



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.

Protandim®

Evidence Summary

May be more useful to take the individual antioxidant ingredients at doses associated with therapeutic benefit than this combination which has no clear clinical value.

Neuroprotective Benefit: No evidence that in this formulation the antioxidants can reach the brain or exert any type of neuroprotective activity *in vivo*.

Aging and related health concerns: Possible minor survival benefit in male mice. Clinical studies show reductions in an oxidative stress marker but no evidence of meaningful clinical benefits.

Safety: No major adverse effects. Doses of ingredients lower than those traditionally used therapeutically, and no evidence that combining them is harmful.

Availability: OTC	Dose: 675mg (1 tablet) daily	Chemical formula: Mixture (milk thistle, bacopa, ashwagandha, green tea, turmeric)
Half-life: Unknown	BBB: Unknown	
Clinical trials: 4 RCTs and 1 non-placebo-controlled study. Trial sizes range from n=29 to n=46. No real clinical benefits found.	Observational studies: None	

What is it? Protandim® is a patented blend of 5 herbal ingredients with antioxidant activity: milk thistle (*Silybum marianum*) extract (225 mg), bacopa (*Bacopa monnieri*) extract (150 mg), ashwagandha (*Withania somnifera*) root (150 mg), green tea (*Camellia sinensis*) extract (75 mg), and turmeric (*Curcuma longa*) extract (75 mg). An *in vitro* study indicated that this combination has a synergistic effect in the induction of the Nrf2 antioxidant pathway [1], but there is no corresponding *in vivo* evidence.

Protandim® Nrf2 synergizer is a supplement sold by LifeVantage Corporation. It is marketed as an anti-aging pill capable of preventing or curing a wide variety of age-related diseases, including neurodegenerative disorders, cardiovascular disorders, and cancer. In 2017, LifeVantage was issued a warning [letter](#) by the FDA indicating that Protandim® is being illegally misbranded as a product intended to treat diseases with no clinical evidence to support these claims.

Neuroprotective Benefit: No evidence that in this formulation the antioxidants can reach the brain or exert any type of neuroprotective activity *in vivo*.

Types of evidence:

- 1 laboratory study

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 only indication of potential benefit in the nervous system comes from a cell culture study examining the effect of Protandim® (30 ug/ml) on preventing oxidative stress (t-BHP induced) on oligodendrocyte precursor cells. The study found that Protandim® increased levels of target genes of the antioxidant Nrf2 (HO-1, NQO1, p62), glutathione (GSH) levels, cell viability, and the percentage of cells differentiating into mature (MBP+) oligodendrocytes [2]. **It is not known whether after oral administration the antioxidants contained in the Protandim® supplement can reach the brain at concentrations that would be therapeutically cytoprotective**, or how this might impact cognitive function.

APOE4 interactions: Unknown

Aging and related health concerns: Possible minor survival benefit in male mice. Clinical studies show reductions in an oxidative stress marker but no evidence of meaningful clinical benefits.

Types of evidence:

- 5 clinical trials (4 placebo-controlled RCTs, 1 non-placebo-controlled study)
- Several laboratory studies

Lifespan: Potential benefit (mice)

Protandim® chow supplementation (equivalent to human supplement dosage) led to a 7% increase in median survival ($p < 0.012$) in male mice but had no effect on survival in females or in maximum survival ($p = 0.1$) of either sex [3]. The study was conducted by the National Institute on Aging Interventions Testing Program and examined genetically heterogeneous mice in 3 testing sites. The survival effect in males was driven by a significant increase ($p = 0.03$) in only 1 of the 3 sites.

Protection against oxidative stress damage: Potential minor/no benefit

Cell culture studies have indicated that Protandim® can protect a variety of cell types (cartilage, heart cells, endothelial cells, chondrocytes) from oxidative stress damage and activate the Nrf2 antioxidant pathway when Protandim® is applied to the cells directly [4; 5; 6]. However, these **results have not translated to clinically meaningful benefits in humans or animal models**. This suggests that the bioavailable levels of the active ingredients may be too low to induce a robust antioxidant response *in vivo*.



