

Nutritional Strategies to Combat Alzheimer's

March 2013

Someone in America develops Alzheimer's every **68 seconds**. This rate is projected to more than double by **2050**, to one every **33 seconds**.¹

Alzheimer's research is accelerating, but there is still no cure.

A vast array of published data, however, shows that making healthy dietary choices, along with proper use of nutrients, hormones, and drugs may dramatically reduce one's risk of developing this mind-destroying killer.

Most recently, an innovative brain scan was unveiled that for the first time can accurately diagnose the brain plaques that are characteristic of Alzheimer's. More than 300 hospitals and imaging centers have the ability to perform this scan.²

The dilemma we face today is that the five drugs approved for Alzheimer's only partially treat some of the symptoms. None of them can slow or stop the progression of the disease itself—let alone reverse it.³

Just because mainstream medicine has no solutions doesn't mean you're powerless against Alzheimer's.

Dozens of compounds have ample research behind them demonstrating their ability to take aim at multiple degenerative steps in the development of Alzheimer's.^{4,5} This may not only prevent the disease from developing, but it can also modify the course of the disease itself—reversing cognitive deficits, restoring memory, delaying the progression of disease, and more.

The Complexity of Alzheimer's

Symptoms of Alzheimer's disease, the most common form of dementia, begin with insidious loss of memory which progresses to involve all aspects of cognition, including confusion and mood swings.^{6,7} After a painful and lingering

illness, Alzheimer's causes death; it's the **6th** leading cause of death in Americans overall, and the **5th** among those over 64.²

Doctors are in a scientific and therapeutic quandary with Alzheimer's. We know a great deal about the disease's risk factors, about the pathological changes that occur in the brain, and about the biochemistry underlying them. We can predict with accuracy the natural course of the disease, once its symptoms become evident.

But to date, conventional medicine can do almost nothing to slow or stop the disease's progression, let alone prevent or reverse it.^{3,7}

Part of the problem is the tremendous complexity of Alzheimer's. Rather than having a single or a few clear-cut causes that can be targeted with individual medicines, a complex presentation of interrelated abnormalities contribute to Alzheimer's disease.⁴ These develop slowly, and most are already in place by the time the first symptom arises.⁶ Ultimately, loss of brain cells and their billions of connections leads to atrophy, or shrinkage, of the brain itself, especially in the hippocampus and cortex, brain areas responsible for memory, cognition, and personality.⁶

No single-targeted synthetic drug can yet address these multiple factors. Nutraceuticals offer an entirely different approach. Rather than a single target, these natural products take aim at multiple steps in the development of Alzheimer's.⁵

The list of researched nutraceuticals that offer hope for modifying the course of Alzheimer's disease is long, and growing. Many of these nutrients attack Alzheimer's at multiple target points.⁸⁻¹⁰

The list is so long, in fact, that it's easy to become overwhelmed and to wonder which nutrients are right for any one individual to choose. That answer, of course, is highly individualized.

What we have done is meticulously compile a listing of supplements grouped by

the kind of evidence available to support their use. The first group includes nutrients with good support from strong human studies. The second group includes those with extensive evidence from epidemiological studies relating intake (or blood levels) to the risk of Alzheimer's disease. The third group is comprised of nutrients for which we have strong laboratory evidence, but for which human studies are still incomplete. The science behind nutritional strategies for preventing Alzheimer's continues to evolve. Here's what we know as of today...

Nutrients with Strong Evidence from Human Studies

Acetyl-L-Carnitine

Acetyl-L-Carnitine is a natural amino acid-derived molecule that contributes to movement of fatty acids and other vital fuels from the cell into mitochondria.¹¹⁻¹³ As such, it contributes to brain mitochondrial health and efficiency.¹²⁻¹⁵

Animal studies show that acetyl-L-carnitine supplementation decreases buildup of **amyloid beta** and **tau proteins**, and speeds degradation of amyloid beta, contributing to its rapid clearance from brain cells.¹⁵⁻¹⁷ At the same time, acetyl-L-carnitine boosts natural cellular antioxidant levels.¹⁵ These changes are accompanied by improved memory, cognition, and behavior, including slowing the rate of deterioration.^{13,18}

Compared to control patients, Alzheimer's patients supplemented with **acetyl-L-carnitine** at doses of **2 to 3 grams/day** for three to six months show slower decline in multiple cognitive functions, reduced attention deficits, and increased energy available to cells as ATP, the universal energy-storage molecule.¹⁹⁻²³ Acetyl-L-carnitine research provides the first demonstration that a nutrient therapy may modify the clinical and central nervous system neurochemical parameters of the disease, unlike any existing drugs, which only influence symptoms.^{3,20}

Acetyl-L-carnitine supplements, like most nutraceuticals, work in the earliest stages of Alzheimer's disease, emphasizing the importance of starting the

supplement well before the onset of detectable symptoms.^{21,22} Studies also show that adding acetyl-L-carnitine to the prescription drugs donepezil or rivastigmine in mild Alzheimer's can improve the response rate to these drugs from **38% to 50%.**¹¹

Ginseng

Panax ginseng and its extracts are used in traditional Chinese medicine to enhance memory and cognition. This natural plant product has multiple mechanisms of action, including reducing amyloid beta plaque formation, enhancing amyloid beta clearance, and reducing brain cell death.²⁴⁻²⁷ Animal studies show that ginseng treatment reverses many of the memory and behavioral abnormalities found in models of Alzheimer's.²⁸

Human clinical trials show good efficacy of ginseng extracts in terms of improving scores on the standard Alzheimer's rating scales.²⁹ One study of ginseng, 4.5 grams/day showed improvements that continued until treatment was stopped, after which scores declined to those of the control group.³⁰

Huperzine

Huperzine A is a biochemical component of the Chinese club moss *Huperzia serrata*. It binds reversibly to the enzyme that destroys the neurotransmitter acetylcholine, helping to maintain the signaling molecule's presence in the synapses, where nerve cells communicate.^{31,32} This mechanism is similar to that of most common Alzheimer's drugs available today, but Huperzine also blocks the excitatory NMDA channels that overstimulate brain cells, offering a path not only to symptom relief but also to slowing the disease itself.³³ Finally, huperzine protects mitochondria from the destructive effects of amyloid beta, and triggers enzymes that degrade the toxic protein.^{34,35}

Human studies of Huperzine at doses of **200 to 400 mcg** twice daily have shown significant improvement,^{31,36-39} with some studies demonstrating

improvements of **61%** to **348%** compared with placebo in scores measuring Alzheimer's disease severity and activities of daily living.^{31,37} Minor side effects such as ankle swelling and insomnia have been reported in **3%** of patients taking huperzine.³⁷

Lipoic Acid

Lipoic acid is a small molecule that's essential for proper mitochondrial energy production.⁴⁰ It boosts natural cellular antioxidant systems.^{40,41} Lipoic acid protects brain cells from death induced by amyloid beta and other oxidizing substances.⁴² It also binds tightly to toxic metal ions, preventing them from inducing oxidant stress.⁴³ Lipoic acid boosts production of acetylcholine in the brain, making more of the neurotransmitter available.⁴⁰ In animal models of aging brains, alpha-lipoic acid slows development of cognitive dysfunction and memory loss, and prevents degeneration of brain cells.⁴⁴⁻⁴⁶

In human studies, alpha-lipoic acid supplementation at **600 mg/day** led to stabilization or slowing of cognitive decline, with Alzheimer's disease scores remaining constant for 1 year and progressing extremely slowly over 4 years.^{47,48} As with most supplements, the effects are more pronounced in patients with early stages of the disease.⁴⁸

Editor's Note: Alpha-lipoic acid is a 50/50 mixture of two different chemical forms of lipoic acid, an "**R**" form and an "**S**" form. Studies show that the "**R**" form is more biologically active and more bioavailable than the "**S**" form—as such, a lower dose of pure R-lipoic acid can be considered.⁴⁹

N-Acetylcysteine (NAC)

N-acetylcysteine (NAC) is an amino acid precursor of the cellular antioxidant glutathione.⁵⁰ As such, it can boost intracellular protection against the ravages of oxidant stress. NAC has been used in the laboratory successfully to clean up reactive oxygen species and ameliorate the behavioral changes seen in older animals and those with features of Alzheimer's.^{41,51}

Social isolation is known to increase the risk of Alzheimer's disease, resulting in increased oxidant stress levels and higher levels of amyloid beta. An intriguing study in mice showed that NAC supplementation could mitigate isolation-induced oxidant stress and amyloid beta formation.⁵²

Human studies, though limited in number, have demonstrated slowing of deterioration in those with Alzheimer's supplemented with n-acetylcysteine (NAC), particularly for cognitive tasks.⁵³

Omega-3 Fatty Acids

People with high intakes of fish oil, rich in omega-3 fatty acids, have lower levels of all kinds of dementia, including Alzheimer's disease. People with lower levels of omega-3 intake have greater Alzheimer's risk.⁵⁴⁻⁵⁷

Omega-3 fatty acids, especially DHA and EPA, reduce inflammation and form important components of brain cell membranes.

