KeenMind®
Traditional Botanical Support for Memory, Concentration, Learning, Mental Clarity, and Calm

**DESCRIPTION**
KeenMind® is a well-researched botanical with a long history of traditional use for enhancing memory, mentation, focus, and calm. KeenMind® contains a powdered enriched extract of the traditional salutary herb *Bacopa monnieri* called CDRI 08®. This broad spectrum CDRI 08® extract contains an array of neuroactive phytochemicals. The principal *Bacopa monnieri* constituents with neurophysiologic activities are bacosides. The CDRI 08® *Bacopa monnieri* extract has been extensively studied and shown to influence neurotransmitter activities, display antioxidant effects, scavenge β-amyloid, modulate inflammatory pathways, chelate metals, enhance microcirculation, and act as an adaptogen. Animal and human studies consistently document enhanced learning and memory, calming effects, and preserved cognitive function. Each vegetarian KeenMind® capsule provides 160 mg of CDRI 08® *Bacopa monnieri* extract standardized to contain at least 55% bacosides.

**OVERVIEW**
Cognitive function is vital throughout the span of life. In childhood, hyperactivity, inattention, and impulsivity may compromise daily performance and learning. With aging, preservation of cognitive function is a major concern. A large Italian epidemiological study of people age 65 to 84 years found a 45% prevalence of diminished cognition without dementia. Clinical interest in botanical support of cognitive function at all ages is increasing worldwide. *Bacopa monnieri* is rich in phytochemical compounds that operate at the molecular level to maintain neuronal structures and enhance neural pathways to support memory, concentration, learning, clarity, focus, and calm.

*Bacopa monnieri* Background and Phytochemistry

*Bacopa monnieri* (L.) Wettst. (syn. *Bacopa monniera* Hayata & Matsum) is a creeping perennial herb indigenous to India, southeast Asia, and Australia. With succulent, elongated leaves and small white or light purple flowers, it is commonly known as Indian pennywort or water hyssop. For over 3,000 years, *Bacopa monnieri* has been used in traditional Ayurvedic medicine to support memory and intellectual function. The sixth century AD Ayurvedic text Caraka Samhita recommends *Bacopa monnieri* for anxiety, inability to concentrate, and poor cognition (literally “mind”). Phytochemical assays have identified well over 30 bioactive compounds in *Bacopa monnieri* including saponins (bacosides, bacopasaponins, hersaponin, and others), sterols (β-sitosterol, σ-sterol), alkaloids (brahmine, nicotine, herpestine), cucurbitacins (bacobitacin A-D, cucurbitacin E), glycosides, phylethanoloid glycosides, D-mannitol, betulinic acid, and a variety of flavanoids. A complex mix of four triglycocidic saponins called bacoside A and four diglycocidic saponins called bacoside B are responsible for most of the neuromodulatory and neuroprotective activities exerted by the standardized CDRI 08® *Bacopa monnieri* extract. The active constituents of *Bacopa monnieri* extract are well absorbed following oral ingestion as evidenced by beneficial effects on information processing and decision times at one and two hours following ingestion. Animal studies show that bacosides readily cross the blood brain barrier (BBB) by lipid-mediated passive diffusion.

Neurophysiological Effects

**Neuroprotective Effects**
*Bacopa monnieri* extract provides support against a variety of potentially harmful compounds including glutamate, aluminum, β-amyloid, and nitric oxide. *Bacopa monnieri* extract restores learned behaviors (Morris water maze latency times) following glutamate excitation. It supports lipid and protein structures in the face of aluminum administration and restores antioxidant enzyme systems. *Bacopa monnieri* extract scavenuges β-amyloid and prevents its aggregation in vitro. *Bacopa monnieri* maintains the function of the critical antioxidant enzymes superoxide dismutase, catalase, and glutathione peroxidase during exposure to MeHg. Isolated bacoside A protects rat brain tissue from oxidative stress due to chronic exposure to cigarette smoke.
Antioxidant Effects
Bacopa monnieri’s neuroprotective effects are mediated in large part by powerful antioxidant properties that control neural oxidative stress. It protects cultured astrocytes against nitric oxide-induced toxicity and has greater antioxidant strength than ascorbic acid. Antioxidant effects of Bacopa monnieri in brain areas involved with memory and decision-making such as the hippocampus, frontal cortex, and striatum have been amply documented. It increases a broad array of antioxidant enzymes as well as decreases the generation of reactive oxygen species. Bacopa monnieri restores normal levels of glutathione and other thiol antioxidants. It consistently reduces malondialdehyde levels, a marker for oxidative stress. Bacopa monnieri prevents deoxyribose oxidation by chelating free iron. Bacosides inhibit the β-amyloid oxidative stress pathway.

