

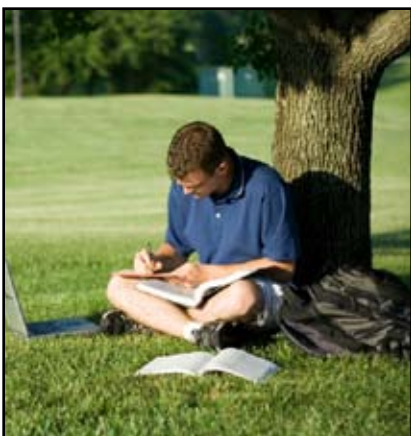
Nutraceutical Supplementation Enhances Mental Cognition

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STRUCTURE/FUNCTION CLAIMS MENTAL COGNITION

- Helps enhance focus and mental stamina*
- Helps promote mental clarity and concentration*



Mental cognition is emerging as a new health platform with strong consumer appeal. Chronic stress, aging, and other factors bring about profound deleterious effects on brain function, leading to impaired quality of life for an increasingly broad segment of the population. These effects include memory loss, difficulty learning new information, and a reduction in the ability to concentrate. Consumers that experience diminished cognitive function range from the elderly and aging Baby Boomers to stressed college students, business professionals, and parents juggling hectic schedules. Experts recommend that people eat a balanced diet, perform regular exercise (both physical and mental), and make other healthy lifestyle choices to promote overall health and well-being, but often this is not enough to maintain optimum brain function. Consumer research indicates that because of this, the public is becoming more educated regarding the beneficial role nutraceutical supplementation can play in enhancing cognitive function and are increasingly seeking natural products with scientifically proven efficacy in this condition-specific area, and which are safe to use. Nutragenesis now sells a superior, cognitive function-enhancing nutraceutical ingredient under the tradename Sensoril® to satisfy this customer demand.*

SENSORIL® - CLINICALLY-PROVEN TO ENHANCE COGNITIVE FUNCTION

Sensoril® is a safe, natural product that is clinically proven to improve memory and the ability to think clearly.* Sensoril® is a multi-patented, standardized extract of Ashwagandha (*Withania somnifera*), an adaptogen that has been used in Ayurvedic medicine for thousands of years to reverse cognitive deficits associated with stress and aging by helping to bring the body back into a state of balance, or homeostasis.* In a recent randomized, double-blind, placebo-controlled clinical trial, ingestion of Sensoril® at the recommended dosage of 250 mg per day reduced the inability to concentrate by 75.8% and forgetfulness by 57.1% (significant at $p < 0.001$ compared to placebo; Figure 1).*

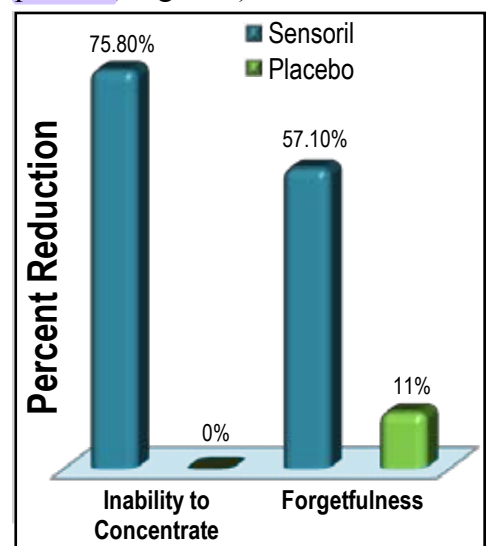


Figure 1. Percent Reduction in Inability to Concentrate and Forgetfulness in Subjects Receiving Sensoril® Compared to a Placebo.

Research has demonstrated that the withanolide bioactives in Sensoril® enhance cognitive function in a multifunctional manner, utilizing several complementary mechanisms of action that improve the overall health of neurons as well as communication between neurons.* In this way, Sensoril® has more comprehensive cognitive-enhancing activity than other products currently sold in this category that rely on single mechanisms of action to promote improvement in only one area of brain health.*

NEUROTRANSMITTERS ARE ESSENTIAL FOR PROPER BRAIN FUNCTION

Boosting neurotransmitter levels in the brain is an important way to enhance cognitive function. Neurotransmitters play a critical role in brain health by facilitating communication between neurons. Neurons are connected to each other across tiny gaps called synapses. Brain activity involves electrical propagation of nerve impulses along the axon of one neuron, transference of the impulse across the synapse via chemical neurotransmitters, and continuation of the electrical message in the dendrite of the next neuron.

