

*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.*

## Bacopa Monnieri

### Evidence Summary

Clinical evidence suggests benefit for cognitive ability. It has a long history of Ayurveda use and may help protect against age-related inflammation and oxidative stress damage.

**Neuroprotective Benefit:** Clinical trials suggest that bacopa is somewhat nootropic and laboratory studies suggest it may have anti-oxidant and anti-inflammatory properties.

**Aging and related health concerns:** Laboratory studies and a long history of use in Ayurveda suggest possible benefits including reduced inflammation, and protection from oxidative stress.

**Safety:** Clinical trials in healthy adults suggest that it is safe and well-tolerated. Longer term use, or use in people with diseases or health risks or other medications have not been studied, but its long-term use in Ayurveda has a good safety record.

**What is it?** Bacopa monnieri (referred to here as bacopa) is an herb with a long history of use in Indian Ayurveda traditional medicine. It is also called Brahmi, waterhyssop, herb of grace, thyme-leaved gratiola, and Indian pennywort although the term 'brahmi' can be misleading – it sometimes refers to very different plants like gotu kola. Ayurveda practitioners have claimed that bacopa can improve cognitive function, promote longevity, and help with a range of ailments including but not limited to anxiety, depression, chronic fatigue, insomnia, stomach ulcers, and asthma and bronchitis.

**Neuroprotective Benefit:** Clinical trials suggest that bacopa is somewhat nootropic and laboratory studies suggest it may have anti-oxidant and anti-inflammatory properties.

*Types of evidence:*

- 2 meta-analyses based on 6-9 RCTs of minimum 12-week duration in non-demented people
- 4 RCTs on acute effects (not in the meta-analyses)
- 2 RCTs of combo supplements in dementia patients (not in meta-analyses)
- 1 uncontrolled open-label study in dementia patients (not in meta-analyses)
- Numerous laboratory studies on possible mechanisms of action

*Prevention of dementia/cognitive aging (human research):* No human research is available on whether the use of bacopa protects against dementia. Studies in the laboratory suggest that bacopa has biological effects that might protect against brain aging and dementia, although we don't yet know if these biological effects will occur in humans (see mechanisms of action below).

Bacopa is widely claimed as a nootropic supplement that improves cognitive function in people whether or not they have an underlying disease that might be causing cognitive decline. Treatment for at least 3 months might be needed to see benefit ([Stough 2001](#))([Nathan 2001](#)) although immediate benefits have been seen on a handful of cognitive tests in a couple small trials ([Benson 2014](#), [Downey 2013](#)) from Australian researchers. In 6-9 trials that tested bacopa for 3 months or longer and were analyzed in meta-analyses ([Pase 2012](#), [Kongkeaw 2014](#)), most cognitive scores were unaffected but some benefits have been observed occasionally in tests on memory and attention. One of the trials that reported modest benefits tested elderly people with memory impairment (MMSE scores of 24+).

*Treatment of dementia or mild cognitive impairment (human research):* Bacopa has not been evaluated on its own in controlled trials as a treatment for patients with dementia. However, it has been tested in an uncontrolled study on bacopa and in a randomized controlled study on a combination of herbs that included bacopa.



Specifically, in an open-label and uncontrolled study from India, Alzheimer's patients showed improved cognitive scores and subjective improvements in quality-of-life, irritability, and insomnia during 6 months of treatment with 600 mg per day of a bacopa extract ([Goswami 2011](#)). In a randomized controlled trial also from India, treatment of Alzheimer's patients with a combination of 3 herb extracts including bacopa for 1 year reportedly improved some aspects of daily function, cognitive ability, and depression and reduced biochemical markers of inflammation and oxidative stress ([Sadhu 2014](#)). Similar benefits were also observed in that trial in healthy elderly participants ([Sadhu 2014](#)).

For patients with mild cognitive impairment, the evidence is also limited. One small trial reported that bacopa modestly improved scores on tests of attention and verbal memory when used for 3 months at 450 mg per day in elderly people with memory complaints but not dementia (Barbhaiya 2008, listed in [Kongkeaw 2014](#)).