Neurotransmitter Effects
Bacopa monnieri extract restores acetylcholine and acetylcholine esterase levels in aging rat brains to those seen in young animals. It appears to increase acetylcholine levels by upregulating acetyltransferase thereby boosting synthesis. Bacopa monnieri also potentiates monoamine neurotransmitters thereby reducing 5-hydroxytryptamine and dopamine to youthful levels. It increases 5-hydroxytryptamine levels in the hypothalamus and cerebral cortex. Bacopa monnieri extract-induced increases in 5-hydroxytryptamine indirectly augment acetylcholine levels. Bacopa monnieri augments the expression of a particular subtype of 5-hydroxytryptamine receptor termed 5-HT3A which facilitates hippocampal-dependent learning.

Synaptic Plasticity Effects
Neuronal communications are effected through specific histologic structures termed synapses. Information is communicated from neuron to neuron via electrochemical signaling involving ion channels, neurotransmitters, vesicles, and receptors. The ability to physically modify synaptic pathways is widely believed to underlie learning and memory. Bacopa monnieri extract has been shown to increase synaptic protein synthesis necessary for solidifying of long-term memories by increasing cyclic adenosine monophosphate (cAMP) activity and the cAMP response element binding (CREB) protein signaling pathway. Bacopa monnieri regulates CREB phosphorylation to favor transcription of CREB targeted genes associated with memory formation. Bacopa monnieri extract increases cholinergic neuronal densities.

Animal Learning Behaviors
Bacopa monnieri extract significantly improves learning in animal models. It enhances parameters of acquisition, consolidation and retention of newly learned behavioral responses. Learned behaviors that are both positively and negatively reinforced are enhanced. A host of studies involving a diverse array of mazes robustly shows Bacopa monnieri improves spatial learning and spatial working memory in rodents. Bacopa monnieri extract reduces latency in reward retrieval and improves discrimination of novel objects.

Human Studies
Bacopa monnieri has been used in over 60 human studies to improve cognition, memory, and learning. Acute administration of 320 mg and 640 mg of CDRI 08® Bacopa monnieri extract in a placebo-controlled, double-blinded study led to improved cognitive function based on performance of a computerized multitasking framework. The tasks include mental arithmetic, stroop (interference with reaction times), letter search, and visual tracking. In addition to improved cognitive function, the KeenMind® CDRI 08® extract improved mood and reduced salivary cortisol levels indicative of reduced stress. A second acute study of KeenMind®, using the Cognitive Demand Battery (CDB) cognitive tests, confirmed the benefit of CDRI 08® Bacopa monnieri on cognitive performance during repeated CDB testing suggesting enhanced attention allocation. Independent review has identified six quality clinical studies involving chronic administration of Bacopa monnieri extract to otherwise healthy adults. Three of these trials used the KeenMind® CDRI 08® extract. While comparison of one study to another is difficult because a variety of different end points were used, extracts of Bacopa monnieri clearly and consistently enhance memory, especially free recall memory, and cognitive speed. Studies of KeenMind® CDRI 08® over 90 days show it improves the speed of information processing and verbal learning as well as reducing anxiety. In children with ADHD, 225 mg of Bacopa monnieri extract daily for six months reduced restlessness and improved self-control and attentiveness in more than 85% of the participants (n=31). Scores for learning problems, impulsivity, and behavioral problems were also reduced in over 50% of the children.
KeenMind® with CDRI 08® is intended for individuals who wish to support memory, learning, concentration, mental clarity, and calm. KeenMind® may be used to support cognitive function during aging. Its adaptogenic properties may be useful to maintain cognitive function under stressful circumstances.

**SUGGESTED USE**
2 capsules daily. Capsules should be taken in the morning with breakfast. Children from age 6 to 12 years should take 1 capsule daily with breakfast.

**ADVERSE REACTIONS**
Symptoms reported significantly more frequently in clinical trials with the CDRI 08® *Bacopa monnieri* extract than with placebo include dry mouth, fatigue, palpitations, nausea, excessive thirst, and indigestion.

**DRUG INTERACTIONS**
*Bacopa monnieri* extract inhibits human cytochrome P450 enzyme isoforms important in drug metabolism. It exhibits non-competitive inhibition of CYP2C19, CYP2C9, CYP1A2; competitive inhibition of CYP3A4; and weak inhibition of CYP2D6. Bacosides show negligible inhibition of the same cytochrome P450 isoforms so other components of the extract are responsible for the cytochrome P450 inhibition. Persons taking immunosuppressant medications, antiarrhythmics, calcium channel blockers, or any other medications known to be metabolized by the cytochrome P450 enzyme isoforms CYP2C19, CYP2C9, CYP1A2, and CYP3A4 should consult with a doctor before using this product.

**CONTRAINDICATIONS**
Known sensitivity to *Bacopa monnieri*.

**HOW SUPPLIED**
60 capsules per bottle.

**STORAGE**
Store in a cool, dry place (59°F to 85°F), away from direct light. Keep out of reach of children.

**REFERENCES**
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.