



Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-indevelopment, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Astragalus

Evidence Summary

Likely safe, with very limited evidence suggesting a potential association with neuroprotection, improved learning and memory, and limited evidence for reduced cellular aging.

Neuroprotective Benefit: Preclinical studies suggest it may help preserve learning and memory by protecting neurons against cellular stressors.

Aging and related health concerns: May improve metabolic measures, such as glucose tolerance and insulin sensitivity, and improve heart function in patients with cardiovascular disease, but clinical evidence is limited.

Safety: Generally considered safe based on short term clinical studies, but long-term effects have not been examined. May interact with other drugs that require the liver for metabolism, and could aggravate autoimmune diseases.

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What is it? Astragalus is a large genus of herb species used in traditional Chinese medicine, with *Astragalus membranaceus* being the most common species used in dietary supplements. While these supplements are directed at a variety of health conditions, the supporting evidence of their effectiveness varies. Astragalus is suggested to stimulate and strengthen the immune system, combat the common cold and upper respiratory infections, and lower blood pressure, although there is little scientific evidence to support these claims. An isolated extract of *A. membranaceus* called TA-65 is a patented product of T.A. Sciences, and acts as a telomerase activator (See TA-65 report).

Neuroprotective benefits: Preclinical studies suggest it may help preserve learning and memory by protecting neurons against cellular stressors.

Types of evidence:

• 5 preclinical *in vitro* and *in vivo* studies.

Multiple preclinical animal studies suggest Astragalus may improve learning and memory through multiple mechanisms. Astragalus treatment reversed A β -induced memory loss and prevented the loss of axons and synapses in the cerebral cortex and hippocampus in mice (<u>Tohda et al, 2006</u>), and showed a statistically significant reduction in stress-induced deficits on learning and memory for spatial memory tasks in rats (<u>Park et al, 2009</u>).

Additionally, it protected mice against damage induced by the drug dexamethasone by inhibiting caspase-3 and caspase-9 activity, resulting in statistically significant improvements in learning and memory (Li et al, 2011). Astragalus also protected mitochondria by scavenging reactive oxygen species in mice (Li et al, 2012), and increased neurocyte survival and decreased the neuron apoptosis rate in mice (Huang et al, 2012). While these results demonstrate potential for Astragalus' neuroprotective properties, these effects have not been tested in human or human cell populations and further research is required.

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Broad aging, mortality, and other diseases: May improve metabolic measures, such as glucose tolerance and insulin sensitivity, and improve heart function in patients with cardiovascular disease, but clinical evidence is limited.

Types of evidence:

- 1 randomized controlled trial
- 1 randomized non-controlled trial
- 5 preclinical *in vitro* and *in vivo* studies.

There is no direct evidence that Astragalus extends lifespan in any human or animal model, however research shows potential for improvement in metabolic measures, such as glucose and insulin, and measures of heart function. There is also preclinical evidence for potential improvement in motor and memory function after impairment.

One double-blind randomized-controlled trial in China randomized 43 participants with recently diagnosed Type II diabetes to a treatment of a traditional Chinese herb compound made up of three kinds of plants, including 30 mg of *Astragalus membranaceus*, for three months. The treated group had significantly improved glucose disposal rate compared to a placebo group (<u>Chao et al, 2009</u>). There is also preclinical evidence from mice studies showing that Astragalus can attenuate insulin resistance and endoplasmic reticulum (ER) stress prompted by high glucose *in vivo* and *in vitro*, respectively (<u>Mao et al, 2009</u>).

A clinical trial where 90 patients with cardiovascular disease were randomized to one of three Astragalus granule treatments twice a day for thirty days, at a low (2.25 g/time), moderate (4.5 g/time), or high (7.5 g/time) dosage, suggests that Astragalus granule treatment results in dose-dependent improvement of heart function grades. Improvements in the high-dose and moderate-dose groups were better than those in the low-dose group. Measures included an increase in left ventricular ejection fraction (LVEF), an increase in walking distance in six minutes, and improvements in Minnesota Living with Heart Failure Questionnaire scores, which assesses the ways heart failure and treatments can affect measures related to quality of life (Yang et al, 2011). These findings are supported by preclinical animal studies that suggest Astragalus blocks extracellular calcium influx and helps to relax endothelium vessels in normal and hypertensive rats (Zhang et al, 2006), reduces blood pressure and triglyceride levels in rats (Li et al., 2005), and also improves glucose tolerance in fructose-fed rats (Zhang et al, 2011).

