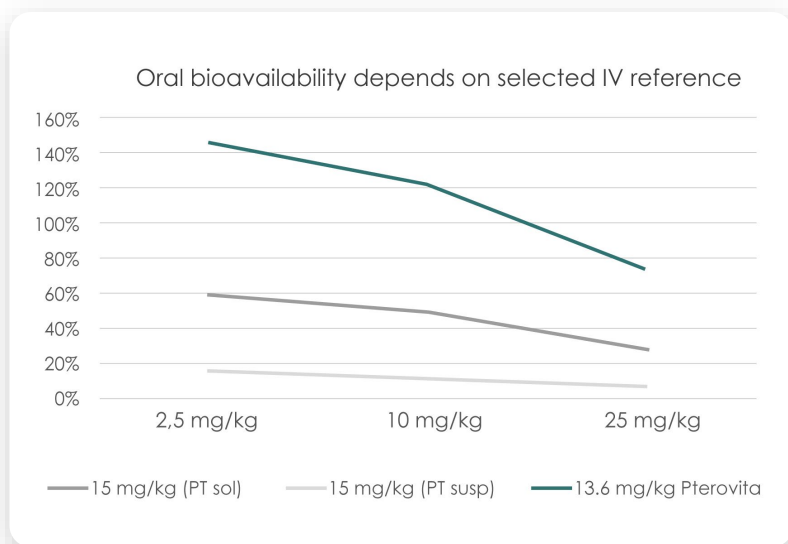
To calculate oral bioavailability, **similar oral and intravenous doses** should be compared to **avoid over/underestimations** (due to a non linear relationship between dose and blood levels).

A 15mg/kg pterostilbene suspension dose in rat (equivalent to **150mg commercial dose in human**) has a **13,5% bioavailability**.



The 20% resveratrol and 80% pterostilbene bioavailabilities were calculated in doses equivalent to ~500 and ~ 1500mg in human (far from commercially available pterostilbene doses) and compared with an intravenous equivalent dose ~100mg, resulting on an overestimation of the bioavailability of resveratrol and pterostilbene.

PTEROVITA achieves >95% bioavailability, much higher than commercial (<15%)



Commercial pterostilbene, presented in solid forms, performs **as the suspension**, less than **15% bioavailable**.

In **solution (non approved nutritional solvents)**, its **bioavailability** is around **40%**, when compared with the right intravenous dose.

Pterovita bioavailability is >95%, much higher than commercial presentations, and potential solution formulations.

These described effects have not been evaluated or validated by FDA, EFSA or any other competent authority. This product is not intended to cure, prevent, diagnose or treat any disease.

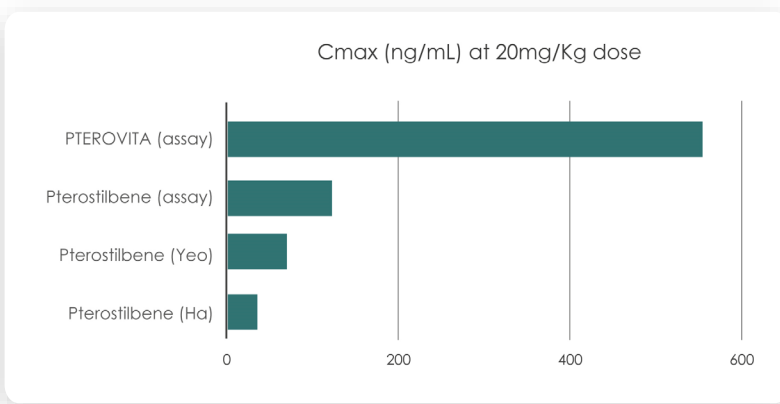


PTEROVITA improves pterostilbene solubility more than 35 fold

→ Dissolution rate of pterostilbene vs cocrystal: 12 vs 427 nmol/min.

But does this translate to a better bioavailability?

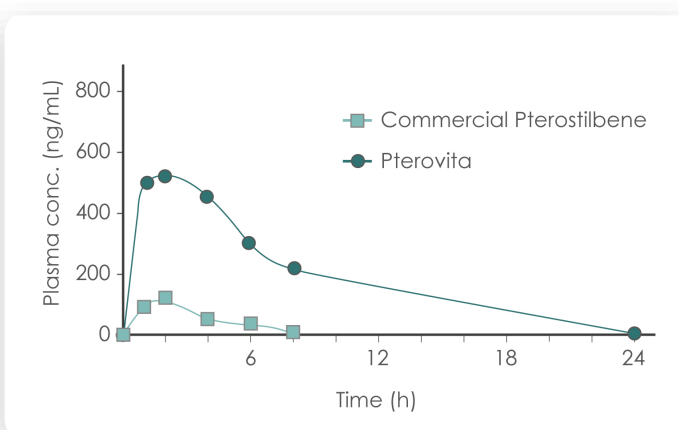
BIOAVAILABILITY STUDIES IN SPRAGUE-DAWLEY RATS, AT 20 MG/KG DOSE



The same amount of **PTEROVITA** achieves much higher levels in blood than pterostilbene or resveratrol, being the **most potent stilbenoid** on the market. A higher bioavailability has been related with superior beneficial activity by many authors.