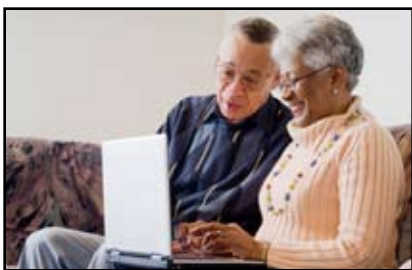
The neurotransmitter, acetylcholine, plays an integral role in facilitating communication between neurons in the hippocampus, which is considered to be the brain's seat of learning and memory consolidation. Normally, acetylcholine is continually synthesized by one group of enzymes, and degraded by another enzyme, acetylcholinesterase, to maintain ideal levels in a balanced equilibrium. As we age or are subjected to chronic stress, acetylcholinesterase activity can rise to a level where the rate of

acetylcholine degradation outpaces its rate of synthesis, resulting in a reduction in acetylcholine below critical levels. Sensoril® enhances cognitive function (particularly that related to learning and memory) because studies have shown that the withanolide bioactives it contains inhibit acetylcholinesterase activity.* This leads to higher levels of acetylcholine in the hippocampus and greater brain activity.*

HIGH CORTISOL LEVELS CAUSED BY STRESS AND AGING UNDERMINE COGNITIVE FUNCTION

Cortisol is a glucocorticoid hormone that is released from the adrenal glands as part of the body's "fight or flight" response to a stressor and is maintained at elevated levels under conditions of chronic stress. Studies have found that cortisol levels also rise in the body as we age, independent of acute stressors. Cortisol is considered by many experts to play a key role in stress-related and aging-related impairment of cognitive function because a large body of research has shown that it produces widespread deleterious effects on brain health.

Cortisol negatively impacts the amount and type of neural connections in the brain (termed "dendritic remodeling") and inhibits neurogenesis (growth of new neurons in specialized areas of the brain). In addition, it causes degeneration of parts of the brain associated with concentration, focus, and memory (the cerebral cortex and hippocampus). Neurons in these areas of the brain are particularly sensitive to rising cortisol levels because they contain large numbers of cortisol receptors. Many people have experienced the harmful effects of cortisol on brain function. For example, when



under stress, it becomes difficult to remember people's names or where the car keys are. In addition, the hippocampus regulates cortisol levels in the body via a negative feedback inhibition loop. Cortisol-induced degradation of the hippocampus reduces the hippocampus' ability to perform this regulation, resulting in even higher cerebral cortisol levels and a compounding of cortisol's deleterious effects on cognitive function.

WITHANOLIDE BIOACTIVES IN SENSORIL® IMPROVE BRAIN HEALTH BY LOWERING CORTISOL LEVELS

As an adaptogen, Ashwagandha promotes resistance to negative stressors and bring the body back into balance, or homeostasis, which is an important mechanism for enhancing cognitive function.* It has long been speculated that a major physiological mechanism responsible for this remarkable activity is the ability of withanolide bioactives to reduce unhealthy levels of cortisol in the body. The results of a recent randomized, double-blind, placebo-controlled clinical trial using Sensoril® (a proprietary extract of Ashwagandha that is standardized to a minimum of 8% withanolides) support this belief. Ingestion of Sensoril® at the recommended dosage of 250 mg per day reduced the level of serum cortisol in subjects by 24.2% (significant at $p < 0.001$ compared to placebo; Figure 2).*

This reduction was probably a factor associated with the observed improvements in variables associated with cognitive functioning (mentioned previously) that occurred in the same clinical trial, including inability to concentrate and forgetfulness. Additional evidence that the

withanolide bioactives in Sensoril® reverse cortisol-related brain tissue degeneration comes from research using *ex vivo* models.* This research demonstrated that withanolides stimulate various components of neural structural plasticity that are critical for learning and memory formation, as well as other higher cognitive functions. These include: neurite outgrowth of axons and dendrites, greater neural connectivity, neurogenesis, and synaptogenesis (the generation of new synapses).