Human studies of omega-3 supplementation are encouraging, but it appears that benefits arise mainly in people with very early Alzheimer's, or mild cognitive impairment, the stage that precedes Alzheimer's itself.⁵⁷⁻⁶⁰ Once the disease has reached the mild to moderate stage, no beneficial effects are seen.⁶¹

Vitamin D

Vitamin D is best known for its role in calcium metabolism and bone health, but the past decade has revealed multiple other crucial effects of the vitamin, which has receptor molecules throughout the body, especially in brain cells.^{62,63}

Vitamin D is now considered a neurohormone, with multiple beneficial effects in the brain.⁶⁴

Older adults, and especially people with Alzheimer's have abnormally low vitamin D levels compared with the healthy population.⁶⁴⁻⁶⁶ Those with the lowest levels have as much as a **25-fold** risk of having the Alzheimer's predecessor, mild cognitive impairment when compared to those with highest vitamin D

levels.⁶⁷

The specific cause and effect relationship remains murky, but it is clear that vitamin D has many different means of protecting brain cells. These include regulation of brain cell calcium channels, nerve growth factor, and nitric oxide synthesis, as well as antioxidant and anti-inflammatory mechanisms.^{62,68-71} Vitamin D also stimulates clearance of amyloid beta, an effect that is boosted by curcumin.^{63,64,72,73}

Studies show an improvement in cognition associated with an improvement in vitamin D status.⁶⁴ Vitamin D has some overlap in mechanisms with the Alzheimer's drug memantine, and a recent study showed that using both the drug and supplement together gave superior results to using either alone.^{70,74}

Ginkgo Biloba

Extracts of Ginkgo biloba have been in use in Europe for more than a decade as a prescription drug to treat degenerative dementias including Alzheimer's disease.⁷⁵ Ginkgo reduces brain cell death and may enhance clearance of the precursor to amyloid beta proteins.^{76,77}

Clinical trials in the US and Europe demonstrate that ginkgo extracts improve cognitive function,⁷⁸⁻⁸⁰ but the findings have not been consistent.^{81,82} One study showed ginkgo extracts can slow progression of early Alzheimer's by up to **25 months**, while also delaying the need for dependence on caregivers.⁷⁹

Several studies compared ginkgo with donepezil, one of the standard drugs for Alzheimer's treatment. Both showed no detectable differences between donepezil **5-10 mg** and ginkgo **160-240 mg** in terms of cognitive improvement, and one showed that the combination of donepezil and ginkgo, while not improving outcomes, did reduce the donepezil-related side effects.^{83,84}

Ginkgo extracts at the higher dose of **240 mg/day** seem to show still more impressive benefits in randomized, placebo-controlled trials, again in patients with mild to moderate Alzheimer's,⁸⁵⁻⁸⁷ but not all human studies show

benefit.81,82

Nutritional Strategies to Combat Alzheimer's

March 2013

Coffee

Many large epidemiological studies show that moderate coffee consumption (3-5 cups of caffeinated coffee/day) is associated with reduced risk for Alzheimer's.⁸⁸⁻⁹¹

People who drank coffee at that level in mid-life had a 65% decrease in Alzheimer's risk later in life.^{91,92} And high blood caffeine levels appear to prevent the progression of minimal cognitive impairment to fully-developed Alzheimer's.⁹³

Studies show that caffeine can reduce brain levels of toxic amyloid beta proteins in animals, while not only slowing but in fact reversing the amyloid beta-associated cognitive impairment.^{89,94,95} Just 1 to 2 months of caffeine treatment restored memory and lowered brain amyloid beta levels in mice.⁸⁹

Coffee's other components, including chlorogenic acid, also have major protective effects on brain cells.^{90,96-99} It is likely, however, that coffee's primary benefit to brain health is related largely to its caffeine content.

Magnesium

Magnesium is a mineral that is essential for myriad human biological functions. It is especially important in the brain.

Increasing brain magnesium using a special compound called **magnesium-L-threonate** restores degraded neuronal connections by increasing **synaptic density**, a process that underlies learning and memory.¹⁰⁰

Lab studies show that magnesium modulates enzymes involved in amyloid beta production; at low levels, magnesium favors amyloid beta buildup, while at higher levels it favors amyloid beta breakdown.^{101,102} There's also evidence

that magnesium opposes the effects of excitotoxic neurotransmitters; this would have the effect of reducing inflammation and perhaps amyloid beta deposition.¹⁰³

Magnesium levels are markedly lower in people with Alzheimer's disease than in healthy controls, and the degree of magnesium deficiency correlates with the severity of the disease.¹⁰⁴⁻¹⁰⁶

Vitamin E

People who have high intakes of vitamin E from food are at lower risk of Alzheimer's than those who don't, but studies of typical vitamin E supplements don't find that effect.^{107,108} The difference is that most supplements are comprised almost solely of the ***alpha tocopherol*** form of vitamin E,^{107,109} whereas the major form of vitamin E from food is ***gamma tocopherol***. More current studies show that the ***gamma*** forms of vitamin E provide needed brain benefits.^{110,111}

Specifically, higher intakes and levels of ***gamma tocopherol*** and ***gamma tocotrienol*** are associated with lower risks for both Alzheimer's and its predecessor, mild cognitive impairment.^{107-109,112}

Nutrients with Strong Laboratory and Theoretical Evidence

Ashwagandha

The Ayurvedic plant, Ashwagandha, has widely-demonstrated beneficial effects, many of which are attributed to several of its antioxidant components, which are more powerful than most commercial antioxidants.¹¹³

Extracts from Ashwagandha's fruit and root protect brain cells in culture from the oxidant effects of amyloid beta; in one study they negated the cell death caused by amyloid beta.¹¹³

Laboratory findings reveal that ashwagandha extract inhibits acetylcholinesterase, an enzyme responsible for breaking down acetylcholine,

one of the brain's key chemical messengers.¹¹⁴ Drugs such as Aricept®, which is currently used in the treatment of Alzheimer's disease, act in this very manner to slow the progression of this mind-robbing disease as well as improve cognition and behavior.¹¹⁵

B-Vitamins

The B vitamins folate (B9), pyridoxine (B6), and cobalamin (B12) are essential for recycling of the molecules that make up DNA; without sufficient B vitamins there is a buildup of the amino acid homocysteine, which is toxic to many tissues. Elevated homocysteine levels are a known risk factor for Alzheimer's disease, though it is still unclear if homocysteine is actually a cause of the condition.¹¹⁶⁻¹¹⁸

Laboratory and human studies show that B vitamin supplements lower homocysteine, slow buildup of abnormal proteins amyloid beta and tau, and reverse the cognitive and memory deficits induced by artificially elevated homocysteine levels.^{119,120}

Blueberries

Blueberries are extremely rich in the beneficial plant molecules called polyphenols, which are powerful antioxidants.¹²¹ Polyphenols can also affect the way genes are expressed, switching on those that offer protection against neuronal damage, and switching off those that signal increased inflammation or other deleterious effects.¹²²

Blueberry extracts' antioxidant actions help protect neurons against the damage done by amyloid beta proteins.^{121,123} They have also been shown to protect neurons and improve animal behavior even when amyloid beta levels are unchanged, meaning that they provide protection "downstream" from amyloid beta's oxidant and inflammatory effects.¹²⁴⁻¹²⁶

CoQ10 and PQQ

Coenzyme Q10 (CoQ10) and pyrroloquinoline quinone (PQQ) are essential

nutrients that help keep mitochondria healthy by improving their efficiency at burning foods to produce energy.¹²⁷⁻¹³⁰

Laboratory studies show that CoQ10 supplementation reduces the amount of amyloid beta plaque formation in brain cells, resulting in improved behavior.^{131,132} PQQ acts after amyloid beta has already accumulated, helping cells recover from amyloid beta-induced oxidant stress, preventing neuronal cell death, and decreasing further production of reactive oxygen species.¹³³

Curcumin

Curcumin is a yellow biomolecule derived from the spice turmeric.¹³⁴ Like other antioxidants, curcumin protects brain cells and their mitochondria against amyloid beta-induced toxicity and inhibits formation of abnormal proteins.¹³⁴⁻¹³⁶

But curcumin also possesses some unique features with regard to Alzheimer's disease. Sophisticated molecular studies reveal that curcumin can prevent amyloid beta molecules from assembling, and can also destabilize amyloid beta plaques after they have formed.^{137,138} This permits the body's natural cleanup cells, macrophages, to rapidly clear amyloid beta fragments before they can reform and damage brain cells. And curcumin stimulates macrophages to make that cleanup process still more rapid and efficient.

Another beneficial mechanism of curcumin is to enhance the health of mitochondria, the tiny cellular power plants that provide energy to all of our cells. Aging mitochondria are thought to be responsible for much of the brain cell death and dysfunction that occurs in Alzheimer's disease.¹³⁹ Curcumin, through its antioxidant actions, scavenges dangerous oxygen free radicals produced by ailing mitochondria, preventing their death and enhancing their action.¹⁴⁰

Finally, curcumin has favorable effects on brain insulin receptors. The balance between glucose levels and insulin in the brain is capturing scientists attention, with some even referring to Alzheimer's disease as "type III diabetes."¹⁴¹ Studies of diabetic animals reveal that curcumin enhances actions of insulin

receptors in brain tissue.^{142,143}

Studies in animal models of Alzheimer's disease demonstrate the value of these multiple mechanisms on learning and memory. Curcumin supplements given even after the onset of Alzheimer's-like symptoms result in fewer mistakes on memory-dependent tasks, and improved performance on mazes that test both reasoning and memory.¹⁴⁴⁻¹⁴⁷ When the animals' brains are examined at the end of such experiments, they demonstrate significantly less brain cell death in memory-processing brain areas.¹⁴⁵

In one of the most dramatic experiments to date, curcumin supplements were found to protect against brain aging in general among mice treated with an age-accelerating compound.¹⁴⁸ These remarkable findings were accompanied by improved performance on cognitive tasks and enhanced locomotion; in these animals' brains improved oxidant defenses and restored mitochondrial enzyme activities were observed as well.

This kind of reversal of Alzheimer's damage is something no existing drug can do.

