



*Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, 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.*

## Sage

### Evidence Summary

Some evidence suggests that the herb Sage can provide acute cognitive benefits, though there are concerns over the standardization of treatment.

**Neuroprotective Benefit:** Clinical studies suggest sage might provide an acute cognitive benefit, but more evidence is needed to determine whether it can slow cognitive decline.

**Aging and related health concerns:** Studies in humans suggest that sage may have a positive effect on blood sugar and lipid profiles.

**Safety:** No reported adverse effects from any of the clinical trials at doses of up to 1332 mg. However, one clinical trial reported increases in blood pressure in 2 patients with existing hypertension.

**What is it?** Sage (or *Salvia officinalis* and *Salvia lavandulaefolia*) is an aromatic herb commonly found in Mediterranean cuisines and essential oils and has been used for many years in Chinese, Ayurvedic, Native American and European herbal medicines for cognitive health ([Tildesley 2005](#) and [Miroddi 2014](#)). Although native to the Mediterranean region, it is cultivated in several European countries and can be found worldwide.

**Neuroprotective Benefit:** Clinical studies suggest sage might provide an acute cognitive benefit, but more evidence is needed to determine whether it can slow cognitive decline.

Types of evidence:

- 1 systematic review of 6 RCTs
- 1 RCT in patients with mild-to-moderate dementia
- 1 single-blind, randomized, controlled trial using “aromatic” sage oil
- 1 open-label, clinical trial in patients with mild-to-moderate Alzheimer’s disease
- Several laboratory studies

Human research to suggest prevention of dementia or cognitive decline?

None

Human research to suggest benefits to patients with dementia

In a double-blind, randomized controlled trial, 39 patients with mild-to-moderate Alzheimer’s disease were given 60 drops of sage extract essential oil or placebo each day over the course of 4 months. By the end of the 4-month treatment period, patients who had received sage experienced statistically significant improvements in ADAS-cog and CDR-SB scores compared to baseline and the placebo group. However, the improvements in cognition seem very high for such a short treatment period, so future studies will have to confirm them ([Akhondzadeh 2003](#)). In a second open-label trial following 11 patients with probable Alzheimer’s disease, 6 weeks of sage essential oil 3 times per day (equivalent to approximately 2.5 g of herb per dose) was generally well-tolerated and resulted in an improvement in behavioral disturbances associated with dementia but no improvement in cognition ([Perry 2003](#)).

More recently, a [clinical trial tested sage](#) in 111 Alzheimer’s patients. Although completed two years ago, the results have not yet been published.

Human research to suggest benefits on cognition in healthy people

Six pilot clinical trials tested the acute effect of sage in healthy adults, aged 20 to 70 years of age, as either an essential oil or in dried capsule form ([Tildesley 2003](#), [Tildesley 2005](#), [Kennedy 2006](#), [Scholey](#)



[2008](#), [Kennedy 2011](#) and [Moss 2010](#)). All six studies demonstrated that patients who received sage treatment experienced some level of cognitive benefit, particularly in the areas of memory enhancement, mood and alertness. However, the systematic review ([Miroddi 2014](#)) harshly criticized the methods used in these trials: “Unfortunately, promising beneficial effects are debased by methodological issues, use of different herbal preparations (extracts, essential oil, use of raw material), lack of details on herbal products used.”

*Mechanisms of action for neuroprotection identified from laboratory and clinical research*

Sage is reported to have anti-oxidant, anti-inflammatory, estrogenic and pro-cholinergic activities ([Scholey 2008](#)). Because of the importance of cholinergic function in learning and memory, particularly short-term memory, the pro-cholinergic activity of sage is likely one mechanism of cognitive enhancement ([Terry 2003](#), [Akhondzadeh 2003](#) and [Kennedy 2011](#)). Sage essential oil has been shown to inhibit acetylcholinesterase (AChE) *in vitro* and *in vivo*, suggesting that it crosses the blood brain barrier ([Scholey 2008](#), [Perry 2002](#), [Perry 2003](#) and [Tildesley 2003](#)).

