

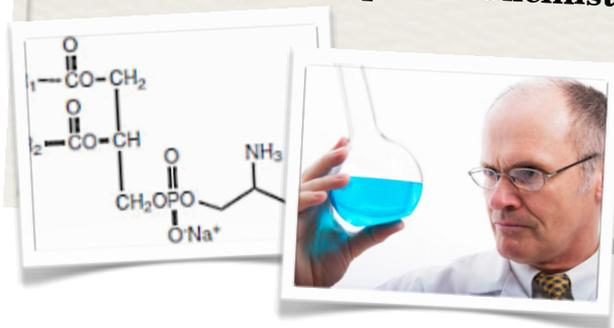
Brain Support

© 2014 TO YOUR HEALTH

LITERATURE EDUCATION SERIES ON DIETARY SUPPLEMENTS

To Your Health

By Chad Brey,
Research & Development Chemist



All Humans Have An Amazing 3lb Chunk of tissue embedded within our skull that controls virtually all biological functions called the brain. With nearly 100 billion neurons making thousands of synaptic connections per neuron, many would admit that the human brain is by far one of the most complex and intricate processing and storage systems on the planet. As impressive as this biological computer might seem, it, like many other body parts, gets old and defective with time. However, both the mature Alzheimer's sufferer and the mentally exhausted college student may be interested in knowing that there are many different natural supplements that can greatly benefit our amazing brains.

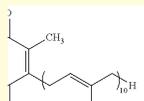
Ginkgo Biloba

Native to China, the maidenhair tree (ginkgo) has many interesting constituents that play different roles in cognitive function. Within the extracts of these ginkgo leaves are found flavone glycosides and different terpenoids which exert different biological effects on the brain and nervous system. One such effect is a reduction in memory loss, as one study suggests regarding the possible effect of ginkgo extract on monoamine oxidase (MAO)¹. This is especially beneficial since one particular monoamine, dopamine, is directly involved in cognitive endurance and memory. In fact, dopamine (and a little involvement of norepinephrine) have been used to treat Alzheimer's disease. So, inhibiting the synaptic reuptake of this neurotransmitter by ginkgo has a very large impact on improving

memory. Interestingly, one of the constituents of the extract of ginkgo leaves, bilobalide, has shown great promise for improving learning and memory. This terpenoid has demonstrated outstanding neuroprotective effects in vivo by increasing superoxide dismutase and glutathione activity, decrease nitric oxide synthase, alleviate neuronal apoptosis (programmed cell death), and decrease TNF-alpha expression in the brain². This 5-hit punch to decreasing cognitive function yields bilobalide a hot commodity to the ginkgo extract. Since ginkgo has also been linked to increased circulation, the outcome of one study that shows ginkgo extract (along with fish oil and multi vitamins) increasing regional cerebral blood flow to healthy individuals³ seems to make sense.

Phosphatidyl Serine

Of all phosphatides found within the cell membrane in humans, phosphatidylserine is one of the most active players in memory and cognitive performance. The amino acid portion of this phospholipid hangs out within the inner cytosolic part of the membrane and has been shown to greatly enhance memory, executive functions, and mental flexibility⁴. Phosphatidylserine seems to work its magic by having a trophic effect on the brain, namely the cerebellum, hippocampus, and other zones. It does this by increasing nerve growth factor (NGF)-receptor density in these areas⁵. Phosphatidylserine also seems to have the ability to improve cognitive function and memory by stimulating the release of dopamine and acetylcholine



TO YOUR HEALTH
Literature Series
By Chad Brey



See More Research Articles:
VivaVitamins.com - click on "Education"



(one of the main neurotransmitters involved in memory) in the striatum and cerebral cortex, respectively⁶. One study even showed how supplementation with phosphatidylserine drastically enhanced the amount of glucose uptake in the temporo-parietal areas of the brain^{7,8}, showing great promise for Alzheimer's sufferers. Although the exact mechanism is not completely understood, phosphatidylserine has also been shown to reduce neural cell degradation caused by free radicals⁹. Much promise has also been given to Attention Deficit Hyperactive Disorder and phosphatidylserine supplementation¹⁰. Throughout all of the various routes of action phosphatidylserine takes on the brain, it seems to be a key player in overall brain performance, especially when taken in conjunction with other cognitive-enhancing supplements.