Grape Seed Extract

Grapes, and particularly their seeds, contain very high levels of proanthocyanidins, clusters of polyphenols that have multiple health benefits including anti-inflammatory and antioxidant effects. But they also have remarkable gene modulating activities, directing protein expression away from that seen in Alzheimer's and towards a more normal state.¹⁴⁹ And they readily cross the blood-brain barrier to be deposited in brain tissue.¹⁵⁰

These effects result in reduction of Amyloid beta formation by several different mechanisms, as well as enhanced amyloid beta clearance.¹⁵¹⁻¹⁵³ Grape seed extracts also reduce inflammation in animal models of Alzheimer's disease.¹⁵⁴

Green Tea

Green tea is rich in a variety of polyphenols, especially one called EGCG, that

has multiple beneficial attributes. EGCG interferes with the Alzheimer's disease process in several important ways.¹⁵⁵

EGCG physically blocks the assembly of amyloid beta proteins, preventing them from clumping together to form plaques.¹⁵⁶ The compound also generates a unique set of stable proteins from the amyloid beta precursor molecule; these proteins can't bind together at all, further reducing the burden of plaque.¹⁵⁷

Intriguingly, EGCG, given before exposure, prevents mitochondrial dysfunction induced by amyloid beta in brain cells, while also normalizing cells' responses to the excitatory neurotransmitter NMDA.^{158,159}

Resveratrol

Resveratrol is a multi-functional polyphenol that plants use as an antifungal compound; it is found abundantly in red grapes.^{8,160-162} Resveratrol has antioxidant characteristics, but scientists are especially excited about its ability to change how genes are expressed.¹⁶³ This so-called epigenetic capability allows resveratrol to affect multiple points in the complex series of events that ultimately produces Alzheimer's symptoms.¹⁶⁴

Studies show that these properties of resveratrol act both before and after amyloid beta protein is deposited in brain tissue. Resveratrol promotes enzyme actions that slow amyloid beta production, and speed its clearance, while it also promotes expression of enzymes that limit the nitric oxide and inflammatory cytokine production that amyloid beta triggers.^{160,165-168}

Glucose utilization is impaired in the brains of Alzheimer's patients, leading to further deterioration of their cells; this is one of the many ways that Alzheimer's and type II diabetes overlap. Breaking research reports that resveratrol can promote glucose utilization in brain cells, potentially mitigating the destructive effect of elevated sugar.¹⁶⁹

Vinpocetine

Vinpocetine is an alkaloid derived from the periwinkle (Vinca) plant.¹⁷⁰ It increases brain blood flow and decreases platelet aggregation through its inhibition of the enzyme PDE1.^{170,171} Vinpocetine also produces higher brain levels of the neurotransmitter acetylcholine that is deficient in Alzheimer's disease.¹⁷¹

By separate mechanisms, vinpocetine provides antioxidant protection to brain cells, and markedly reduces mitochondrial dysfunction.¹⁷⁰⁻¹⁷² These combined mechanisms, and perhaps others, contribute to vinpocetine's ability to prevent neuronal damage and improve impaired learning and memory in animal models of Alzheimer's.¹⁷¹

Nutrient Combinations

The multifactorial nature of Alzheimer's disease makes it a natural condition for combinations of nutrients that, together, can target many, if not most, of the underlying molecular damage.¹⁷³

Studies of a mouse model of Alzheimer's reveal so much improvement in learning in supplemented mice that their performance could not be distinguished from that of healthy mice. The supplement contained curcumin, piperine, epigallocatechin gallate, alpha-lipoic acid, n-acetylcysteine, B vitamins, vitamin C, and folate.¹⁷⁴

Several human studies have been done with a supplement containing curcumin, piperine, EGCG, alpha-lipoic acid, N-acetylcysteine, B vitamins, vitamin C, and folate in those with mild to moderate Alzheimer's disease. Patients' performance on standard neuropsychiatric measures were equivalent to those on donepezil, and exceeded those of galantamine, drugs in current use for Alzheimer's.¹⁷⁵ Even in institutionalized patients with later-stage disease, this formulation produced an improvement of about 30% on the standard neuropsychiatric inventory.¹⁷⁶ This formulation has also been shown to improve cognitive performance in people without dementia, demonstrating the power of combined supplementation.¹⁷⁷

One proprietary nutritional product (containing Ashwagandha, blueberry, grape seed extract, ginger, vinpocetine, and phosphatidylserine plus alpha-glycerol phosphoryl choline and other ingredients) has also now been shown to improve cognition in adults with memory and cognition problems and improve working memory, executive function, and inspection time (a measure of decision-making), in an open clinical trial.¹⁷⁸

Summary

Alzheimer's is a complex, multifactorial, and progressive disease that steals mind and memory. To date, mainstream medicine remains baffled by the condition, with just 5 drugs on the market, none of which can modify or slow disease progression.

Nutritional supplements, on the other hand, have multiple mechanisms, offering a broader front on which to attack Alzheimer's. Many different supplements show great promise by acting on several or many different targets in the disease's progression. Combining many nutrients together is proven to offer even greater impact.

Using a combination of multitargeted supplements may be the only way to stop or slow Alzheimer's disease, and prevent it from taking away your personality.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.



evancy)

LIFE EXTENSION MAGAZINE

Nutritional Strategies to Combat Alzheimer's

March 2013

By Liam Hawkins

References

1. 2012 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2012;8(2):131-68.
2. Available at: <http://www.nytimes.com/2012/11/16/health/for-alzheimers-detection-advances-outpace-treatment-options.html> (<http://www.nytimes.com/2012/11/16/health/for-alzheimers-detection-advances-outpace-treatment-options.html>). Accessed December 6, 2012.
3. Available at: http://www.alz.org/research/science/alzheimers_disease_treatments.asp (http://www.alz.org/research/science/alzheimers_disease_treatments.asp). Accessed November 9, 2012.
4. Suchy J, Chan A, Shea TB. Dietary supplementation with a combination of alpha-lipoic acid, acetyl-L-carnitine, glycerophosphocoline, docosahexaenoic acid, and phosphatidylserine reduces oxidative damage to murine brain and improves cognitive performance. *Nutr Res*. 2009 Jan;29(1):70-4.
5. da Rocha MD, Viegas FP, Campos HC, et al. The role of natural products in the discovery of new drug candidates for the treatment of neurodegenerative disorders II: Alzheimer's disease. *CNS Neurol Disord Drug Targets*. 2011 Mar;10(2):251-70.
6. Kidd PM. Alzheimer's disease, amnesic mild cognitive impairment, and age-associated memory impairment: current understanding and progress toward integrative prevention. *Altern Med Rev*. 2008 Jun;13(2):85-115.
7. Available at: <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001767/> (<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001767/>). Accessed November 9, 2012.
8. Howes MJ, Perry E. The role of phytochemicals in the treatment and prevention of dementia. *Drugs Aging*. 2011 Jun 1;28(6):439-68.
9. Zhao Y, Zhao B. Natural antioxidants in prevention and management of

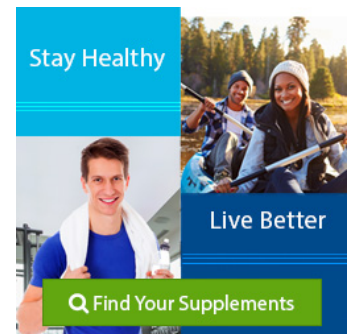
Health Concerns

» [Alzheimer's](#)

[Disease](#)

(/Protocols/Neurological

Disease/Page-01).



(/Pages/SupplementGui

- Alzheimer's disease. *Front Biosci (Elite Ed)*. 2012;4:794-808.
10. Grover A, Shandilya A, Agrawal V, Bisaria VS, Sundar D. Computational evidence to inhibition of human acetyl cholinesterase by withanolide a for Alzheimer treatment. *J Biomol Struct Dyn*. 2012 Feb;29(4):651-62.
 11. Bianchetti A, Rozzini R, Trabucchi M. Effects of acetyl-L-carnitine in Alzheimer's disease patients unresponsive to acetylcholinesterase inhibitors. *Curr Med Res Opin*. 2003;19(4):350-3.
 12. Acetyl-L-carnitine. Monograph. *Altern Med Rev*. 2010 Apr;15(1):76-83.
 13. Inazu M, Matsumiya T. Physiological functions of carnitine and carnitine transporters in the central nervous system. *Nihon Shinkei Seishin Yakurigaku Zasshi*. 2008 Jun;28(3):113-20.
 14. Palacios HH, Yendluri BB, Parvathaneni K, et al. Mitochondrion-specific antioxidants as drug treatments for Alzheimer disease. *CNS Neurol Disord Drug Targets*. 2011 Mar;10(2):149-62.
 15. Abdul HM, Calabrese V, Calvani M, Butterfield DA. Acetyl-L-carnitine-induced up-regulation of heat shock proteins protects cortical neurons against amyloid-beta peptide 1-42-mediated oxidative stress and neurotoxicity: implications for Alzheimer's disease. *J Neurosci Res*. 2006 Aug 1;84(2):398-408.
 16. Traina G, Federighi G, Brunelli M. Up-regulation of kinesin light-chain 1 gene expression by acetyl-L-carnitine: therapeutic possibility in Alzheimer's disease. *Neurochem Int*. 2008 Dec;53(6-8):244-7.
 17. Zhou P, Chen Z, Zhao N, et al. Acetyl-L-carnitine attenuates homocysteine-induced Alzheimer-like histopathological and behavioral abnormalities. *Rejuvenation Res*. 2011 Dec;14(6):669-79.
 18. Shenk JC, Liu J, Fischbach K, et al. The effect of acetyl-L-carnitine and R-alpha-lipoic acid treatment in ApoE4 mouse as a model of human Alzheimer's disease. *J Neurol Sci*. 2009 Aug 15;283(1-2):199-206.
 19. Sano M, Bell K, Cote L, et al. Double-blind parallel design pilot study of acetyl levocarnitine in patients with Alzheimer's disease. *Arch Neurol*. 1992 Nov;49(11):1137-41.
 20. Pettegrew JW, Klunk WE, Panchalingam K, Kanfer JN, McClure RJ. Clinical and neurochemical effects of acetyl-L-carnitine in Alzheimer's disease. *Neurobiol Aging*. 1995 Jan-Feb;16(1):1-4.
 21. Thal LJ, Carta A, Clarke WR, et al. A 1-year multicenter placebo-controlled study of acetyl-L-carnitine in patients with Alzheimer's disease. *Neurology*. 1996 Sep;47(3):705-11.
 22. Brooks JO, 3rd, Yesavage JA, Carta A, Bravi D. Acetyl L-carnitine slows decline in younger patients with Alzheimer's disease: a reanalysis of a double-blind, placebo-controlled study using the trilinear approach. *Int Psychogeriatr*. 1998 Jun;10(2):193-203.
 23. Gavrilova SI, Kalyn Ia B, Kolykhalov IV, Roshchina IF, Selezneva ND.

