

Boosting Memory with Huperzine A Supplementation

James Meschino DC, MS, ROHP

Huperzine A is an extract from a club moss (from the Lycopodiaceae family) that has been used for centuries in Chinese folk medicine for a variety of conditions. In modern times Huperzine A research has focused on its ability to raise brain levels of the memory chemical acetylcholine, hence its potential role in the treatment and prevention of Alzheimer's disease, dementia and other cases of memory and learning impairment.^{1, 2}

Principle Active Constituents

Huperzine A or HupA is a specific alkaloid compound that is found in very low concentrations in the moss where it occurs naturally at only a 1% concentration. Thus, when used therapeutically, Huperzine A is given as a concentrated extract. Commercially available extracts contain up to 95% HupA concentration.^{1,2,3} HupA was first synthesized in 1990, which has helped to increase its availability in the marketplace.³

Biological Action in Memory Support

HupA is rapidly absorbed by the brain where it acts as a potent, reversible and selective inhibitor of the enzyme acetylcholinesterase, which breaks down the memory chemical acetylcholine. By inhibiting this enzyme, brain concentrations of acetylcholine are increased, thereby facilitating improvements in memory and learning capacity. A hallmark feature of Alzheimer's disease is reduced concentrations of acetylcholine in specific areas of the brain involved with memory and other cognitive functions. Huperzine A supplementation appears to help increase acetylcholine levels in Alzheimer's patients in cases where the condition has not yet advanced to the point where brain cells are permanently damaged.

Studies show that Huperzine A provides a longer acting effect than the drugs tacrine and donepezil, which are used in Alzheimer's disease, and it also appears to produce fewer side effects. This is due to the fact that only very small doses of Huperzine A are required due to its high specificity for the acetylcholinesterase enzyme. As such, HupA is under intensive investigation as a viable intervention in the prevention and treatment of Alzheimer's disease, dementia, and other conditions involving learning and memory impairment.^{1,4,5,6} Further, it has recently been reported that HupA also reduces neuronal death (death of nerve cells) caused by glutamate (glutamate toxicity results in seizures associated with exposure to nerve gas), suggesting that HupA may act to protect brain cells from various types of degenerative damage and chemical insults. The dual bio-activities (preserving acetylcholine and protecting nerve cells) make HupA an attractive agent to study as a potentially important therapeutic agent for Alzheimer's disease.¹

Clinical Applications

1. Alzheimer's disease and Dementia

In a double-blind trial with Alzheimer's disease patients, the group given 200 mcg of Huperzine A, twice per day for eight weeks demonstrated significant improvement in memory, cognitive and behavioral functions.⁷ Huperzine A has been used successfully in a clinical setting with approximately 100,000 Alzheimer's and dementia patients in China.³ At Beijing's Institute of Mental Health, Huperzine A was tested against foline in 101 patients with benign senescent forgetfulness (age-related memory impairment). After four weeks of supplementation, 70% of the group receiving Huperzine A showed significant improvement in their memory as measured by memory quotient (MQ). An additional 111 Alzheimer's patients were also included in the study. Overall, the group receiving HupA demonstrated a 10% improvement in the memory quotient over the four-week test period, and significant improvement in other measures of cognitive function. Side effects occurred in only 3% of these patients, with the most frequent side effects involving dizziness and gastrointestinal symptoms.⁴ In a study done at Zhejiang Medical University in Shanghai, 103 patients with Alzheimer's disease were given 200 mcg of HupA per day or a placebo. After eight weeks, 58% of those receiving HupA showed marked improvement in mental function, compared to 36% in the placebo group.² In another double-blind study, the administration of Huperzine A at 100-150 mcg two to three times per day, was shown to be more effective than the drug piracetam in a trial involving patients with age-related cognitive decline.⁸ Animal research shows that Huperzine A has a greater ability to preserve acetylcholine levels than may be available through the use of some prescription drugs that act as acetylcholinesterase inhibitors.^{9,10}

2. Learning Enhancement

Animal studies show that Huperzine A supplementation provides animals with memory-enhancement and a broad range of improved cognitive behaviors.⁵ There is some suggestion that Huperzine A supplementation in otherwise normal individuals can enhance memory and recall ability as well as learning capacity. In a small controlled trial of adolescent middle school students, the administration of 100 mcg of Huperzine A two times per day, was shown to be effective in improving memory and learning performance over a four week period. Although no side effects were reported, the researchers caution that this was a high dose of Huperzine A for subjects with no apparent signs of acetylcholine deficiency and the long term safety of such a practice needs to be established before young, healthy individuals should ingest doses in this range in an attempt to boost their learning capacity.¹¹

Dosage and Standardized Grade

1. Alzheimer's disease: 150 to 200 mcg, one to two times per day in divided doses^{2,12}
2. Early Memory Loss: 50 to 150 mcg one to two times per day in divided doses^{3,12}