Bacopa monniera

Various alkaloids, saponins, and flavonoids found in the leaves of water hyssop have been shown to improve memory and cognitive endurance. Although many studies performed on Bacopa monniera extract seem to include co-supplementation with other herbs and phytonutrients, it packs a very powerful punch on improving memory when administered alone. One of the routes in which it is postulated to improve memory dysfunction for example, is through decreasing neuronal oxidative stress, neuroinflammation, and neuronal loss¹¹. Specifically, it has been shown to do this by increasing acetylcholinesterase inhibition in the brain (extending the synaptic half life of one of the most abundant neurotransmitters involved in memory) and by enhancing synaptic plasticity-related signaling (neural firing) within hippocampal regions¹². Bacopa monniera has been used traditionally in India and other

parts of the world as an Ayurvedic treatment for many different disorders, but has recently been discovered for its use in cognitive dysfunction.

Huperzine

The primary source of the sesquiterpene alkaloid Huperzine A is extracted from the Huperzia serrata plant and has been used in Asia for many years to treat different ailments. Just recently, huperzine has been explored in the United States for its dynamic role in memory loss. Much insight has been uncovered thanks to scientific research as to its pharmacology and how it does what it does. Recent studies have shown huperzine to act in a similar manner to many prescription drugs for Alzheimer's disease. It does this by acting as a cholinesterase inhibitor and is actually used so as a treatment for Alzheimer's in China and parts of the United States¹³. Huperzine also exhibits its fascinating work on reducing oxidative stress and glutamate-induced damaged in the brain by antagonizing n-methyl-d-aspartate (NMDA) receptors¹⁴, which benefits both Alzheimer's sufferers and the rest of the population alike. All in all, this alkaloid packs a powerful one-two punch to both neural stimulation and protection simultaneously.



Vinpocetine

As a derivative of the alkaloid vincamine from the periwinkle plant, vinpocetine has been used worldwide with recent focus in the United States for its vasodilative properties, especially in the brain.

Additionally, as an anti-inflammatory, vinpocetine has shown neuroprotective properties in the brain by inhibiting microglial inflammation mediated by the usual proinflammatory culprits (IL-1 β , TNF- α , and IL-6)¹⁵. This kind of inflammation is seen in Parkinson's and Alzheimer's disease sufferers. Further, vinpocetine acts as a phosphodiesterase inhibitor¹⁶, which is where it gets its vasodilating effects – vasorelaxing smooth muscle cells in the brain. In fact, many other prescription medications work in this manner with their aim toward the same outcome.

Alpha GPC

L- α -glycerylphosphorylcholine (alpha-GPC) is an enzymatically derived choline source that has shown much promise in enhancing cognitive function. As phosphatidylcholine gets its fatty acids chemically or enzymatically clipped off and then rearranged, alpha-GPC is born and becomes a source of choline delivered across the blood-brain barrier to be used as brain food. Besides just being a source of choline (namely acetylcholine), high levels of alpha-GPC within hippocampal regions of the brain have been found to have a significant impact on memory capacity and permanency in healthy human brains as well as Alzheimer's sufferers¹⁷. Further, clinical trials show prolonged beneficial effects in Alzheimer's patients on cholinergic therapies supplementing with alpha-GPC¹⁸. So, we can almost think of alpha-GPC as being a dual functioning form of choline for memory enhancement.

Gotu Kola

Native to many different countries, the *Centella asiatica* plant has many culinary uses, but it is most known for its usefulness in mental acuity promotion. One interesting aspect of this extract is its unique neuritogenic ability (nerve growth). *Centella asiatica* has shown to be able to actually stimulate neurite outgrowth in human neuroblastoma cells¹⁹. The neuroprotective properties of Gotu Kola may also be attributed to its phospholipase A2-blocking actions²⁰ acting as an anti-inflammatory within cortical neurons. This would be especially helpful for people who are suffering from memory loss due to a variety of different physiological circumstances.