- Acetyl-L-carnitine (carnicetine) in the treatment of early stages of Alzheimer's disease and vascular dementia. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2011;111(9):16-22.
24. Fang F, Chen X, Huang T, Lue LF, Luddy JS, Yan SS. Multi-faced neuroprotective effects of Ginsenoside Rg1 in an Alzheimer mouse model. *Biochim Biophys Acta*. 2012 Feb;1822(2):286-92.
 25. Chen LM, Lin ZY, Zhu YG, et al. Ginsenoside Rg1 attenuates beta-amyloid generation via suppressing PPARgamma-regulated BACE1 activity in N2a-APP695 cells. *Eur J Pharmacol*. 2012 Jan 30;675(1-3):15-21.
 26. Yang L, Hao J, Zhang J, et al. Ginsenoside Rg3 promotes beta-amyloid peptide degradation by enhancing gene expression of neprilysin. *J Pharm Pharmacol*. 2009 Mar;61(3):375-80.
 27. Hu SQ, Yu HM, Liu TS, Yang DJ, Chen XZ, He CJ. Neuroprotective effects of water extracts of American Ginseng on SH-SY5Y cells apoptosis induced by Amyloid beta25-35. *Zhong Yao Cai*. 2008 Sep;31(9):1373-7.
 28. Wang Y, Liu J, Zhang Z, Bi P, Qi Z, Zhang C. Anti-neuroinflammation effect of ginsenoside Rb1 in a rat model of Alzheimer disease. *Neurosci Lett*. 2011 Jan 3;487(1):70-2.
 29. Heo JH, Lee ST, Chu K, et al. An open-label trial of Korean red ginseng as an adjuvant treatment for cognitive impairment in patients with Alzheimer's disease. *Eur J Neurol*. 2008 Aug;15(8):865-8.
 30. Lee ST, Chu K, Sim JY, Heo JH, Kim M. Panax ginseng enhances cognitive performance in Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2008 Jul-Sep;22(3):222-6.
 31. Desilets AR, Gickas JJ, Dunican KC. Role of huperzine a in the treatment of Alzheimer's disease. *Ann Pharmacother*. 2009 Mar;43(3):514-8.
 32. Ha GT, Wong RK, Zhang Y. Huperzine a as potential treatment of Alzheimer's disease: an assessment on chemistry, pharmacology, and clinical studies. *Chem Biodivers*. 2011 Jul;8(7):1189-204.
 33. Gordon RK, Nigam SV, Weitz JA, Dave JR, Doctor BP, Ved HS. The NMDA receptor ion channel: a site for binding of Huperzine A. *J Appl Toxicol*. 2001 Dec;21 Suppl 1:S47-51.
 34. Gao X, Zheng CY, Yang L, Tang XC, Zhang HY. Huperzine A protects isolated rat brain mitochondria against beta-amyloid peptide. *Free Radic Biol Med*. 2009 Jun 1;46(11):1454-62.
 35. Wang CY, Zheng W, Wang T, et al. Huperzine A activates Wnt/beta-catenin signaling and enhances the nonamyloidogenic pathway in an Alzheimer transgenic mouse model. *Neuropsychopharmacology*. 2011 Apr;36(5):1073-89.
 36. Xu SS, Gao ZX, Weng Z, et al. Efficacy of tablet huperzine-A on

- memory, cognition, and behavior in Alzheimer's disease. *Zhongguo Yao Li Xue Bao*. 1995 Sep;16(5):391-5.
37. Zhang Z, Wang X, Chen Q, Shu L, Wang J, Shan G. Clinical efficacy and safety of huperzine Alpha in treatment of mild to moderate Alzheimer disease, a placebo-controlled, double-blind, randomized trial. *Zhonghua Yi Xue Za Zhi*. 2002 Jul 25;82(14):941-4.
 38. Wang BS, Wang H, Wei ZH, Song YY, Zhang L, Chen HZ. Efficacy and safety of natural acetylcholinesterase inhibitor huperzine A in the treatment of Alzheimer's disease: an updated meta-analysis. *J Neural Transm*. 2009 Apr;116(4):457-65.
 39. Rafii MS, Walsh S, Little JT, et al. A phase II trial of huperzine A in mild to moderate Alzheimer disease. *Neurology*. 2011 Apr 19;76(16):1389-94.
 40. Holmquist L, Stuchbury G, Berbaum K, et al. Lipoic acid as a novel treatment for Alzheimer's disease and related dementias. *Pharmacol Ther*. 2007 Jan;113(1):154-64.
 41. Moreira PI, Harris PL, Zhu X, et al. Lipoic acid and N-acetyl cysteine decrease mitochondrial-related oxidative stress in Alzheimer disease patient fibroblasts. *J Alzheimers Dis*. 2007 Sep;12(2):195-206.
 42. Zhang L, Xing GQ, Barker JL, et al. Alpha-lipoic acid protects rat cortical neurons against cell death induced by amyloid and hydrogen peroxide through the Akt signalling pathway. *Neurosci Lett*. 2001 Oct 26;312(3):125-8.
 43. Lovell MA, Xie C, Xiong S, Markesbery WR. Protection against amyloid beta peptide and iron/hydrogen peroxide toxicity by alpha lipoic acid. *J Alzheimers Dis*. 2003 Jun;5(3):229-39.
 44. Cui X, Zuo P, Zhang Q, et al. Chronic systemic D-galactose exposure induces memory loss, neurodegeneration, and oxidative damage in mice: protective effects of R-alpha-lipoic acid. *J Neurosci Res*. 2006 Aug 15;84(3):647-54.
 45. Quinn JF, Bussiere JR, Hammond RS, et al. Chronic dietary alpha-lipoic acid reduces deficits in hippocampal memory of aged Tg2576 mice. *Neurobiol Aging*. 2007 Feb;28(2):213-25.
 46. Cho JY, Um HS, Kang EB, et al. The combination of exercise training and alpha-lipoic acid treatment has therapeutic effects on the pathogenic phenotypes of Alzheimer's disease in NSE/APPsw-transgenic mice. *Int J Mol Med*. 2010 Mar;25(3):337-46.
 47. Hager K, Marahrens A, Kenkies M, Riederer P, Munch G. Alpha-lipoic acid as a new treatment option for Alzheimer [corrected] type dementia. *Arch Gerontol Geriatr*. 2001 Jun;32(3):275-82.
 48. Hager K, Kenkies M, McAfoose J, Engel J, Munch G. Alpha-lipoic acid as a new treatment option for Alzheimer's disease--a 48 months follow-up analysis. *J Neural Transm Suppl*. 2007 (72):189-93.

49. Available at: <http://lpi.oregonstate.edu/infocenter/othernuts/la/> (<http://lpi.oregonstate.edu/infocenter/othernuts/la/>). Accessed December 27, 2012.
50. Pocernich CB, Butterfield DA. Elevation of glutathione as a therapeutic strategy in Alzheimer disease. *Biochim Biophys Acta*. 2012 May;1822(5):625-30.
51. Huang Q, Aluise CD, Joshi G, et al. Potential in vivo amelioration by N-acetyl-L-cysteine of oxidative stress in brain in human double mutant APP/PS-1 knock-in mice: toward therapeutic modulation of mild cognitive impairment. *J Neurosci Res*. 2010 Sep;88(12):2618-29.
52. Hsiao YH, Kuo JR, Chen SH, Gean PW. Amelioration of social isolation-triggered onset of early Alzheimer's disease-related cognitive deficit by N-acetylcysteine in a transgenic mouse model. *Neurobiol Dis*. 2012 Mar;45(3):1111-20.
53. Adair JC, Knoefel JE, Morgan N. Controlled trial of N-acetylcysteine for patients with probable Alzheimer's disease. *Neurology*. 2001 Oct 23;57(8):1515-7.
54. Samieri C, Feart C, Letenneur L, et al. Low plasma eicosapentaenoic acid and depressive symptomatology are independent predictors of dementia risk. *Am J Clin Nutr*. 2008 Sep;88(3):714-21.
55. Lopez LB, Kritz-Silverstein D, Barrett Connor E. High dietary and plasma levels of the omega-3 fatty acid docosahexaenoic acid are associated with decreased dementia risk: the Rancho Bernardo study. *J Nutr Health Aging*. 2011 Jan;15(1):25-31.
56. Phillips MA, Childs CE, Calder PC, Rogers PJ. Lower omega-3 fatty acid intake and status are associated with poorer cognitive function in older age: A comparison of individuals with and without cognitive impairment and Alzheimer's disease. *Nutr Neurosci*. 2012 Jul 19.
57. Freund-Levi Y, Eriksdotter-Jonhagen M, Cederholm T, et al. Omega-3 fatty acid treatment in 174 patients with mild to moderate Alzheimer disease: OmegAD study: a randomized double-blind trial. *Arch Neurol*. 2006 Oct;63(10):1402-8.
58. Chiu CC, Su KP, Cheng TC, et al. The effects of omega-3 fatty acids monotherapy in Alzheimer's disease and mild cognitive impairment: a preliminary randomized double-blind placebo-controlled study. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008 Aug 1;32(6):1538-44.
59. Yurko-Mauro K, McCarthy D, Rom D, et al. Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline. *Alzheimers Dement*. 2010 Nov;6(6):456-64.
60. Lee LK, Shahar S, Chin AV, Yusoff NA. Docosahexaenoic acid-concentrated fish oil supplementation in subjects with mild cognitive impairment (MCI): a 12-month randomised, double-blind, placebo-controlled trial. *Psychopharmacology (Berl)*. 2012 Aug 30.