*Mechanisms of action for neuroprotection:* Laboratory studies have identified several possible mechanisms of action by which bacopa could protect against dementia and cognitive aging. Whether these biological effects can occur in humans has not yet been tested although one trial reported that treatment with a combination of 3 herb extracts, which included bacopa, reduced biochemical markers of inflammation and oxidative stress ([Sadhu 2014](#)). Bacopa was shown to protect against oxidative stress or inflammation in rodent and *in vitro* studies (for example, [Priyanka 2013](#), [Singh 2012](#), [Dwivedi 2013](#), [Williams 2014](#)). The effects on oxidative stress may occur by activating Nrf2 via Keap1 expression, thereby upregulating glutathione and preserving cellular redox homeostasis (e.g. [Singh 2012](#), [Dwivedi 2013](#)). Bacopa reduced beta-amyloid levels in one study ([Holcolmb 2006](#)) and protected against cell death caused by beta-amyloid in another ([Limp 2008](#)). Bacopa treatment for three months was also reported in one study to protect against brain aging in rats as measured by lipofuscin accumulation, glutathione levels and glutathione reductase activity, and changes in some neurotransmitter levels ([Rastogi 2012](#)).

*APOE4 interactions:* No research is available on whether or not the effects of Bacopa differ in people with and without the APOE4 risk factor for Alzheimer's disease.

**Aging and related health concerns:** Laboratory studies and a long history of use in Ayurveda suggest possible benefits including reduced inflammation, and protection from oxidative stress.

*Types of evidence:*

- 1 RCT using bacopa in combination with 2 other herbs
- numerous laboratory studies suggesting anti-inflammatory and anti-oxidant benefits



- handful of laboratory studies hinting at potential benefit on cancer, arthritis or cardiovascular disease
- Only 1 lifespan study (in *C. elegans*)

In traditional Ayurveda, bacopa has been claimed to promote longevity and protect against various aspects of aging. The limited research done in either humans or laboratory models suggests it may have anti-inflammatory and anti-oxidant effects.

In one randomized trial tested Alzheimer's patients and healthy elderly, a combination of 3 herbs including bacopa taken for 1 year reportedly reduced biochemical markers of inflammation like homocysteine, CRP, TNF $\alpha$  and reduced markers of oxidative stress like decreased TBARS, glutathione peroxidase, and superoxide dismutase with increased glutathione GSH. The herb extracts used were bacopa (whole plant extract), hippophae rhamnoides (leaves & fruit), dioscorea bulbifera (bulbils) ([Sadhu 2014](#)).

A handful of laboratory studies support the idea that bacopa can protect against age-related oxidative stress and inflammation, possibly by activating Nrf2. In *C. elegans*, one study reported that an aqueous extract of bacopa could upregulate a stress-associated gene that can promote longevity during stress conditions (hsp-16.2) and increase lifespan during exposure to stress (thermal or oxidative stress) but not under standard laboratory conditions ([Phulara 2015](#)). In aged rats, bacopa treatment for 3 months led to a dose-dependent reduction of lipofuscin in the brain, a putative biomarker of aging through accumulated oxidation of fatty acids ([Rastogi 2012](#)). The study didn't evaluate lipofuscin build-up in other areas of the body although a separate mouse study reported less lipofuscin accumulation in the prostate ([Kalamade 2008](#)). Bacopa was also reported to protect against other biochemical markers of aging like pro-inflammatory cytokine levels and iNOS expression and protect against age-related changes to behavior like immobility during tail suspension (a model of depression) and total activity in a closed field ([Rastogi 2012](#)).

For specific age-related diseases, a couple laboratory studies hint at possible benefits to **arthritis** ([Vijayan 2011](#), [Viji 2010](#)) and **cancer** ([Peng 2010](#), [Janani 2010](#), [Kalamade 2008](#)) but the laboratory work is very preliminary, tends to rely on the oxidative or inflammatory pathways, and have never been tested in humans in a trial or observational study. The research is also very preliminary for **cardiovascular health** but bacopa was reported to reduce stress and/or salivary cortisol levels in one clinical trial ([Benson 2014](#)) and some isolated rodent studies suggest that it could reduce blood pressure ([Kamkaew 2011](#)), protect against high cholesterol ([Kamesh 2012](#)), or protect against the heart against ischemia-

reperfusion injury ([Mohanty 2010](#)), with increased heart muscle expression of antioxidants and heat-shock protein 72 in healthy rats ([Mohanty 2010](#)).