Other possible mechanisms of neuroprotection by sage may also exist. A preclinical study suggested that a component of sage, rosmarinic acid, and protected memory in mice that had been injected with Abeta 25-35 peptide by scavenging peroxynitrite (OONO<sup>-</sup>), an oxidant that leads to cell death by damaging DNA and proteins ([Alkam 2007](#)). Similarly, extracts of sage and rosmarinic acid prevented the neurotoxicity induced by Abeta42 in rat PC-12 cells by reducing reactive oxygen species and lipid peroxidation, reducing tau hyperphosphorylation, and by inhibiting caspase-3 activation and DNA fragmentation that can lead to cell apoptosis ([Iuvone 2006](#)).

*APOE4 interactions:*

None reported.

**Aging and related health concerns:** Studies in humans suggest that sage may have a positive effect on blood sugar and lipid profiles.

*Types of evidence:*

- 3 clinical trials in Type 2 diabetic and/or hyperlipidemic patients
- Several preclinical studies, a number in STZ-induced diabetic rodents

#### *Details:*

Sage is reputed not only for its neuroprotective properties, but also for antioxidant, anti-inflammatory, anti-hyperglycemic, anti-hyperlipidemic and estrogenic activity, some of which could play a role in delaying the aging process ([Perry 2003](#), [Kianbakht 2013](#)). In three clinical trials in diabetic, hyperlipidemic or healthy participants, consumption of sage (500mg-1500mg sage/day) over 1-3 months was associated with significant decreases blood glucose and improvements in lipid profiles. In a small pilot study, sage increased activities of superoxide dismutase (SOD) and catalase (CAT) antioxidant enzymes and increased levels of Hsp70 ([Sa 2009](#), [Kianbakht 2011](#) and [Kianbakht 2013](#)).

In addition, one recent study in STZ-induced diabetic rats found that supplementing with 600-800 mg of sage extract for 30 days, after the onset of diabetes, alleviated the negative impact of diabetes on learning and memory, reduced hyperglycemia, reduced levels of malondialdehyde (a measure of lipid peroxidation), and increased activities of SOD and CAT enzymes ([Hasanein 2016](#)). Combined with the observations of no adverse effects in the clinical trials, these results suggest that sage consumption might be beneficial for aging-related conditions such as diabetes and cardiovascular disease. However, larger trials will have to confirm this.

**Safety:** No reported adverse effects from any of the clinical trials at doses of up to 1332 mg. However, one clinical trial reported increases in blood pressure in 2 patients with existing hypertension.

#### Types of evidence:

- Several short clinical studies

#### Details.

None of the clinical studies reported adverse effects of sage in doses of sage extract up to 1332 mg per day. Our analysis found that the longest duration of sage treatment in clinical trials was 4 months, therefore the safety and efficacy of long-term sage treatment requires further investigation. In addition, there is a lack of standardization in preparation of the extract between studies, so it is unclear what would be the proper dose ([Miroddi 2014](#)). However, it is a common herb that is widely used and sold in supplement stores.

#### **Sources and dosing:**

Sage is widely available as a leafy herb in grocery stores, and sage leaf extracts are also available from numerous sources online and in natural food stores. One company, Nexira, sells a powdered combination of *Salvia officinalis* and *Salvia lavandulaefolia* as “Cognivia™” for cognitive health,



recommending doses of 400-600 mg of the powder. The clinical studies involving sage and cognition typically found doses between 300 and 600 mg to be most effective for memory enhancement ([Miroddi 2014](#)).

#### **Research underway:**

There is currently one clinical trial in progress, studying the effects of sage on cognition, focused specifically on Alzheimer's disease patients. The results are pending.

#### **Search terms:**

Google, Google Scholar or Pubmed:

- Sage
- Salvia officinalis
- Salvia lavandulaefolia
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + cognition
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + Alzheimer's
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + cognitive impairment
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + dementia
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + MCI
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + diabetes
- Sage (or Salvia officinalis or Salvia lavandulaefolia) + cardiovascular disease

Clinicaltrials.gov

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- Sage (or Salvia officinalis or Salvia lavandulaefolia) + MCI



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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 [INFO@alzdiscovery.org](mailto:INFO@alzdiscovery.org). To view our official ratings, visit [Cognitive Vitality's Rating page](#).*