61. Quinn JF, Raman R, Thomas RG, et al. Docosahexaenoic acid supplementation and cognitive decline in Alzheimer disease: a randomized trial. *JAMA*. 2010 Nov 3;304(17):1903-11.
62. Lehmann DJ, Refsum H, Warden DR, Medway C, Wilcock GK, Smith AD. The vitamin D receptor gene is associated with Alzheimer's disease. *Neurosci Lett*. 2011 Oct 24;504(2):79-82.
63. Soni M, Kos K, Lang IA, Jones K, Melzer D, Llewellyn DJ. Vitamin D and cognitive function. *Scand J Clin Lab Invest Suppl*. 2012 Apr;243:79-82.
64. Annweiler C, Beauchet O. Vitamin D-mentia: randomized clinical trials should be the next step. *Neuroepidemiology*. 2011;37(3-4):249-58.
65. Evatt ML, DeLong MR, Khazai N, Rosen A, Triche S, Tangpricha V. Prevalence of vitamin d insufficiency in patients with Parkinson disease and Alzheimer disease. *Arch Neurol*. 2008 Oct;65(10):1348-52.
66. Balion C, Griffith LE, Striffler L, et al. Vitamin D, cognition, and dementia: A systematic review and meta-analysis. *Neurology*. 2012 Sep 25;79(13):1397-405.
67. Annweiler C, Fantino B, Schott AM, Krolak-Salmon P, Allali G, Beauchet O. Vitamin D insufficiency and mild cognitive impairment: cross-sectional association. *Eur J Neurol*. 2012 Jul;19(7):1023-9.
68. Lu'o'ng KV, Nguyen LT. The beneficial role of vitamin D in Alzheimer's disease. *Am J Alzheimers Dis Other Demen*. 2011 Nov;26(7):511-20.
69. Riascos D, de Leon D, Baker-Nigh A, et al. Age-related loss of calcium buffering and selective neuronal vulnerability in Alzheimer's disease. *Acta Neuropathol*. 2011 Nov;122(5):565-76.
70. Annweiler C, Beauchet O. Possibility of a new anti-alzheimer's disease pharmaceutical composition combining memantine and vitamin D. *Drugs Aging*. 2012 Feb 1;29(2):81-91.
71. Eyles DW, Burne TH, McGrath JJ. Vitamin D, effects on brain development, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. *Front Neuroendocrinol*. 2012 Jul 11.
72. Masoumi A, Goldenson B, Ghirmai S, et al. 1alpha,25-dihydroxyvitamin D3 interacts with curcuminoids to stimulate amyloid-beta clearance by macrophages of Alzheimer's disease patients. *J Alzheimers Dis*. 2009;17(3):703-17.
73. Mizwicki MT, Menegaz D, Zhang J, et al. Genomic and nongenomic signaling induced by 1alpha,25(OH)2-vitamin D3 promotes the recovery of amyloid-beta phagocytosis by Alzheimer's disease macrophages. *J Alzheimers Dis*. 2012;29(1):51-62.
74. Annweiler C, Herrmann FR, Fantino B, Brugg B, Beauchet O. Effectiveness of the combination of memantine plus vitamin d on cognition in patients with Alzheimer disease: a pre-post pilot study.

75. Luo Y. Ginkgo biloba neuroprotection: Therapeutic implications in Alzheimer's disease. *J Alzheimers Dis.* 2001 Aug;3(4):401-07.
76. Colciaghi F, Borroni B, Zimmermann M, et al. Amyloid precursor protein metabolism is regulated toward alpha-secretase pathway by Ginkgo biloba extracts. *Neurobiol Dis.* 2004 Jul;16(2):454-60.
77. Cong W, Sheng L, Li Y, Li P, Lin C, Liu J. Protective effects of ginseng-ginkgo extracts combination on rat primary cultured neurons induced by Amyloid beta(1-40). *Zhongguo Zhong Yao Za Zhi.* 2011 Apr;36(7):908-11.
78. Kanowski S, Hoerr R. Ginkgo biloba extract EGb 761 in dementia: intent-to-treat analyses of a 24-week, multi-center, double-blind, placebo-controlled, randomized trial. *Pharmacopsychiatry.* 2003 Nov;36(6):297-303.
79. Haan J, Horr R. Delay in progression of dependency and need of care of dementia patients treated with Ginkgo special extract EGb 761. *Wien Med Wochenschr.* 2004 Nov;154(21-22):511-4.
80. Napryeyenko O, Sonnik G, Tartakovsky I. Efficacy and tolerability of Ginkgo biloba extract EGb 761 by type of dementia: analyses of a randomised controlled trial. *J Neurol Sci.* 2009 Aug 15;283(1-2):224-9.
81. Vellas B, Coley N, Ousset PJ, et al. Long-term use of standardised Ginkgo biloba extract for the prevention of Alzheimer's disease (GuidAge): a randomised placebo-controlled trial. *Lancet Neurol.* 2012 Oct;11(10):851-9.
82. Snitz BE, O'Meara ES, Carlson MC, et al. Ginkgo biloba for preventing cognitive decline in older adults: a randomized trial. *JAMA.* 2009 Dec 23;302(24):2663-70.
83. Mazza M, Capuano A, Bria P, Mazza S. Ginkgo biloba and donepezil: a comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study. *Eur J Neurol.* 2006 Sep;13(9):981-5.
84. Yancheva S, Ihl R, Nikolova G, Panayotov P, Schlaefke S, Hoerr R. Ginkgo biloba extract EGb 761(R), donepezil or both combined in the treatment of Alzheimer's disease with neuropsychiatric features: a randomised, double-blind, exploratory trial. *Aging Ment Health.* 2009 Mar;13(2):183-90.
85. Scripnikov A, Khomenko A, Napryeyenko O. Effects of Ginkgo biloba extract EGb 761 on neuropsychiatric symptoms of dementia: findings from a randomised controlled trial. *Wien Med Wochenschr.* 2007;157(13-14):295-300.
86. Janssen IM, Sturtz S, Skipka G, Zentner A, Velasco Garrido M, Busse R. Ginkgo biloba in Alzheimer's disease: a systematic review. *Wien Med Wochenschr.* 2010 Dec;160(21-22):539-46.

87. Ihl R, Tribanek M, Bachinskaya N. Efficacy and tolerability of a once daily formulation of Ginkgo biloba extract EGb 761(R) in Alzheimer's disease and vascular dementia: results from a randomised controlled trial. *Pharmacopsychiatry*. 2012 Mar;45(2):41-6.
88. Barranco Quintana JL, Allam MF, Serrano Del Castillo A, Fernandez-Crehuet Navajas R. Alzheimer's disease and coffee: a quantitative review. *Neurol Res*. 2007 Jan;29(1):91-5.
89. Arendash GW, Cao C. Caffeine and coffee as therapeutics against Alzheimer's disease. *J Alzheimers Dis*. 2010;20 Suppl 1:S117-26.
90. Dostal V, Roberts CM, Link CD. Genetic mechanisms of coffee extract protection in a *Caenorhabditis elegans* model of beta-amyloid peptide toxicity. *Genetics*. 2010 Nov;186(3):857-66.
91. Eskelinen MH, Kivipelto M. Caffeine as a protective factor in dementia and Alzheimer's disease. *J Alzheimers Dis*. 2010;20 Suppl 1:S167-74.
92. Eskelinen MH, Ngandu T, Tuomilehto J, Soininen H, Kivipelto M. Midlife coffee and tea drinking and the risk of late-life dementia: a population-based CAIDE study. *J Alzheimers Dis*. 2009;16(1):85-91.
93. Cao C, Loewenstein DA, Lin X, et al. High Blood caffeine levels in MCI linked to lack of progression to dementia. *J Alzheimers Dis*. 2012;30(3):559-72.
94. Arendash GW, Mori T, Cao C, et al. Caffeine reverses cognitive impairment and decreases brain amyloid-beta levels in aged Alzheimer's disease mice. *J Alzheimers Dis*. 2009;17(3):661-80.
95. Chu YF, Chang WH, Black RM, et al. Crude caffeine reduces memory impairment and amyloid beta(1-42) levels in an Alzheimer's mouse model. *Food Chem*. 2012 Dec 1;135(3):2095-102.
96. Kotyczka C, Boettler U, Lang R, et al. Dark roast coffee is more effective than light roast coffee in reducing body weight, and in restoring red blood cell vitamin E and glutathione concentrations in healthy volunteers. *Mol Nutr Food Res*. 2011 Oct;55(10):1582-6.
97. Kwon SH, Lee HK, Kim JA, et al. Neuroprotective effects of chlorogenic acid on scopolamine-induced amnesia via anti-acetylcholinesterase and anti-oxidative activities in mice. *Eur J Pharmacol*. 2010 Dec 15;649(1-3):210-7.
98. Ho L, Varghese M, Wang J, et al. Dietary supplementation with decaffeinated green coffee improves diet-induced insulin resistance and brain energy metabolism in mice. *Nutr Neurosci*. 2012 Jan;15(1):37-45.
99. Cao C, Wang L, Lin X, et al. Caffeine synergizes with another coffee component to increase plasma GCSF: linkage to cognitive benefits in Alzheimer's mice. *J Alzheimers Dis*. 2011;25(2):323-35.
100. 100. Slutsky I, Abumaria N, Wu LJ, et al. Enhancement of learning and memory by elevating brain magnesium. *Neuron*. 2010 Jan

28;65(2):165-77.

