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File: ■ Dementia
■ Brain Aging
■ Cognition

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RE: Evidence of Benefits from Herbal Preparations for Improving Cognition and Behavioral and Psychological Symptoms of Dementia in the Elderly

Perry E, Howes M-J R. Medicinal plants and dementia therapy: Herbal hopes for brain aging? *CNS Neurosci Ther*. 2011;17(6):683-698.

Dementia is associated with cognitive impairment, psychosis, agitation, anxiety, sleep disorders, and depression. Cognition involves memory as well as attention, executive function, and ability to form new memories. There are only a few pharmaceuticals used to treat cognitive impairment in dementia; namely, acetylcholinesterase (AChE) and/or butyrylcholinesterase (BuChE) inhibitors, and memantine (a glutamate N-methyl-D-aspartic acid [NMDA] receptor antagonist). Other drugs are used to treat the behavioral and psychological symptoms of dementia, such as antipsychotics, antidepressants, tranquillizers, and hypnotics. There are herbal remedies as well. The purpose of this review article was to discuss the plant extracts or components with promising human clinical evidence for treating dementia. The review does not include *all* herbal or phytochemical approaches. The study inclusion criteria were not explained. The authors provide top-line summaries of the herbal remedies, rather than in-depth study details.

Products derived from European plants for improving cognition
Galantamine, an AChE inhibitor, was originally derived from the snowdrop (*Galanthus* spp.), and is also present in bulbs of daffodil (*Narcissus* spp.) and other Amaryllidaceae plants not commonly used as medicines. It is now synthesized, and it is a licensed drug for the treatment of Alzheimer's disease (AD). Galantamine improves cognitive and behavioral symptoms and activities of daily living for people with AD. It is not effective for patients with mild cognitive impairment.

Sage (*Salvia officinalis*) or Spanish sage (*S. lavandulifolia*), traditionally used for memory problems, has in vitro and in vivo anti-AChE activity. Sage oil and extracts enhance memory in studies with young and elderly normal volunteers, and have been shown to have positive cognitive and behavioral effects in clinical studies of patients with AD.

Lemon balm (*Melissa officinalis*) has a reputation of being used to enhance and restore memory, produce calmness, and have antidepressant properties. In normal, young adult

volunteers, the dried leaf improved memory, calmness, and anxiety, and increased cognitive function under experimental stress. Lemon balm standardized extract has been shown to reduce cognitive impairment in patients with AD.

Lesser periwinkle (*Vinca minor*) aerial plant and its synthetic alkaloid vinpocetine have been shown to improve blood flow to the brain. Vinpocetine may be able to enhance cognition in patients with dementia, and enhanced memory and learning in patients with vascular dementia.

Herbal products derived from traditional Chinese medicine (TCM) that improve cognition
Ginkgo (*Ginkgo biloba*) leaf standardized extract has more published dementia-related research than any other plant species. Nonetheless, the evidence for enhancing cognition in AD is equivocal, according to the authors. Many reviews conclude that ginkgo improves cognition, including activities of daily living, selective attention, and executive function, while other reviews indicate these findings are inconsistent. There may be a risk of adverse interactions between ginkgo extract and antiplatelet or anticoagulant drugs.

Asian ginseng (*Panax ginseng*) has many in vivo and in vitro studies that demonstrate pertinent activity for improving dementia. However, according to the authors, though effective as an adjunct in treating AD, robust clinical studies are lacking. The authors state that Asian ginseng may be more effective for cognition before dementia has developed.

Huperzine A is a potent anti-AChE alkaloid from toothed clubmoss (*Huperzia serrata*) that also protects neurons from β-amyloid peptide associated with AD. According to the authors, clinical studies have only been conducted in China. A meta-analysis of these studies concluded that huperzine A improved cognition with minimal adverse events. The authors state that the results need to be verified.