3. General Brain Support (by age 50-55): Consider 25 to 50 mcg per day: With age, the brain tends to make less acetylcholine, which largely accounts for age-related memory loss that patients often complain about. At age 54, I personally take one capsule per day of a Memory Support Supplement that contains four proven memory-boosting natural agents (each capsule contains):
 - A. CDP – choline – 50 mg
 - B. Phosphatidylserine – 100 mg (50% std grade)
 - C. Bacopa Monnieri – 50 mg (std to 20% bacosides)
 - D. Huperzine A – 25 mcg

Adverse Side Effects, Toxicity and Contraindications

Huperzine A inhibits the breakdown of acetylcholine by reversibly inhibiting the enzyme acetylcholinesterase. This gives rise to the potential to increase acetylcholine levels to toxic levels, if the dosage is too high.^{1,13} Excessive levels of acetylcholine in the brain can result in cholinergic syndrome, which manifests as a slowing of the heart rate (bradycardia), contraction of the pupil of the eye (miosis), sweating, increased movement of intestinal tract contents (hyperperistalsis), as well as wheezing, excessive salivation, urinary incontinence and excessive discharge of mucus from the air passages of the lungs (bronchorrhea).¹⁴ To date, none of the human trials using Huperzine A have produced cholinergic syndrome in any subject. However, the potential for this to occur remains plausible and thus, dosage recommendations should be strictly adhered to and patients and practitioners should closely monitor response to the use of this bioactive agent.¹⁵

Side effects are rare at recommended doses, but may include dizziness and gastrointestinal symptoms.^{4,8,10}

Drug-Nutrient Interactions

Acetylcholinesterase Inhibitors, such as Donepezil and Tacrine - These drugs also inhibit the breakdown of acetylcholine and therefore, the addition of Huperzine A may potentiate their effects, increasing the likelihood of developing cholinergic syndrome as a serious side effect.^{17,18} These drugs on their own are noted for the side effects of vomiting, excess saliva and tear production, and increased sweating, which indicate their tendency to over stimulate the cholinergic system.¹⁵

1. Bai DL, et al. Huperzine A, a potential therapeutic agent for treatment of Alzheimer's disease. *Curr Med Chem*, Mar2000;7(3):355-74
2. Dworkin N. Restoring memory. *Psychology Today*, Jul/Aug00;32(4):p28
3. Pirisi, Angela. Plant wisdom: Memory moss. *Yoga Journal*, 08/31/1999;147:p95
4. McCaleb R. Huperzia looks promising for improving memory. *HerbalGram*, 10/31/1995;35:p14
5. Tang XC. Huperzine A (shuangyiping): A promising drug for Alzheimer's disease. *Chung Kuo Yao Li Hsueh Pao*, Nov1996;17(6):481-4
6. Ashani Y, Peggins JO, Doctor BP. Mechanism of inhibition of cholinesterases by huperzine A. *Biochem Biophys Res Commun*, 1992;184:719-26

7. Xu SS, Gao, ZX, Weng Z et al. Efficacy of tablet huperzine-A on memory, cognition, and behavior in Alzheimer's disease. *Chung Kuo Yao Li Hsueh Pao*, 1995;16:391-5
8. Wang Z, Ren G, Zhao Y et al. A double-blind study of huperzine A and piracetam in patients with age-associated memory impairment and dementia. In: Kanba S, Richelson E (eds.) *Herbal Medicines for Nonpsychiatric Diseases*. Tokyo: Seiwa Choten Publishers, 1999:39-50
9. Cheng DH, Tang XC. Comparative studies of huperzine A, E2020, and tacrine on behavior and cholinesterase activities. *Pharmacol Biochem Behav*, 1998;60:377-86
10. Cheng DH, Ren H, Tang XC. Huperzine A, a novel promising acetylcholinesterase inhibitor. *Neuroreport*, 1996;8:97-101
11. Sun QQ, Xu SS, Pan JL, et al. Huperzine-A capsules enhance memory and learning performance in 34 pairs of matched adolescent students. *Acta Pharmacol Sin*, 1999;20:601-3
12. Qian BC, Wang M, Zhou ZF, et al. Pharmacokinetics of tablet huperzine A in six volunteers. *Chung Kuo Yao Li Hsueh Pao*, 1005;16:396-8
13. Huperzine A for memory enhancement? NCRHI Newsletter, 04/30/2000;23(2):3-4 [Pharmacist's Letter]
14. *Current Medical Diagnosis and Treatment*. 33rd Annual Revision, 1994. Lange Medical Books. Appleton and Lange:p1323
15. 2001 Healthnotes, Inc. www.healthnotes.com: Huperzine A
16. Skolnick AA. Old Chinese herbal medicine used for fever yields possible new Alzheimer disease therapy. *JAMA*, Mar1997;277(10):p776
17. Cheng DH et al. Huperzine A, a novel promising acetylcholinesterase inhibitor. *Neuroreport*, Dec1996;8(1):97-101
18. Liu J, et al. Inhibitory effects of huperzine B on cholinesterase activity in mice. *Chung Kuo Yao Li Hsueh Pao*, Feb1999;20(2):141-4