101. Ho M, Hoke DE, Chua YJ, et al. Effect of metal chelators on gamma-secretase indicates that calcium and magnesium ions facilitate cleavage of Alzheimer amyloid precursor substrate. *Int J Alzheimers Dis.* 2010;2011:950932.
102. Yu J, Sun M, Chen Z, et al. Magnesium modulates amyloid-beta protein precursor trafficking and processing. *J Alzheimers Dis.* 2010;20(4):1091-106.
103. Lee M, Jantaratnotai N, McGeer E, McLarnon JG, McGeer PL. Mg²⁺ ions reduce microglial and THP-1 cell neurotoxicity by inhibiting Ca²⁺ entry through purinergic channels. *Brain Res.* 2011 Jan 19;1369:21-35.
104. Cilliler AE, Ozturk S, Ozbakir S. Serum magnesium level and clinical deterioration in Alzheimer's disease. *Gerontology.* 2007;53(6):419-22.
105. Vural H, Demirin H, Kara Y, Eren I, Delibas N. Alterations of plasma magnesium, copper, zinc, iron and selenium concentrations and some related erythrocyte antioxidant enzyme activities in patients with Alzheimer's disease. *J Trace Elem Med Biol.* 2010 Jul;24(3):169-73.
106. Barbagallo M, Belvedere M, Di Bella G, Dominguez LJ. Altered ionized magnesium levels in mild-to-moderate Alzheimer's disease. *Magnes Res.* 2011 Sep;24(3):S115-21.
107. Morris MC, Evans DA, Tangney CC, et al. Relation of the tocopherol forms to incident Alzheimer disease and to cognitive change. *Am J Clin Nutr.* 2005 Feb;81(2):508-14.
108. Mangialasche F, Xu W, Kivipelto M, et al. Tocopherols and tocotrienols plasma levels are associated with cognitive impairment. *Neurobiol Aging.* 2012 Oct;33(10):2282-90.
109. Usoro OB, Mousa SA. Vitamin E forms in Alzheimer's disease: a review of controversial and clinical experiences. *Crit Rev Food Sci Nutr.* 2010 May;50(5):414-9.
110. Frank J, Chin XW, Schrader C, Eckert GP, Rimbach G. Do tocotrienols have potential as neuroprotective dietary factors? *Ageing Res Rev.* 2012 Jan;11(1):163-80.
111. Catalgol B, Batirel S, Ozer NK. Cellular protection and therapeutic potential of tocotrienols. *Curr Pharm Des.* 2011;17(21):2215-20.
112. Mangialasche F, Kivipelto M, Mecocci P, et al. High plasma levels of vitamin E forms and reduced Alzheimer's disease risk in advanced age. *J Alzheimers Dis.* 2010;20(4):1029-37.
113. Jayaprakasam B, Padmanabhan K, Nair MG. Withanamides in *Withania somnifera* fruit protect PC-12 cells from beta-amyloid responsible for Alzheimer's disease. *Phytother Res.* 2010 Jun;24(6):859-63.
114. Choudhary MI, Yousuf S, Nawaz SA, Ahmed S, Atta uR. Cholinesterase inhibiting withanolides from *Withania somnifera*. *Chem*

- Pharm Bull (Tokyo). 2004 Nov;52(11):1358-61.
115. Wilkinson DG, Francis PT, Schwam E, Payne-Parrish J. Cholinesterase inhibitors used in the treatment of Alzheimer's disease: the relationship between pharmacological effects and clinical efficacy. *Drugs Aging*. 2004;21(7):453-78.
 116. Ho RC, Cheung MW, Fu E, et al. Is high homocysteine level a risk factor for cognitive decline in elderly? A systematic review, meta-analysis, and meta-regression. *Am J Geriatr Psychiatry*. 2011 Jul;19(7):607-17.
 117. Wei W, Liu YH, Zhang CE, et al. Folate/vitamin-B12 prevents chronic hyperhomocysteinemia-induced tau hyperphosphorylation and memory deficits in aged rats. *J Alzheimers Dis*. 2011;27(3):639-50.
 118. de Jager CA, Oulhaj A, Jacoby R, Refsum H, Smith AD. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2012 Jun;27(6):592-600.
 119. Flicker L, Martins RN, Thomas J, et al. B-vitamins reduce plasma levels of beta amyloid. *Neurobiol Aging*. 2008 Feb;29(2):303-5.
 120. Smith AD, Smith SM, de Jager CA, et al. Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. *PLoS One*. 2010;5(9):e12244.
 121. Joseph JA, Shukitt-Hale B, Casadesus G. Reversing the deleterious effects of aging on neuronal communication and behavior: beneficial properties of fruit polyphenolic compounds. *Am J Clin Nutr*. 2005 Jan;81(1 Suppl):313S-16S.
 122. Williams RJ, Spencer JP. Flavonoids, cognition, and dementia: actions, mechanisms, and potential therapeutic utility for Alzheimer disease. *Free Radic Biol Med*. 2012 Jan 1;52(1):35-45.
 123. Ramassamy C. Emerging role of polyphenolic compounds in the treatment of neurodegenerative diseases: a review of their intracellular targets. *Eur J Pharmacol*. 2006 Sep 1;545(1):51-64.
 124. Joseph JA, Denisova NA, Arendash G, et al. Blueberry supplementation enhances signaling and prevents behavioral deficits in an Alzheimer disease model. *Nutr Neurosci*. 2003 Jun;6(3):153-62.
 125. Joseph JA, Fisher DR, Carey AN. Fruit extracts antagonize Amyloid beta- or DA-induced deficits in Ca²⁺ flux in M1-transfected COS-7 cells. *J Alzheimers Dis*. 2004 Aug;6(4):403-11; discussion 43-9.
 126. Zhu Y, Bickford PC, Sanberg P, Giunta B, Tan J. Blueberry opposes beta-amyloid peptide-induced microglial activation via inhibition of p44/42 mitogen-activation protein kinase. *Rejuvenation Res*. 2008 Oct;11(5):891-901.
 127. Spindler M, Beal MF, Henchcliffe C. Coenzyme Q10 effects in

- neurodegenerative disease. *Neuropsychiatr Dis Treat*. 2009;5:597-610.
128. Ohwada K, Takeda H, Yamazaki M, et al. Pyrroloquinoline quinone (PQQ) prevents cognitive deficit caused by oxidative stress in rats. *J Clin Biochem Nutr*. 2008 Jan;42:29-34.
129. Orsucci D, Mancuso M, Ienco EC, LoGerfo A, Siciliano G. Targeting mitochondrial dysfunction and neurodegeneration by means of coenzyme Q10 and its analogues. *Curr Med Chem*. 2011;18(26):4053-64.
130. Choi H, Park HH, Koh SH, et al. Coenzyme Q10 protects against amyloid beta-induced neuronal cell death by inhibiting oxidative stress and activating the P13K pathway. *Neurotoxicology*. 2012 Jan;33(1):85-90.
131. Yang X, Dai G, Li G, Yang ES. Coenzyme Q10 reduces beta-amyloid plaque in an APP/PS1 transgenic mouse model of Alzheimer's disease. *J Mol Neurosci*. 2010 May;41(1):110-3.
132. Dumont M, Kipiani K, Yu F, et al. Coenzyme Q10 decreases amyloid pathology and improves behavior in a transgenic mouse model of Alzheimer's disease. *J Alzheimers Dis*. 2011;27(1):211-23.
133. Zhang JJ, Zhang RF, Meng XK. Protective effect of pyrroloquinoline quinone against Amyloid beta-induced neurotoxicity in human neuroblastoma SH-SY5Y cells. *Neurosci Lett*. 2009 Oct 30;464(3):165-9.
134. Verma M, Sharma A, Naidu S, Bhadra AK, Kukreti R, Taneja V. Curcumin Prevents Formation of Polyglutamine Aggregates by Inhibiting Vps36, a Component of the ESCRT-II Complex. *PLoS One*. 2012;7(8):e42923.
135. Wang J, Zhang YJ, Du S. The protective effect of curcumin on Amyloid beta induced aberrant cell cycle reentry on primary cultured rat cortical neurons. *Eur Rev Med Pharmacol Sci*. 2012 Apr;16(4):445-54.
136. Huang HC, Xu K, Jiang ZF. Curcumin-Mediated Neuroprotection Against Amyloid-beta-Induced Mitochondrial Dysfunction Involves the Inhibition of GSK-3beta. *J Alzheimers Dis*. 2012 Aug 9.
137. Zhao LN, Chiu SW, Benoit J, Chew LY, Mu Y. The effect of curcumin on the stability of Amyloid beta dimers. *J Phys Chem B*. 2012 Jun 28;116(25):7428-35.
138. Sparks S, Liu G, Robbins KJ, Lazo ND. Curcumin modulates the self-assembly of the islet amyloid polypeptide by disassembling alpha-helix. *Biochem Biophys Res Commun*. 2012 Jun 15;422(4):551-5.
139. Eckert GP, Renner K, Eckert SH, et al. Mitochondrial dysfunction--a pharmacological target in Alzheimer's disease. *Mol Neurobiol*. 2012 Aug;46(1):136-50.
140. Sood PK, Nahar U, Nehru B. Curcumin attenuates aluminum-induced oxidative stress and mitochondrial dysfunction in rat brain. *Neurotox*

Res. 2011 Nov;20(4):351-61.

