

# Nrf2 Activator™

Antioxidant & Detoxification Support Formula\*



Available in 30 capsules & 60 capsules

## Discussion

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 cellular insult. 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 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

## Clinical Applications

- » Antioxidant Support\*
- » Attenuates the Expression and Release of Damaging Cytokines, Such as NF- $\kappa$ B\*
- » Supports the Body's Natural Detoxification Pathways\*

*Nrf2 Activator™, developed by Dr. David Perlmutter, is an exclusive formula designed to activate the Nrf2 genetic pathway. This pathway regulates the production of important molecules that impart antioxidant activity, such as glutathione and superoxide dismutase (SOD). It also regulates the production of detoxification enzymes, including glutathione S-transferase, and downregulates signaling factors such as NF- $\kappa$ B. Each ingredient in this formula is backed by extensive research in peer-reviewed journals.\**

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 Activator is a promising approach to increasing antioxidant defenses by transcriptionally increasing the activity of the Nrf2/ARE pathway and positively affecting the transcription of damaging cytokine 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.\*

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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.

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## Nrf2 Activator™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Glucoraphanin (from broccoli extract)( <i>Brassica oleracea italica</i> )(seed) (SGS™)	60 mg	**
Turmeric Extract ( <i>Curcuma longa</i> )(rhizome)(95% curcuminoids)	400 mg	**
Green Tea Aqueous Extract ( <i>Camellia sinensis</i> )(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	400 mg	**
<i>trans</i> -Pterostilbene (pTeroPure®)	100 mg	**
Black Pepper Extract ( <i>Piper nigrum</i> )(fruit)(BioPerine®)	4 mg	**
** Daily Value (DV) not established.		

**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.

**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.

**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.

**STORAGE:** Keep tightly closed in a cool, dry place out of reach of children.



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.



## References

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Additional references available upon request

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All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

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