All of the *in vivo* studies assess antioxidant activity by measuring levels of thiobarbituric acid reactive substances (TBARS), which are a byproduct of lipid peroxidation, but is generally considered a poor marker of oxidative stress.

One study in healthy volunteers (age 20-78) found that 30 days of Protandim® supplementation (1 tablet daily) decreased plasma TBARS by 40% (1.82 ± 0.15 to $1.10 \pm 0.05 \mu\text{M}$ $P=0.001$) [7]. At baseline there was a correlation between increased age and TBARS levels, which was eliminated following supplementation. It is unknown whether this decrease in TBARS was clinically beneficial in any way. All other studies have failed to show any benefits.

Protandim® decreased TBARS by 48% in a mouse model of muscular dystrophy but provided no clinical benefit to muscle function [8]. In older adults (avg age 67), Protandim® supplementation offered no clinical benefits toward age-associated muscle decline in terms of promoting muscle synthesis and protecting against oxidative stress or inflammation [9]. In elite runners (age 25-46), Protandim® supplementation had no effect on athletic performance or antioxidant capacity [10]. Protandim® also had no effects on an overweight population of adults (age 45-60) [11] or the lung function of alcoholics [12].

Cancer: Potential minor/no benefit (mice)

Protandim® supplemented chow (600 mg/kg for 3 weeks) was partially effective in a mouse skin cancer model (DMBA + TPA induced) [13]. Protandim® supplementation decreased tumor incidence by 33% and tumor multiplicity by 57%, however, the majority of the mice still developed tumors, suggesting that Protandim® would not be useful in preventing or treating cancer.

Safety: No major adverse effects. Doses of ingredients lower than those traditionally used therapeutically, and no evidence that combining them is harmful.

Types of evidence:

- 5 clinical trials (4 placebo-controlled RCTs, 1 non-placebo-controlled study)
- Several laboratory studies

No adverse effects were reported in any of the animal or clinical studies testing Protandim®.

An ALSUntangled report on Protandim® noted that the family practitioner Dr. N. Marvin estimates that 8% of the 18,000 people who have taken Protandim® have experienced side effects, with the most

common being loose stools and rash [14]. There is no evidence of hospitalizations or deaths linked to Protandim® use.

On 'Patients like me' the most common use for Protandim® was for ALS (19 people), followed by general health (7 people). Of the 4 evaluations for general health – 1 indicated major effectiveness, and 2 indicated moderate effectiveness. Most (28/32) reported no side effects. Reported side effects were bloating and burning sensation. The most common reason for stopping use was “does not seem to work”.

ConsumerLab.com did not give Protandim® a positive rating and noted that in 2012 certain lots of the product were recalled due to the presence of metal fragments.

Sources and dosing:

Protandim® Nrf2 synergizer is a supplement sold by LifeVantage Corporation. The recommended dosing is one 675 mg capsule daily. However, a dose that is safe and effective to activate Nrf2 *in vivo* in humans has not been established. The negative results of the clinical studies suggest the recommended dose is too low. This may be because the compounds may not have enough bioavailability to be active at this concentration, as the amounts of the individual components are much lower than their recommended therapeutic doses.

Research underway:

There are no known clinical studies underway or projected.

Search terms:

Pubmed, Google: Protandim +

aging, lifespan, neurodegeneration, clinical trial, cardiovascular, safety, meta-analysis, Nrf2

Websites visited for Protandim:

- [Clinicaltrials.gov](https://clinicaltrials.gov)
- [ConsumerLab.com](https://consumerlab.com)
- [Patientslikeme.com](https://patientslikeme.com)



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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact INFO@alzdiscovery.org. To view our official ratings, visit [Cognitive Vitality's Rating page](#).