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Additional preclinical studies show that Astragalus can significantly improve motor and memory impairment following D-galactose induced senescence in mice, which suggests anti-aging effects and possibly a delay in senility of middle-aged mice (Lei et al, 2003).

Safety: Generally considered safe based on short term clinical studies, but long-term effects have not been examined. May interact with other drugs that require the liver for metabolism, and could aggravate autoimmune diseases.

The Astragalus species in most dietary supplements and herbal medicine is generally considered safe for most adults. However, there is a lack of information on possible adverse effects when used in combination with other herbs and supplements (NIH). Based on the clinical trials reviewed, doses ranging from 30 mg, and 2.5 g to 7.5 g daily have proved to be generally safe when taken for 1-3 months (Chao et al, 2009; Yang et al, 2011). A double-blind, randomized controlled clinical trial examining the effect of Astragalus on allergies reported few adverse effects using an 80 mg dose for six weeks (Matkovic et al, 2010). Additionally, a review of 22 studies, conducted in China, evaluated the effects of Astragalus, as a crude herb, extract, and as part of a combination of other extracts, on patients with chronic kidney disease. The results demonstrate that injections of Astragalus were generally safe with few reported adverse effects (Zhang et al, 2014). While Astragalus injection is permitted in mainland China, it is generally not approved for use elsewhere. There is no available research on long-term consumption.

Astragalus has the potential to interfere with drug metabolism through inhibition of CYP3A4, a liver enzyme key to the metabolism of many common drugs (<u>Or et al, 2012</u>; <u>Pao et al, 2012</u>) but it has not been evaluated beyond that for drug interactions in humans. There is a lack of research on the safety of Astragalus on humans during pregnancy and who are breast-feeding, and avoidance of use has been recommended. Additionally, strong caution should be taken regarding individuals with autoimmune diseases, as Astragalus has the potential to increase activity in the immune system, which can therefore aggravate symptoms (WebMD).

It should also be noted that some Astragalus species, which are not typically found in dietary supplements intended for humans, can be toxic. For example, certain species in the United States contain the neurotoxin swainsonine and have caused "locoweed" poisoning in animals, and other species contain potentially harmful levels of selenium (<u>NIH</u>).

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Dosing and Sources:

There is not enough available evidence to suggest that one form of Astragalus supplementation is superior to another. Dosing depends on the specified use, the source of the supplement, and various other factors (<u>Drugs.com</u>). Astragalus root extract supplements are distributed by various manufacturers and are available in capsules and tablets in doses ranging from 400mg-1000mg. Currently, no specific dose has been shown to promote cognitive health, and there is insufficient scientific evidence to establish an appropriate dose range for Astragalus (<u>WebMD</u>).

Future Studies: Currently there is an ongoing Phase 3 randomized controlled trial at LanZhou University in China, whose aim is to investigate the effect of different doses of Astragalus treatment on metabolic syndrome, which is a strong risk factor for dementia (NCT01847807).

For future research, it is important to ensure isolated treatment of Astragalus so as to optimize the probability that observed results are due to Astragalus exposure, although the efficacy and safety of combination treatments might also be tested.

Search Terms:

Pubmed: "Astragalus" + "Alzheimer's", "Astragalus" + "dementia", "Astragalus" + "cognitive", "Astragalus" + "aging", "Astragalus" + "neuroprotective", "Astragalus" + "longevity", "Astragalus" + "diabetes", "Astragalus" + "memory", "Astragalus" + "cardiovascular disease" + "Astragalus" + "kidney disease", "Astragalus" + "safety", "Astragalus" + "mortality", "Astragalus" + "side effects"

Clinicaltrials.gov: "Astragalus" + "aging", "Astragalus" + "dementia", "Astragalus" + "Alzheimer's", "Astragalus"

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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact <u>INFO@alzdiscovery.org</u>. To view our official ratings, visit <u>Cognitive Vitality's Rating page</u>.

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