“Comparison pharmacokinetics of resveratrol and pterostilbene in animals revealed that pterostilbene exhibited a superior pharmacokinetic profile than that of resveratrol, which could be a good explanation of why in vitro and/or in vivo pharmacological activities of pterostilbene are usually found to be superior than that of resveratrol.”
(Wang et al. 2018, Metabolism and pharmacokinetics of resveratrol and pterostilbene)

CIRCE SCIENTIFIC COMPARATIVE BIOAVAILABILITY STUDY IN SPRAGUE-DAWLEY RATS



20mg/kg of PTEROVITA, containing 68% of pterostilbene, **achieves much higher levels in blood than 20mg/kg of regular pterostilbene.**

This may lead to improved activity, and to a dose reduction to achieve equivalent blood levels. **A dose reduction will also generate free volume to include additional ingredients on the capsule, if desired.**

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PTEROSTILBENE POTENTIAL HEALTH BENEFITS DESCRIBED IN SCIENTIFIC LITERATURE

Pterostilbene is an emerging antioxidant that is attracting a lot of attention since evidences suggest that many human diseases which include neurological, cardiovascular, metabolic, and hematologic disorders are related with oxidative stress. Thus, PTEROVITA may help in preventive programs for a healthy ageing.

HEALTHY LONGEVITY



- May fight free radicals provoked by oxidative stress
- May increase sirtuin activation (sirtuin are known as the "longevity genes")
- May help fight radiation-associated damage

BRAIN HEALTH



- May reduce oxidative stress in brain
- May reduce inflammation in brain
- May improve cognitive functions
- May improve motor function
- May slow rate of cognitive decline

CARDIOVASCULAR HEALTH



- It helps maintain blood pressure in healthy levels, thus promoting a better heart health
- May improve cardiac function
- May help reduce platelet aggregation needed for thrombus formation
- May help achieve sugar levels by improving insulin sensitivity
- May be useful as support in weight control

Pterostilbene is generally safe for use in humans at doses up to 250mg per day. Pterostilbene is well-tolerated at a twice daily dosing frequency. (Riche et al. 2013, Analysis of Safety from a Human Clinical Trial with Pterostilbene")

In addition to the clinical trials already performed with pterostilbene (reduction of blood pressure, sun protection, skin brightening, antiaging...) there are many ongoing human trials with pterostilbene being studied as aid in neurodegeneration prevention, muscle regeneration, exercise performance...).

PTEROSTILBENE HAS MANY APPLICATION AREAS

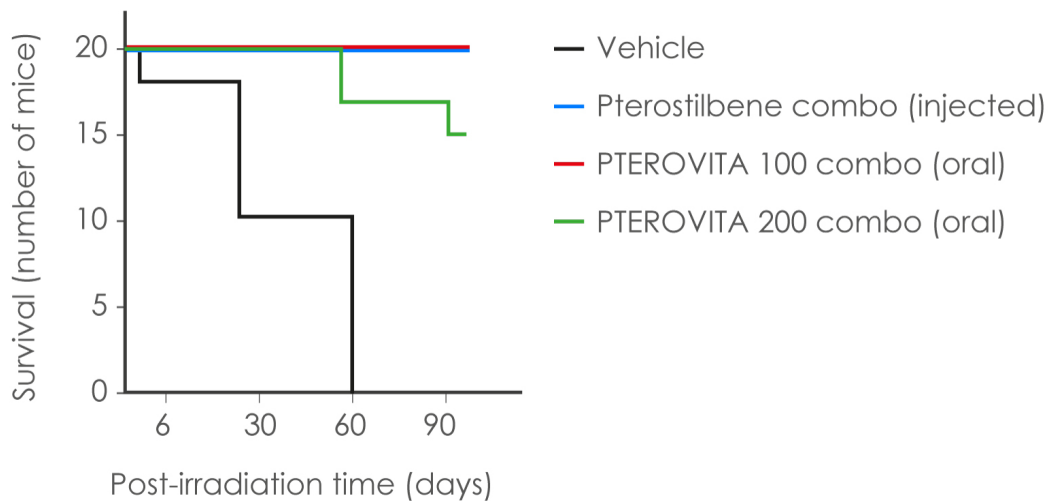
PTEROVITA bring significant improvements and benefits to the longevity healthcare sector.