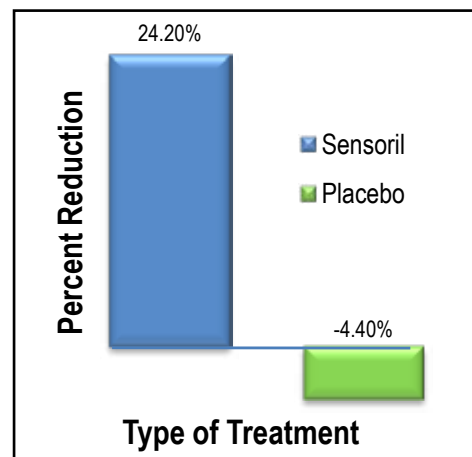


Figure 2. Percent Reduction in the Level of Serum Cortisol in Subjects Receiving Sensoril® Compared to a Placebo.

ANTIOXIDANTS REDUCE FREE RADICAL-INDUCED OXIDATIVE DAMAGE OF NEURONS

Free radicals are reactive oxygen species that oxidize and damage cellular components of neurons including cell membranes, DNA, protein, and mitochondria. An additional damaging effect of cortisol in the brain is that it increases the generation of free radicals while at the same time depressing levels of important antioxidant enzymes that protect the brain against oxidative attack by free radicals, including superoxide dismutase, catalase, and glutathione peroxidase. Regions of the brain that are important for cognitive



function, including the cerebral cortex and hippocampus, are particularly vulnerable to oxidative stress. By lowering cortisol levels, Sensoril® produces increased concentrations of the brain's antioxidant enzymes and greater protection of neurons from free radicals.* Sensoril's antioxidant properties also inhibit oxidative damage by neutralizing free radicals directly.*

DHEA IS A MENTAL COGNITION BOOSTER

Dehydroepiandrosterone (DHEA) is an important hormone that boosts mental cognition by protecting the brain against the harmful effects of cortisol. DHEA stimulates neurogenesis and increases the density of synaptic connections between neurons. It reduces the number of cortisol receptors in the hippocampus as well, making that part of the brain less susceptible to degradation by cortisol. DHEA is produced in the adrenal glands, as well as by cranial neurons and astrocytes (cells that perform important supportive roles in the brain). DHEA decreases in concentration in the body under conditions of chronic stress and also with aging, thereby contributing to impaired cognitive function. In the same randomized, double-blind, placebo-controlled clinical trial mentioned previously, ingestion of Sensoril® at the recommended dosage of 250 mg per day increased the level of serum DHEA in subjects by 32.2% (significant at $p < 0.001$ compared to placebo; Figure 3).* This result provides further insight into the mechanism by which Sensoril® improves cognitive function in the body.*

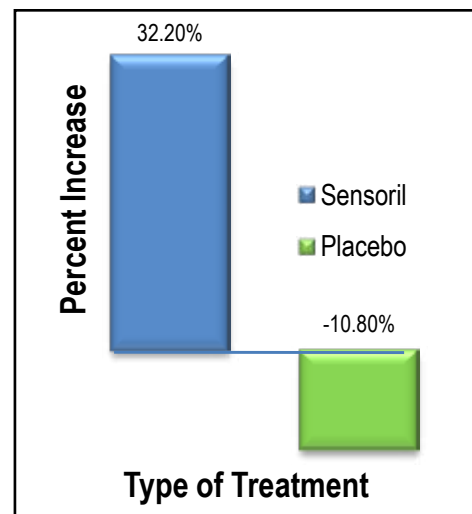


Figure 3. Percent Increase in the Level of DHEA in Subjects Receiving Sensoril® Compared to a Placebo.

SENSORIL® - A SUPERIOR MENTAL COGNITION-ENHANCING NUTRACEUTICAL

Multi-patented Sensoril® is clinically proven to enhance cognitive function by counteracting the deleterious effects of stress and aging in the brain.* By improving neuron health and connectivity, and raising levels of the neurotransmitter, acetylcholine, Sensoril® boosts the ability to concentrate and memory retention.* Based on its multifunctionality and supportive science, Sensoril® provides dietary supplement marketers with a superior choice when developing new cognitive function products.* ■

— Dr. Abedon received his M.S. and PhD in plant genetics from the University of Wisconsin-Madison and a B.S. in Biochemistry from the University of Massachusetts-Amherst. Dr. Abedon may be contacted through NutraGenesis at 802-257-5345, or bruce@nutragenesis.com.

* 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.