



Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Pterostilbene

Evidence Summary

While more bioavailable than resveratrol, very little is known about either safety or efficacy or whether it could either help or harm.

Neuroprotective Benefit: More likely to reach the brain than resveratrol but very limited data.

Aging and related health concerns: Due to higher bioavailability, it is expected to be more effective than resveratrol but its effects in humans are largely unknown and it was reported to increase LDL.

Safety: Used as a supplement but very little clinical data exist.

What is it? Pterostilbene (PTE) is an anti-fungal agent naturally created by plants like red sandalwood, blueberries, and grapes. It is also a major phenolic compound of darakchasava, an herbal preparation used in traditional Indian Ayurvedic medicine. Pterostilbene and resveratrol are structurally very similar but pterostilbene is believed to have much stronger anti-fungal properties and better bioavailability ([Estrela 2013](#)).

Some of the concerns around resveratrol also apply to pterostilbene. The effects are difficult to predict because the compounds and their metabolites may affect many biological pathways (e.g. [Estrela 2013](#), [Poulose 2015](#)) yet those pathways can be difficult to identify because the compounds are pan-assay interference (PAIN) compounds, leading to many false-positive hits *in vitro* assays ([Baell & Walters 2014](#)).

Neuroprotective Benefit: More likely to reach the brain than resveratrol but very limited data.

Types of evidence:

- 0 meta-analyses, systematic reviews
- 0 RCTs and 0 observational studies
- 3 rodent studies; 1 cell culture study, and mechanisms of action reported in other cell types

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function? None

Human research to suggest benefits to patients with dementia: None

Mechanisms of action for neuroprotection identified from laboratory and clinical research

The primary rationale for PTE comes from evidence on resveratrol, which is believed to have similar but less potent effects than PTE. However, the effects of resveratrol in a clinical trial on dementia patients was mixed with some biomarkers suggesting benefit but others suggesting harm.

For PTE specifically, in a mouse model of accelerated aging (SAMP8), PTE, but not resveratrol, improved cognitive function, with measured effects on markers of cellular stress, inflammation, Alzheimer's-like pathology, and increased PPAR alpha activity. Oddly, neither PTE nor resveratrol activated SIRT1 ([Chang 2012](#)). Another study in aged rats reported benefit to cognitive aging and specifically working memory ([Joseph 2008](#)). Other than that, some *in vitro* studies suggest relevant mechanisms of action like on



inflammation and oxidative stress but no effects have yet been confirmed in humans (reviewed in [Poulose 2015](#)).

APOE4 interactions: None known

Aging and related health concerns: Due to higher bioavailability, it is expected to be more effective than resveratrol but its effects in humans are largely unknown and it was reported to increase LDL.

Types of evidence:

- 1 trial on PTE; 1 trial on combination therapy
- some laboratory studies on age-related conditions like cancer

Only two clinical trials have reported relevant results for PTE. In hypercholesterolemic patients, it was reported to have both benefits and harm on cardiovascular risk factors. Specifically, it increased LDL, but decreased blood pressure ([Riche 2014](#)). In another short-term cross-over trial, a combination of 5 supplements decreased some blood biomarkers of cardiovascular disease and oxidative stress in the elderly ([Qureshi 2013](#)).

PTE is being pursued as a more effective therapeutic than resveratrol (see resveratrol report), acting on virtually all the same pathways. No studies have tested whether PTE increases lifespan. Resveratrol itself has little effect on healthy mammals but may help mitigate the risks of the metabolic syndrome and diabetes. Like resveratrol, PTE is being investigated for cancer prevention and treatment ([McCormack 2012](#); [Dhar 2016](#)) but human data is lacking and the *in vitro* studies are criticized for the same reason as resveratrol – PTE is a PAIN (pan-assay interference compound) that causes false positive hits in many assays ([Baell & Walters 2014](#)).

Safety: Used as a supplement but very little clinical data exist.

Types of evidence:

- 1 clinical trial
- consumer use of available supplement and history of herbal use in Ayurveda
- some presumed toxicology studies



Companies have been seeking GRAS status for purified PTE (pTeroPure), suggesting that they have substantial toxicology data available. Pterostilbene has been tested in one Chromadex-sponsored clinical trial in patients with hypercholesterolemia at 50 or 125 mg bid for 6-8 weeks. No adverse reactions or side effects were reported. The treatment did increase LDL levels ([Riche 2013](#)). It was also used in a combination therapy in young adults with no safety concerns raised ([Joy 2016](#)). In multiple myeloma patients, a trial on a related compound (a bioavailable formation of resveratrol) was terminated early due to safety concerns of kidney damage ([GSK SRT501](#)). High doses of drakshasava, an herbal Ayurvedic medicine that contains pterostilbene, is reported online to cause diarrhea and gastrointestinal discomfort.

Sources and dosing: PTE is available as a supplement from numerous companies. The only clinical trial to-date used 50 to 175 mg bid. The supplement Elysium includes PTE and nicotinamide riboside based on the theory that the increase in NAD+ caused by nicotinamide riboside will lead to much stronger SIRT1 activation by PTE. However, to date, no studies have been published that either confirm or counter this hypothesis for a synergistic effect.

Learn more

- perspective on Scientific American [blog](#) on Elysium

Research underway: A clinical trial is testing the safety, tolerability, and general health effects of Elysium at 250 or 500 mg/day versus placebo in healthy elderly people.

Search terms:

- Pubmed - pterostilbene with trial, Alzheimer, brain, cognitive, cancer, metabolic, lifespan
- Google or other – pterostilbene purified; Elysium forum supplement
- Clinicaltrials.gov - pterostilbene



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