141. Lue LF, Andrade C, Sabbagh M, Walker D. Is There Inflammatory Synergy in Type II Diabetes Mellitus and Alzheimer's Disease? *Int J Alzheimers Dis.* 2012;2012:918680.
142. Isik AT, Celik T, Ulusoy G, et al. Curcumin ameliorates impaired insulin/IGF signalling and memory deficit in a streptozotocin-treated rat model. *Age (Dordr).* 2009 Mar;31(1):39-49.
143. Agrawal R, Mishra B, Tyagi E, Nath C, Shukla R. Effect of curcumin on brain insulin receptors and memory functions in STZ (ICV) induced dementia model of rat. *Pharmacol Res.* 2010 Mar;61(3):247-52.
144. Pan R, Qiu S, Lu DX, Dong J. Curcumin improves learning and memory ability and its neuroprotective mechanism in mice. *Chin Med J (Engl).* 2008 May 5;121(9):832-9.
145. Ishrat T, Hoda MN, Khan MB, et al. Amelioration of cognitive deficits and neurodegeneration by curcumin in rat model of sporadic dementia of Alzheimer's type (SDAT). *Eur Neuropsychopharmacol.* 2009 Sep;19(9):636-47.
146. Ahmed T, Enam SA, Gilani AH. Curcuminoids enhance memory in an amyloid-infused rat model of Alzheimer's disease. *Neuroscience.* 2010 Sep 1;169(3):1296-306.
147. Kawamoto EM, Scavone C, Mattson MP, Camandola S. Curcumin Requires Tumor Necrosis Factor alpha Signaling to Alleviate Cognitive Impairment Elicited by Lipopolysaccharide. *Neurosignals.* 2012 May 9.
148. Kumar A, Prakash A, Dogra S. Protective effect of curcumin (*Curcuma longa*) against D-galactose-induced senescence in mice. *J Asian Nat Prod Res.* 2011 Jan;13(1):42-55.
149. Deshane J, Chaves L, Sarikonda KV, et al. Proteomics analysis of rat brain protein modulations by grape seed extract. *J Agric Food Chem.* 2004 Dec 29;52(26):7872-83.
150. Ferruzzi MG, Lobo JK, Janle EM, et al. Bioavailability of gallic acid and catechins from grape seed polyphenol extract is improved by repeated dosing in rats: implications for treatment in Alzheimer's disease. *J Alzheimers Dis.* 2009;18(1):113-24.
151. Dasilva KA, Shaw JE, McLaurin J. Amyloid-beta fibrillogenesis: structural insight and therapeutic intervention. *Exp Neurol.* 2010 Jun;223(2):311-21.
152. Ho L, Pasinetti GM. Polyphenolic compounds for treating neurodegenerative disorders involving protein misfolding. *Expert Rev Proteomics.* 2010 Aug;7(4):579-89.
153. Liu P, Kemper LJ, Wang J, Zahs KR, Ashe KH, Pasinetti GM. Grape seed polyphenolic extract specifically decreases amyloid beta*56 in the brains of Tg2576 mice. *J Alzheimers Dis.* 2011;26(4):657-66.
154. Wang YJ, Thomas P, Zhong JH, et al. Consumption of grape seed

- extract prevents amyloid-beta deposition and attenuates inflammation in brain of an Alzheimer's disease mouse. *Neurotox Res.* 2009 Jan;15(1):3-14.
155. Mandel SA, Weinreb O, Amit T, Youdim MB. Molecular mechanisms of the neuroprotective/neurorescue action of multi-target green tea polyphenols. *Front Biosci (Schol Ed).* 2012;4:581-98.
156. Sinha S, Du Z, Maiti P, et al. Comparison of three amyloid assembly inhibitors: the sugar scyllo-inositol, the polyphenol epigallocatechin gallate, and the molecular tweezer CLR01. *ACS Chem Neurosci.* 2012 Jun 20;3(6):451-8.
157. Lopez del Amo JM, Fink U, Dasari M, et al. Structural properties of EGCG-induced, nontoxic Alzheimer's disease Amyloid beta oligomers. *J Mol Biol.* 2012 Aug 24;421(4-5):517-24.
158. Dragicevic N, Smith A, Lin X, et al. Green tea epigallocatechin-3-gallate (EGCG) and other flavonoids reduce Alzheimer's amyloid-induced mitochondrial dysfunction. *J Alzheimers Dis.* 2011;26(3):507-21.
159. He Y, Cui J, Lee JC, et al. Prolonged exposure of cortical neurons to oligomeric amyloid-beta impairs NMDA receptor function via NADPH oxidase-mediated ROS production: protective effect of green tea (-)-epigallocatechin-3-gallate. *ASN Neuro.* 2011;3(1):e00050.
160. Li F, Gong Q, Dong H, Shi J. Resveratrol, a neuroprotective supplement for Alzheimer's disease. *Curr Pharm Des.* 2012;18(1):27-33.
161. Lopez-Miranda V, Soto-Montenegro ML, Vera G, Herradon E, Desco M, Abalo R. Resveratrol: a neuroprotective polyphenol in the Mediterranean diet. *Rev Neurol.* 2012 Mar 16;54(6):349-56.
162. Wight RD, Tull CA, Deel MW, et al. Resveratrol effects on astrocyte function: Relevance to neurodegenerative diseases. *Biochem Biophys Res Commun.* 2012 Sep 14;426(1):112-5.
163. Liu GS, Zhang ZS, Yang B, He W. Resveratrol attenuates oxidative damage and ameliorates cognitive impairment in the brain of senescence-accelerated mice. *Life Sci.* 2012 Oct 29;91(17-18):872-7. doi: 10.1016/j.lfs.2012.08.033. Epub 2012 Sep 12.
164. Davinelli S, Sapere N, Zella D, Bracale R, Intrieri M, Scapagnini G. Pleiotropic protective effects of phytochemicals in Alzheimer's disease. *Oxid Med Cell Longev.* 2012;2012:386527.
165. Huang TC, Lu KT, Wo YY, Wu YJ, Yang YL. Resveratrol protects rats from Amyloid beta-induced neurotoxicity by the reduction of iNOS expression and lipid peroxidation. *PLoS One.* 2011;6(12):e29102.
166. Braidy N, Jayasena T, Poljak A, Sachdev PS. Sirtuins in cognitive ageing and Alzheimer's disease. *Curr Opin Psychiatry.* 2012 May;25(3):226-30.
167. Capiralla H, Vingtdoux V, Zhao H, et al. Resveratrol mitigates

- lipopolysaccharide- and Amyloid beta-mediated microglial inflammation by inhibiting the TLR4/NF-kappaB/STAT signaling cascade. *J Neurochem*. 2012 Feb;120(3):461-72.
168. Ge JF, Qiao JP, Qi CC, Wang CW, Zhou JN. The binding of resveratrol to monomer and fibril amyloid beta. *Neurochem Int*. 2012 Sep 7.
169. Zhang JQ, Wu PF, Long LH, et al. Resveratrol promotes cellular glucose utilization in primary cultured cortical neurons via calcium-dependent signaling pathway. *J Nutr Biochem*. 2012 Jul 20.
170. Vinpocetine. Monograph. *Altern Med Rev*. 2002 Jun;7(3):240-3.
171. Deshmukh R, Sharma V, Mehan S, Sharma N, Bedi KL. Amelioration of intracerebroventricular streptozotocin induced cognitive dysfunction and oxidative stress by vinpocetine -- a PDE1 inhibitor. *Eur J Pharmacol*. 2009 Oct 12;620(1-3):49-56.
172. Pereira C, Agostinho P, Oliveira CR. Vinpocetine attenuates the metabolic dysfunction induced by amyloid beta-peptides in PC12 cells. *Free Radic Res*. 2000 Nov;33(5):497-506.
173. Bolognesi ML, Rosini M, Andrisano V, et al. MTDL design strategy in the context of Alzheimer's disease: from lipocrine to memoquin and beyond. *Curr Pharm Des*. 2009;15(6):601-13.
174. Parachikova A, Green KN, Hendrix C, LaFerla FM. Formulation of a medical food cocktail for Alzheimer's disease: beneficial effects on cognition and neuropathology in a mouse model of the disease. *PLoS One*. 2010;5(11):e14015.
175. Chan A, Paskavitz J, Remington R, Rasmussen S, Shea TB. Efficacy of a vitamin/nutraceutical formulation for early-stage Alzheimer's disease: a 1-year, open-label pilot study with an 16-month caregiver extension. *Am J Alzheimers Dis Other Dement*. 2008 Dec-2009 Jan;23(6):571-85.
176. Remington R, Chan A, Paskavitz J, Shea TB. Efficacy of a vitamin/nutraceutical formulation for moderate-stage to later-stage Alzheimer's disease: a placebo-controlled pilot study. *Am J Alzheimers Dis Other Dement*. 2009 Feb-Mar;24(1):27-33.
177. Chan A, Remington R, Kotyla E, Lepore A, Zemianek J, Shea TB. A vitamin/nutraceutical formulation improves memory and cognitive performance in community-dwelling adults without dementia. *J Nutr Health Aging*. 2010 Mar;14(3):224-30.
178. R&D Department BioActive Ingredients Division Enzymotec Ltd. An open-label study to assess the efficacy of Cognitex with Neuroprotection Complex (Life Extension, USA) in middle age to elderly subjects who display subjective memory complaints; Statistical Analysis of Clinical Study Results. March 2012.
179. Available at:
http://www.lef.org/protocols/neurological/alzheimers_disease_01.htm

(/protocols/neurological/alzheimers_disease_01.htm). Accessed October 5, 2012.