L-tyrosine

It is well known that the non-essential amino acid L-tyrosine can be manufactured by the body from adequate amounts of phenylalanine and can be used to biologically synthesize norepinephrine and dopamine (the feel-good neurotransmitters). However, there is evidence that this particular amino acid has the capacity to target cognitive-control operations and promote performance in working memory²¹. Apart from indirectly helping with focus and concentration due to mood enhancement via norepinephrine and dopamine production, tyrosine in and of itself seems to be able to improve mental endurance, memory, and overall cognitive performance in a number of subject groups in different environmental and physiological circumstances^{22,23}. So tyrosine, while multi functional, seems to be able to increase certain areas of mental capacity as a solo player or in conjunction with other supplements.

L-Glutamine

Glutamine is one of the most multi functional amino acids in the human body. Of specific interest to neurology, it is the chief supplier of

glutamate, the main excitatory neurotransmitter in the central nervous system²⁴. Glutamine readily gets converted by quick deamination (an NH₃ gets removed) to glutamate within presynaptic neurons via the glutamine-glutamate cycle. This in turn provides the amino acid responsible for the formation and retrieval of memories, spatial recognition and the maintenance of consciousness²⁵. Too much glutamate within the synaptic cleft, and we create a problem with excitotoxicity. Fortunately, our bodies have a very intricate system of regulating the amount of glutamate being produced from glutamine via this cycle. This is why it would be extremely dangerous to administer large amounts of glutamate by itself²⁶. So in this sense, it would seem obvious - and studies also show, that glutamine as a precursor to glutamate, along with other nutrients, seems to improve cognitive function – especially in learning²⁷

References:

1. Tanaka K et. al., "Ginkgo biloba extract in an animal model of Parkinson's disease: a systematic review." *Curr Neuropharmacol*. 2013 Jul;11(4):430-5.
2. Li WZ et al, "Protective effect of bilobalide on learning and memory impairment in rats with vascular dementia." *Mol Med Rep*. 2013 Sep; 8(3):935-41
3. Amen DG, Taylor DV, Ojala K. "Effects of brain-directed nutrients on cerebral blood flow and neuropsychological testing: a randomized, double-blind, placebo-controlled, crossover trial." *Adv Mind Body Med*. 2013 Spring;27(2): 24-33.
4. Richter Y., Herzog Y., et al., "The effect of soybean-derived phosphatidylserine on cognitive performance in elderly with subjective memory complaints: a pilot study." *Clin Interv Aging*. 2013;8:557-63
5. Nunzi M, Guidolin D, Petrelli L, et al. "Behavioral and morpho-

functional correlates of brain aging: a preclinical study with phosphatidylserine." In: Bazan NG, ed. *Neurobiology of Essential Fatty Acids*. New York, NY: Plenum Press; 1992;393-398.

6. Nunzi MG, Milan F, Guidolin D, et al. "Effects of phosphatidylserine administration of aged-related structural changes in the rat hippocampus and septal complex." *Pharmacopsychiatry* 1989;22:S125-S128.
7. Heiss WD, Kessler J, Mielke R, et al. "Long-term effects of phosphatidylserine, pyritinol, and cognitive training in Alzheimer's disease." A neuropsychological, EEG, and PET investigation. *Dementia* 1994;5:88-98.
8. Klinkhammer P, Szeliés B, Heiss WD. "Effect of phosphatidylserine on cerebral glucose metabolism in Alzheimer's disease." *Dementia* 1990;1:197-201.
9. Latorraca S, Piersanti P, Tesco G, et al. "Effect of phosphatidylserine on free radical susceptibility in human diploid fibroblasts." *J Neural Transm Park Dis Dement Sect* 1993;6:73-77.
10. Vaisman N, Kaysar N, Zaruk-Adasha Y, Pelled D, Brichon G, Zwingelstein G, Bodennec J (2008). "Correlation between changes in blood fatty acid composition and visual sustained attention performance in children with inattention: effect of dietary n-3 fatty acids containing phospholipids." *The American Journal of Clinical Nutrition* 87 (5): 1170–1180.
11. Dwivedi S. et al., "Standardized Extract of *Bacopa monniera* Attenuates Okadaic Acid Induced Memory Dysfunction in Rats: Effect on Nrf2 Pathway." *Evid Based Complement Alternat Med*. 2013;2013:294501
12. Le XT et al., "Bacopa monnieri ameliorates memory deficits in olfactory bulbectomized mice: possible involvement of glutamatergic and cholinergic systems." *Neurochem Res*. 2013 Oct;38(10):2201-15
13. Huang XT et al., "Reducing iron in the brain: a novel pharmacologic mechanism of huperzine A in the treatment of Alzheimer's disease." *Neurobiol Aging*. 2013. Nov 13.