Other traditional Chinese and Japanese herbal medicines
In TCM and traditional Japanese medicine (TJM), combinations of herbs are prescribed. This makes it difficult to interpret the efficacy of individual herbs. Several herbal combinations used in China or Japan show promise in preliminary research. The authors conclude that additional controlled trials are needed.

Herbal products for behavioral and psychological symptoms
For behavioral and psychological symptoms of dementia, the authors highlight certain herbs. They conclude that galantamine needs additional research in this arena because clinical trials did not include patients primarily affected by behavioral and psychological symptoms of dementia. There is substantial evidence in favor of ginkgo for treatment of behavioral and psychological symptoms of dementia, with studies showing ginkgo-related improvement in apathy/indifference, anxiety, irritability/lability, sleep/nighttime behavior and depression/dysphoria. The authors also highlight the TJM yokukansan, which is composed of cang-zhu atractylodes (*Atractylodes lancea*) rhizome, cnidium (*Cnidium* spp.) rhizome, *Uncaria* spp. twig/branch, angelica (*Angelica* spp.) root, bupleurum (*Bupleurum* spp.) root, licorice (*Glycyrrhiza* spp.) root, and poria (*Wolfiporia cocos* syn. *Poria cocos*) fungus. Yokukansan improved psychiatric symptoms, daily living, and sleep structure in small, open-label studies.

The following herbs have efficacy for behavioral and psychological symptoms in patients without dementia, and therefore should be evaluated in patients with dementia: St. John's wort (SJW; *Hypericum perforatum*) for depression and generalized anxiety, kava (*Piper methysticum*) for generalized anxiety, passionflower (*Passiflora incarnata*) for generalized anxiety, lavender (*Lavandula angustifolia*) for sleep, valerian (*Valeriana officinalis*) for sleep, and chamomile (*Matricaria recutita*) for sleep. Kava and SJW can have potential adverse effects. SJW can interfere with prescription medications; therefore, doctors who provide medication prescriptions should be informed of SJW use.

Agitation
The authors highlight some herbs that benefit agitation of dementia. Aromatherapy with lavender or lemon balm essential oils has been shown to be helpful. They also state that cannabis (*Cannabis sativa*) is frequently associated with psychosis, but the constituent cannabidiol (CBD), the constituent Δ^9-tetrahydrocannabinol (THC), and the synthetic cannabinoid receptor agonist nabilone, may help dementia-related agitation. Cannabis constituents may produce adverse side effects.

Botanical substances for dementia prevention/stabilization
The authors describe studies evaluating ginkgo, curcumin (from turmeric [*Curcuma longa*]), coffee, caffeine, red wine (from grapes [*Vitis vinifera*]), and nicotine that show some benefit for dementia prevention/stabilization, but the results are inconclusive. Increased consumption of fruits and vegetables, especially as part of a traditional Mediterranean diet including use of olive (*Olea europaea*) oil, is associated with a decreased risk of AD and other forms of dementia, though the degree of protection is uncertain.

Conclusion
The authors conclude that herbal remedies for dementia are promising. They explain that two of the four drugs licensed to treat cognitive treatments in dementia are derived from plants. However, it may be too simplistic to create drugs from single plant constituents; rather plants more than likely have numerous components that work together to produce a beneficial effect. The authors recommend that future research should focus on normal, elderly populations rather than populations with established dementia, since this reflects the traditional use and has a much wider potential application that could contribute to delaying dementia progression in the early stages. They also advocate for an accessible, authoritative database on herbal applications for dementia to provide practitioners and caregivers with a resource describing clinical evidence, specific herbal preparations, dosage, and quality sources, and addressing safety issues and potential for interactions.

—*Heather S. Oliff, PhD*

Peer Reviewer's Comments:
The benefits of galantamine and huperzine A are stronger than the other herbs. The evidence base for them is also more solid. In clinical practice, the natural *Galanthus* spp. extract is more effective and better tolerated than the synthetic galantamine.

The American Botanical Council has chosen not to reprint the original article.