180. Kurz A, Perneczky R. Amyloid clearance as a treatment target against Alzheimer's disease. *J Alzheimers Dis.* 2011;24 Suppl 2:61-73.
181. Pocernich CB, Lange ML, Sultana R, Butterfield DA. Nutritional approaches to modulate oxidative stress in Alzheimer's disease. *Curr Alzheimer Res.* 2011 Aug;8(5):452-69.
182. Magrone T, Marzulli G, Jirillo E. Immunopathogenesis of neurodegenerative diseases: current therapeutic models of neuroprotection with special reference to natural products. *Curr Pharm Des.* 2012;18(1):34-42.
183. Mancuso C, Siciliano R, Barone E, Preziosi P. Natural substances and Alzheimer's disease: from preclinical studies to evidence based medicine. *Biochim Biophys Acta.* 2012 May;1822(5):616-24.
184. Stewart WF, Kawas C, Corrada M, Metter EJ. Risk of Alzheimer's disease and duration of NSAID use. *Neurology.* 1997 Mar;48(3):626-32.
185. Yip AG, Green RC, Huyck M, Cupples LA, Farrer LA. Nonsteroidal anti-inflammatory drug use and Alzheimer's disease risk: the MIRAGE Study. *BMC Geriatr.* 2005;5:2.
186. Cote S, Carmichael PH, Verreault R, Lindsay J, Lefebvre J, Laurin D. Nonsteroidal anti-inflammatory drug use and the risk of cognitive impairment and Alzheimer's disease. *Alzheimers Dement.* 2012 May;8(3):219-26.
187. Babiloni C, Frisoni GB, Del Percio C, et al. Ibuprofen treatment modifies cortical sources of EEG rhythms in mild Alzheimer's disease. *Clin Neurophysiol.* 2009 Apr;120(4):709-18.
188. Aisen PS, Schafer KA, Grundman M, et al. Effects of rofecoxib or naproxen vs placebo on Alzheimer disease progression: a randomized controlled trial. *JAMA.* 2003 Jun 4;289(21):2819-26.
189. Breitner JC, Baker LD, Montine TJ, et al. Extended results of the Alzheimer's disease anti-inflammatory prevention trial. *Alzheimers Dement.* 2011 Jul;7(4):402-11.
190. Leoutsakos JM, Muthen BO, Breitner JC, Lyketsos CG. Effects of non-steroidal anti-inflammatory drug treatments on cognitive decline vary by phase of pre-clinical Alzheimer disease: findings from the randomized controlled Alzheimer's Disease Anti-inflammatory Prevention Trial. *Int J Geriatr Psychiatry.* 2012 Apr;27(4):364-74.
191. Ibanez-Hernandez MG, Macias-Islas MA, Zavalza-Gomez AB, Pacheco-Moises FP, Ortiz GG. [The effect of ibuprofen and acetylsalicylic acid on cognitive impairment, total antioxidant power and isoprostane serum]. *Gac Med Mex.* 2008 Nov-Dec;144(6):497-502.
192. Ciabattini G, Porreca E, Di Febbo C, et al. Determinants of platelet

- activation in Alzheimer's disease. *Neurobiol Aging*. 2007 Mar;28(3):336-42.
193. Pomponi M, Bria P. Is Alzheimer's disease a synaptic disorder? *J Alzheimers Dis*. 2008 Feb;13(1):39-47.
194. Pomponi MF, Gambassi G, Pomponi M, Di Gioia A, Masullo C. Why docosahexaenoic acid and aspirin supplementation could be useful in women as a primary prevention therapy against Alzheimer's disease? *Ageing Res Rev*. 2011 Jan;10(1):124-31.
195. Graham GG, Punt J, Arora M, et al. Clinical pharmacokinetics of metformin. *Clin Pharmacokinet*. 2011 Feb;50(2):81-98.
196. Hadden DR. Goat's rue - French lilac - Italian fitch - Spanish sainfoin: gallega officinalis and metformin: the Edinburgh connection. *J R Coll Physicians Edinb*. 2005 Oct;35(3):258-60.
197. Grzybowska M, Bober J, Olszewska M. Metformin - mechanisms of action and use for the treatment of type 2 diabetes mellitus. *Postepy Hig Med Dosw (Online)*. 2011;65:277-85.
198. Gupta A, Bisht B, Dey CS. Peripheral insulin-sensitizer drug metformin ameliorates neuronal insulin resistance and Alzheimer's-like changes. *Neuropharmacology*. 2011 May;60(6):910-20.
199. Kickstein E, Krauss S, Thornhill P, et al. Biguanide metformin acts on tau phosphorylation via mTOR/protein phosphatase 2A (PP2A) signaling. *Proc Natl Acad Sci U S A*. 2010 Dec 14;107(50):21830-5.
200. Li J, Deng J, Sheng W, Zuo Z. Metformin attenuates Alzheimer's disease-like neuropathology in obese, leptin-resistant mice. *Pharmacol Biochem Behav*. 2012 Jun;101(4):564-74.
201. Magri F, Cravello L, Barili L, et al. Stress and dementia: the role of the hypothalamic-pituitary-adrenal axis. *Aging Clin Exp Res*. 2006 Apr;18(2):167-70.
202. Ferrari E, Cravello L, Muzzoni B, et al. Age-related changes of the hypothalamic-pituitary-adrenal axis: pathophysiological correlates. *Eur J Endocrinol*. 2001 Apr;144(4):319-29.
203. Krysiak R, Frysz-Naglak D, Okopien B. Current views on the role of dehydroepiandrosterone in physiology, pathology and therapy. *Pol Merkur Lekarski*. 2008 Jan;24(139):66-71.
204. Wang MJ, Huang HM, Chen HL, Kuo JS, Jeng KC. Dehydroepiandrosterone inhibits lipopolysaccharide-induced nitric oxide production in BV-2 microglia. *J Neurochem*. 2001 May;77(3):830-8.
205. Bastianetto S, Ramassamy C, Poirier J, Quirion R. Dehydroepiandrosterone (DHEA) protects hippocampal cells from oxidative stress-induced damage. *Brain Res Mol Brain Res*. 1999 Mar 20;66(1-2):35-41.
206. Leblhuber F, Neubauer C, Peichl M, et al. Age and sex differences of

- dehydroepiandrosterone sulfate (DHEAS) and cortisol (CRT) plasma levels in normal controls and Alzheimer's disease (AD). *Psychopharmacology (Berl)*. 1993;111(1):23-6.
207. Barger SW, Chavis JA, Drew PD. Dehydroepiandrosterone inhibits microglial nitric oxide production in a stimulus-specific manner. *J Neurosci Res*. 2000 Nov 15;62(4):503-9.
 208. Aly HF, Metwally FM, Ahmed HH. Neuroprotective effects of dehydroepiandrosterone (DHEA) in rat model of Alzheimer's disease. *Acta Biochim Pol*. 2011;58(4):513-20.
 209. Azizi H, Mehrjardi NZ, Shahbazi E, Hemmesi K, Bahmani MK, Baharvand H. Dehydroepiandrosterone stimulates neurogenesis in mouse embryonal carcinoma cell- and human embryonic stem cell-derived neural progenitors and induces dopaminergic neurons. *Stem Cells Dev*. 2010 Jun;19(6):809-18.
 210. Vallee M, Mayo W, Le Moal M. Role of pregnenolone, dehydroepiandrosterone and their sulfate esters on learning and memory in cognitive aging. *Brain Res Brain Res Rev*. 2001 Nov;37(1-3):301-12.
 211. Farr SA, Banks WA, Uezu K, Gaskin FS, Morley JE. DHEAS improves learning and memory in aged SAMP8 mice but not in diabetic mice. *Life Sci*. 2004 Oct 22;75(23):2775-85.

Page
1 (/Magazine/2013/3/Nutritional-Strategies-to-Combat-Alzheimers/Page-01)
2 (/Magazine/2013/3/Nutritional-Strategies-to-Combat-Alzheimers/Page-02)
3 (/Magazine/2013/3/Nutritional-Strategies-to-Combat-Alzheimers/Page-03)



Start the discussion...

Be the first to comment.

ALSO ON LIFE EXTENSION

[How to Delay Brain Aging by 11 Years](#)

6 comments • 5 months ago •



Price Weston — Butter is quite different than margine. Do the swiss who eat a ton ...

[Topical Vitamin C for Skin Rejuvenation](#)

1 comment • 4 months ago •



Ella Darling — Awesome, well-written article. Thank you!

[A Multi-Targeted Approach to Reduce the Risk of ...](#)

1 comment • 5 months ago •



Matthew Smith — There is a relationship between Alzheimer's and pernicious ...


[Enhance Eyelashes Naturally](#)

3 comments • 5 months ago •



Mark Miller — Eyelashes also protect the eyes (cornea) from particulates and add some ...

 [Subscribe](#)  [Add Disqus to your site](#) [Add Disqus](#) [Add Disqus](#) **DISQUS**
 [Privacy](#)

 [1-800-544-4440 \(tel:18005444440\)](tel:18005444440)

**These statements have not been evaluated by the Food and Drug Administration.
These products are not intended to diagnose, treat, cure, or prevent any disease.**

[About Us \(/welcome\)](#) [Contact Us \(/quest-com\)](#) [FAQs \(/FAQ\)](#) [Blog \(http://blog.lifeextension.com/\)](#)
[Affiliate Program \(/aff\)](#) [Privacy Policy \(/Legal/Privacy-Policy\)](#) [Terms of Use \(/Legal/Legal-Notices_01\)](#) [Site Map \(/sitemap\)](#)

All Contents Copyright ©2016 Life Extension® All rights reserved