Product application is broad and can be also used in the sport and pet industries.

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PTEROVITA: same activity as injected pterostilbene



Obrador et al. recently described an injected pterostilbene-based combination exerting a **high protection against lethal γ radiation in mice**. However, this effect can be observed **only** when pterostilbene bioavailability was increased by **intraperitoneal administration** of pterostilbene phosphate disodium salt to achieve relevant levels in blood.

When Obrador reproduced the same experiment with PTEROVITA, with **oral administration**, it was able to exert the same level of protective activity. This proves that **PTEROVITA, in addition to its confirmed ability to increase oral bioavailability to 99%, also maintains the expected activity.**



At CIRCE Scientific, by applying our proprietary Crystal Engineering Technology, we aim to dramatically optimize the undesirable physicochemical properties boosting the health benefits of recognized nutraceutical ingredients in order to offer to our customer premium ingredients for the development of innovative nutraceutical products in emerging health and longevity markets.

CIRCE Scientific's qualified team leads the development of new ingredients, its patent protection, transfer to industrial plant and regulatory development to provide innovative and safe ingredients.

PTEROVITA is produced at a cGMP plant holding relevant certifications, according to a strict quality policy, and audited by globally respected bodies.



REFERENCES:

Bofill L, Barbas R, de Sande D, Font-Bardia M, Ràfols C, Albertí J, Prohens R. A Novel, Extremely Bioavailable Cocrystal of Pterostilbene. *Crystal Growth & Design* 2021 21 (4), 2315-2323. DOI: 10.1021/acs.cgd.0c01716

Yeo SC, Ho PC, Lin HS (2013) Pharmacokinetics of pterostilbene in Sprague-Dawley rats: the impacts of aqueous solubility, fasting, dose escalation, and dosing route on Bioavailability. *Mol Nutr Food Res.* 57(6):1015-1025

Ha ES, Choi DH, Baek IH, Park H, Kim MS. Enhanced Oral Bioavailability of Resveratrol by Using Neutralized Eudragit E Solid Dispersion Prepared via Spray Drying. *Antioxidants (Basel).* 2021 Jan 11;10(1):90

Wang P, Sang S. Metabolism and pharmacokinetics of resveratrol and pterostilbene. *Biofactors.* 2018 Jan;44(1):16-25. doi: 10.1002/biof.1410. Epub 2018 Jan 8. PMID: 29315886

Majeed M, Majeed S, Jain R, Mundkur L, Rajalakshmi H, Lad P, Neupane P. (2020). An Open-Label Single-Arm, Monocentric Study Assessing the Efficacy and Safety of Natural Pterostilbene (*Pterocarpus marsupium*) for Skin Brightening and Antiaging Effects. *Clinical, Cosmetic and Investigational Dermatology.* Volume 13. 105-116. 10.2147/CCID.S238358

Majeed M, Majeed S, Jain R, Mundkur L, Rajalakshmi H, Lad P, Neupane P. (2020). A Randomized Study to Determine the Sun Protection Factor of Natural Pterostilbene from *Pterocarpus Marsupium*. *Cosmetics.* 7. 16. 10.3390/cosmetics7010016.

Riche D, Riche K, Blackshear C, McEwen C, Sherman J, Wofford M, Griswold M, (2014). Pterostilbene on Metabolic Parameters: A Randomized, Double-Blind, and Placebo-Controlled Trial. *Evidence-based complementary and alternative medicine : eCAM.* 2014. 459165. 10.1155/2014/459165

Amarnath Satheesh M, Pari L. The antioxidant role of pterostilbene in streptozotocin-nicotinamide-induced type 2 diabetes mellitus in Wistar rats. *J Pharm Pharmacol.* 2006;58(11):1483-1490. doi:10.1211/jpp.58.11.0009

Obrador E, Salvador-Palmer R, Pellicer B, López-Blanch R, Sirerol JA, Villaescusa J, Montoro A, Dellinger R, Estrela J (2022). Combination of natural polyphenols with a precursor of NAD+ and a TLR2/6 ligand lipopeptide protects mice against lethal γ radiation. *Journal of Advanced Research.* 10.1016/j.jare.2022.05.005.



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