14. Coleman, BR; Ratcliffe, RH; Oguntayo, SA; Shi, X; Doctor, BP; Gordon, RK; Nambiar, MP (2008). "+-Huperzine A treatment protects against N-methyl-D-aspartate-induced seizure/status epilepticus in rats." *Chemico-biological interactions* **175** (1-3): 387–95
15. Zhao YY et al., "TSPO-specific ligand vinpocetine exerts a neuroprotective effect by suppressing microglial inflammation." *Neuron Glia Biol.* 2011 May;7(2-4):187-97
16. Hagiwara M, Endo T, Hidaka H (1984). "Effects of vinpocetine on cyclic nucleotide metabolism in vascular smooth muscle". *Biochemical Pharmacology* **33** (3): 453–7
17. Kozlovskiy, S., Vartanov, A., and Pyasik, M. (2013). Human memory and glycerophosphocholine level in hippocampus. In The 13th European Congress of Psychology. European Federation of Psychologists' Associations Stockholm, Sweden.
18. Amenta F et al., "The ASCOMALVA trial: association between the cholinesterase inhibitor donepezil and the cholinergic precursor choline alfoscerate in Alzheimer's disease with cerebrovascular injury: interim results." *J Neurol Sci.* 2012 Nov 15;322 (1-2):96-101
19. Wanakhachornkrai O et al., "Neuritogenic effect of standardized extract of *Centella asiatica* ECA233 on human neuroblastoma cells." *BCM Complement Altern Med.* 2013 Aug 4;13 (1):204
20. Defillipo PP et al., "Inhibition of cPLA2 and sPLA2 activities in primary cultures of rat cortical neurons by *Centella asiatica* water extract." *Nat Prod Commun.* 2012 Jul;7(7):841-3
21. Colzato LS, Jongkees BJ, Sellaro R, Hommel B. "Working memory reloaded: tyrosine repletes updating in the N-back task." *Front Behav Neurosci.* 2013 Dec 16;7:200
22. Neri DF, Wiegmann D, Stanny RR, et al. The effects of tyrosine on cognitive performance during extended wakefulness. *Avit Space Environ Med.* 1995;66:313-319.
23. Deijen JB, Wientjes CJ, Vullings HF, et al. Tyrosine improves cognitive performance and reduces blood pressure in cadets after one week of a combat training course. *Brain Res Bull.* 1999;48:203-209.
24. Erecinska, M. & Silver, I. A. (1990) Metabolism and role of glutamate in mammalian brain. *Prog. Neurobiol.* 35: 245–296.
25. McEntee, W. J. & Crook, T. H. (1993) Glutamate: its role in learning, memory, and the aging brain. *Psychopharmacology* 111: 391–401.
26. Kristian, T. & Siesjo, B. K. (1998) Calcium in ischemic cell death. *Stroke* 29: 705–718.
27. Aldo AM Lima, et al., "Zinc, vitamin A, and glutamine supplementation in Brazilian shantytown children at risk for diarrhea results in sex-specific improvements in verbal learning." *Clinics Sao Paulo.* 2013 March; 68(3): 351–358

To Your Health is a free series of educational literature. Although copyrighted, this literature may be photocopied and distributed, but may not be altered in any way. To Your Health is not intended as medical advice. For diagnosis and treatment of any medical condition, consult your physician.

By Chad Brey,
Research & Development Chemist
 holds a B.S. degree in biochemistry from California State University, Northridge. Chad has worked as a chemist in various fields including Inorganic chemistry- U.S. Borax, pharmaceutical biochemistry research - Amgen, Analytical chemistry - Baxter Biosciences, organic/silicone chemistry