



HerbClip™

Darren Early
Heather S Oliff, PhD

Shari Henson

Brenda Milot, ELS
Densie Webb, PhD

Executive Editor – Mark Blumenthal *Consulting Editors* - Steven Foster, Roberta Lee, MD, Allison Turner, MS

Managing Editor – Lori Glenn

Funding/Administration – Wayne Silverman, PhD *Production* – George Solis/Kathleen Coyne

FILE: ■ Alzheimer's Disease

HC050448-264

Date: September 15, 2004

RE: Potential of Botanical Derivatives for Use in Alzheimer's Disease

Abascal K, Yarnell E. Alzheimer's disease. Part 1 – biology and botanicals. *Altern Complement Ther.* 2004; February:18-21.

Abascal K, Yarnell E. Alzheimer's disease. Part 2 – A botanical treatment plan. *Altern Complement Ther.* 2004; April:67-72.

Alzheimer's disease (AD) is a progressive disease that causes memory loss, behavioral changes, disorientation, depression, and death. Increasing age is the greatest risk factor for the disease, and more than 22 million people worldwide are expected to suffer from AD by the year 2025. AD is characterized by two major changes in the brain: (1) senile plaques, which are an accumulation of nerve cell fragments and a protein called beta-amyloid and (2) neurofibrillary tangles, which are tangled fibers made up of the tau protein.

There is no cure for AD. Drugs that inhibit acetylcholinesterase, known as ACE inhibitors, are approved by the FDA for the treatment of AD. These drugs help maintain levels of acetylcholine, a neurotransmitter that plays a critical role in memory and mental function. While ACE inhibitors reduce some symptoms of AD, they do not halt or slow progression of the disease. They may be of limited benefit in early stages of the disease and cause serious side effects in some people. Another possible explanation for the pathology of AD is toxicity caused by accumulation of pro-oxidant substances in the brain. Research is now focusing on ways to provide the brain with suitable antioxidants to prevent or reduce the toxicity.

Certain herbs have been used in the treatment of AD because they contain natural inhibitors of acetylcholinesterase. However, these herbs may not be safer or more effective than their synthetic counterparts. The authors review four such herbs and herbal compounds.

The first plant-based compound is physostigmine, an alkaloid from the seed of the calabar bean (*Physostigma venenosum*). Although this compound is not considered safe enough for clinical use, some practitioners have had good results with it. The second herbal component is galantamine, an alkaloid found in snow drop (*Galanthus nivalis*), daffodil (*Narcissus tazetta*), and snowflake (*Leucojum aestivum*). Galantamine is one of the FDA approved drugs for use in AD, but effects of these herbs or whole herb extracts are unknown. All three herbs are considered to be moderately toxic. The third herbal alkaloid is huperzine A, isolated from huperzia (*Huperzia*

serrata). Clinical trials conducted in China indicate that huperzine A produces a prolonged increase in acetylcholine levels in the brain and has milder side effects than synthetic drugs. The fourth herbal compound is pilocarpine, an alkaloid isolated from the leaves of *Pernambuco jaborandi* (*Pilocarpus jaborandi*). Pilocarpine appears to have a different mechanism of action than the other alkaloids and has not been tested in clinical trials.

The authors conclude that herbs containing acetylcholinesterase inhibitors may be helpful for people in the later stages of AD, but that botanicals with antioxidant properties may be more effective in people in the early and middle stages of AD. Although antioxidant defense is a plausible therapy, the authors do not review the published literature on the use of antioxidants in AD and do not provide strong evidence to support this conclusion.

Part 2 of the article focuses on botanicals and AD. The paper describes a treatment plan for patients with AD, which includes ginkgo (*Ginkgo biloba*), turmeric (*Curcuma longa*), lemon balm (*Melissa officinalis*), Spanish sage (*Salvia lavendulifolia*), rosemary (*Rosmarinus officinalis*), and ashwagandha (*Withania somnifera*) along with a diet rich in fruits and vegetables, particularly blueberries (*Vaccinium pallidum*) and beets (*Beta vulgaris*), and vitamins C and E.