**Safety:** Clinical trials in healthy adults suggest that it is safe and well-tolerated. Longer term use, or use in people with diseases or health risks or other medications have not been studied, but its long-term use in Ayurveda has a good safety record.

*Types of evidence:*

- 1 meta-analysis of 9 RCTs of 12+ week duration
- biochemical data on bacopa accumulation of mercury and other metals

Bacopa has been used for centuries in traditional Indian medicine. In clinical trials, the use of Bacopa extracts for three months in healthy adults has been safe and well-tolerated with no serious adverse events but occasional gastrointestinal discomfort like nausea, increased stools or diarrhea, and abdominal cramps, as well as dry mouth or flu-like symptoms ([Kongkeaw 2014](#)). The extracts of bacopa used in these trials varied. The doses averaged at around 300 mg/day but ranged from 250 to 600 mg/day. In one trial, adverse events like heart palpitations, muscular fatigue, and the frequency of urination were more common in people given bacopa instead of placebo but the difference between the groups might have been due to chance (i.e. it was not significant) ([Stough 2001](#)). The safety of bacopa has generally not been researched in people with specific health risks or diseases or in people who take other medications. According to the US Pharmacopeia material safety data sheet, heart problems and thyroid problems might be exacerbated by bacopa and chronic use of bacopa may lead to hypersensitization ([usp.org](#)).

Bacopa might inhibit acetylcholinesterase and increased acetylcholine levels which means that people who are taking medications that affect those pathways (e.g. acetylcholinesterase inhibitors, cholinergic drugs, or anticholinergic drugs) might be at risk of either greater side effects or less benefit from their medications. One animal study also reported that bacopa might affect thyroid hormones levels so people who take thyroid medication should be particularly careful ([Kar 2002](#)). Other drug interactions with bacopa might occur but are generally unstudied and unknown.

Some sources of bacopa might be unsafe. The plant is known to accumulate toxins like mercury and has even been promoted as a tool to clean up the environment. So, depending on where the plant is grown, its extracts might contain mercury, lead, and other heavy metals ([Srikanth 2013](#)). In 2008, a random evaluation of Ayurveda supplements sold online concluded that roughly 20% of Ayurveda

supplements manufactured in either the United States or India contained lead, mercury, or arsenic ([Saper 2008](#)).

**Sources and dosing:** Bacopa preparations vary widely in their components and their preparation. All parts of the plant have been used in Ayurveda. The putative bioactive components are steroidal saponins called Bacoside A and Bacoside B and some standardized preparations of bacopa track the concentration of the bacosides. (Side note: one study suggested that the metabolic derivatives of the bacosides are more likely to affect the brain than bacosides, [Ramasamy 2015](#)).

In clinical trials, bacopa extracts have been used at doses between 250 mg to 600 mg/day, most commonly at 300 mg/day, but the type of extract has varied and the bacoside concentrations are not always reported. Alcohol extracts or alcohol + water extracts are common, but some trials have not reported how the extract was generated. Specific brand names that have been used in clinical trials include KeenMind, BacoMind, and MediHerb (table in [Kongkeaw 2014](#)).

**Future research:** A clinical trial in Australia is currently testing whether 300 mg/day of bacopa for 12 months might benefit healthy elderly people with outcomes that include cognitive, neuropsychological and mood scores, cardiovascular health, and biochemical measures of inflammation, oxidative stress, telomere length, and safety ([ANZCTR12611000487910](#)). As of June 2015, scientists were recruiting subjects for this year-long trial with results anticipated at the end of 2016.

#### Search terms:

Pubmed:

- Bacopa filtered by clinical trial, meta-analysis, and systematic review
- Bacopa plus the following terms in separate searches: amyloid, tau, cognitive, dementia, Alzheimer, oxidative, telomere, autophagy, mitochondria, lifespan, mortality, arthritis, cancer, cardiovascular, mercury.

Google: Ayurveda & bacopa; Ayurveda & bacopa & safety

Natural Medicines database: bacopa

Clinicaltrials.gov: bacopa

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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](#).*