Nrf2 (NF-E2-related factor 2), a transcription factor in humans that is encoded by the NFE2L2 gene, regulates the expression of a set of antioxidant and detoxifying genes, protecting the body from the ravages of oxidative stress-related conditions, including (but not limited to) those affecting the brain and nervous system. In an unstressed state, Nrf2 is anchored in the cytoplasm by its specific inhibitor Keap1 (kelch-like ECH-associated protein 1). Keap1 functions as a sensor for oxidants and electrophilic xenobiotics. In the presence of any of these substances, Keap1 gives up its inhibition of Nrf2. This action stabilizes Nrf2, allowing it to accumulate in the nucleus and bind to the antioxidant response element (ARE) located in the enhancers of its target genes. Under this circumstance, Nrf2 then upregulates a variety of antioxidant enzymes and detoxifying proteins.

A variety of natural substances have been shown to activate Nrf2:

Sulforaphane (SGS), a naturally occurring isothiocyanate derived from cruciferous vegetables, induces phase 2 cytoprotective enzymes, supporting the body’s response to oxidative stress and inflammation. SGS may modify critical cysteine residues of Keap1, leading to Nrf2 stabilization and activation of the ARE and thereby inducing phase 2 enzymes. Research demonstrates that sulforaphane, through induction of Nrf2-dependent phase 2 enzymes, protects the brain against hypoxic-ischemic injury and may improve cognitive function when administered following traumatic brain injury.

Pterostilbene, a naturally occurring phenolic compound/analog of resveratrol that has comparatively better oral bioavailability, has been shown to possess cytotoxic, cytokine-inhibiting, and antioxidant properties. Resveratrol has also been shown to increase the protein and mRNA expression of Nrf2. There is evidence that Nrf2-mediated attenuation of oxidative stress and inflammatory cytokine induction could be partially responsible for resveratrol’s potential effect on cell-life regulation. In rat and animal studies, resveratrol/pterostilbene have been shown to upregulate a significant number of genes involved in mitochondrial function as well as to modulate cholinergic neurotransmission and improve cognition.

Curcumin’s array of biological activities stems from its cytokine-balancing activity, antioxidant properties, and induction of phase 2 detoxifying enzymes such as heme oxygenase-1 (HO-1). Purification of curcumin yields the curcuminoids demethoxy curcumin (DMC) and bisdemethoxy curcumin (BDMC). DMC has been shown to induce HO-1 more effectively than curcumin. The ability of DMC and BDMC to induce the expression of HO-1 and to translocate Nrf2 to the nucleus of pancreatic beta cells in mice suggests that they may play a role in cellular defense. Human studies showed a significant increase in curcumin absorption when co-administered with BioPerine®, a patented black pepper extract.

Green Tea’s major polyphenol, (-)-epigallocatechin-3-gallate (EGCG), has been shown to induce expression of glutathione S-transferase, glutathione peroxidase, glutamate cysteine ligase, HO-1, and other enzymes, thereby protecting a variety of cells, including cultured neurons, against oxidative stress-induced cell death. EGCG modulates the redox-sensitive transcription factor Nrf2, which plays a key role in activating detoxifying enzyme HO-1 as well as other phase 2 enzymes.

In summary, NRF2 OPTIMIZER is a promising approach to increasing antioxidant defenses by transcriptionally increasing the activity of the Nrf2/ARE pathway and positively affecting the transcription of inflammatory and antioxidant genes. Green tea, curcumin, and resveratrol (pterostilbene) have also been shown to influence amyloid formation; this influence further increases the potential of this innovative formula.
**Supplement Facts**

**Serving Size:** 2 Capsules  
**Servings Per Container:** 30

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>%DV</th>
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| Glucoraphanin (from broccoli extract)  
(Brassica oleracea italica)(seed)(SGS™)  
(Brassica oleracea italica)(seed)(SGS™) | 60 mg | ** |
| Turmeric Extract  
(Curcuma longa)(rhizome)(95% curcuminoids) | 400 mg | ** |
| Green Tea Aqueous Extract  
(Gamelia sinensis)(leaf)  
(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine) | 400 mg | ** |
| trans-Pterostilbene (pTeroPure®) | 100 mg | ** |
| Black Pepper Extract  
(Piper nigrum)(fruit)(BioPerine®) | 4 mg | ** |

**Other Ingredients:** HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglycerides.

BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.  

pTeroPure is a trademark of ChromaDex, Inc.  

Produced under US patents 5,725,895; 5,968,505; 5,968,567; 6,177,122; and 6,242,018 licensed from Brassica Protection Products LLC. SGS is a trademark of Brassica Protection Products LLC.

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### Directions

Take one to two capsules daily, or as directed by your healthcare practitioner.

Children, pregnant and lactating women, and individuals using blood thinners or receiving cancer treatment should consult their healthcare practitioner prior to use. Do not use if tamper seal is damaged.

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### References


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### Does Not Contain:

Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs) artificial colors, artificial sweeteners, or preservatives.

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*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*