Ginkgo is popular in Europe as a treatment of the symptoms of early stage AD and vascular dementias (condition of diminished cognition caused by strokes). Meta-analyses and systematic reviews indicate that ginkgo may improve cognition and function in patients with AD. One study concluded that ginkgo might delay the progression of AD by nine months compared to placebo. However, a well-designed study of patients with age-associated memory impairment or very mild dementia failed to show a benefit of ginkgo. There are several large studies in progress that should be more definitive. Nearly all of the clinical studies use a concentrated ginkgo extract standardized to contain 24% ginkgo flavonoid glycosides, 6% terpene lactones, and no more than 5ppm ginkgolic acids. A typical dose was 120-240 mg/day, in divided doses. Ginkgo may be contraindicated in patients with bleeding disorders.

A majority of the evidence supporting the use of turmeric for the treatment of AD symptoms comes from animal studies. There are no clinical studies on turmeric's benefit for patients with AD. However, epidemiologic studies show a 4.4-fold lower incidence of AD in places such as India where turmeric is commonly part of the diet. A typical dose of tincture is 5 mL, 3 times/day.

Lemon balm leaves have historically been used as an anxiolytic and a support for memory. Two randomized, placebo-controlled, double-blind studies indicate that lemon balm may be of benefit for AD. In the studies lemon balm improved attention, cognitive function, and produced calmness. Lower doses appear to be more effective for AD. The typical adult dose is fresh-herb tincture 2-5 mL, 3 times/day.

Sage leaves are traditionally used to support memory. Spanish sage is naturally very low in thujone, a potentially toxic compound. Many studies evaluate Spanish sage in patients with AD because of the low thujone content. Since the herb will be used long-term to treat AD, a species with low thujone content is necessary. There are several small clinical trials in patients with mild-to-moderate AD, which show a positive effect on cognitive function. A typical dose is 3-5 mL, 3 times per day. Sage may worsen gastroesophageal reflux in some people and should be used with caution in people with seizure disorders.

Rosemary is used historically as a memory enhancer, but research on it is lacking. A typical adult dose of fresh-herb tincture used alone is 3-5 mL, 3 times/day.

Ashwagandha is an adaptogen—an agent that nonspecifically strengthens both the body and mind. Historically adaptogens have been used to offset the symptoms of aging. In vitro, ashwagandha stimulated neurite outgrowth in human brain cells, which may help damaged neuronal circuits in the demented brain. Human trials are lacking. Ashwagandha has a calming effect and is indicated for people with AD plus agitation. For patients that are more catatonic (immobile), a different adaptogen may be better suited.

The risk for developing dementia is lower in people with a diet rich in flavonoids. Therefore a diet rich in a variety of fruits and vegetables is an important part of AD treatment. Blueberries are on the top of the list of foods that contain constituents that enhance neuronal function. Beets are high in betaine, which helps lower homocysteine levels. Homocysteine may be the link between hypertension and dementia.

The authors recommend the following regimen for addressing AD: (1) Ginkgo leaf extract containing 24% ginkgo flavonoid glycosides, 6% terpene lactones, and no more than 5 ppm ginkgolic acids, 120-240 mg/day, in divided doses; (2) 10 mL of the formula with the following components in divided doses, 3 times/day: 30% turmeric tincture of fresh rhizome, 15% sage tincture of fresh leaf, 15% lemon balm tincture of fresh herb, 10% rosemary tincture of fresh herb, and 30% ashwagandha tincture of fresh root; (3) 400 IU vitamin E and 1000 mg vitamin C taken together, may be divided doses; (4) blueberries 1 cup/day as berries or juice; (5) beets ½ cup daily or every other day; and (6) regular physical and mental exercise.

The treatment plan described in this study is one example of how antioxidant herbs, adaptogens, diet, and exercise may be used in attempt to treat the symptoms of AD.

—Heather S. Oliff, Ph.D.

Enclosure: Referenced articles reprinted with permission from Mary Ann Liebert, Inc., 2 Madison Ave., Larchmont, NY 10438; Telephone (914)834-3100; Fax (914)834-3582; email: info@liebertpub.com.

The American Botanical Council provides this review as an educational service. By providing this service, ABC does not warrant that the data is accurate and correct, nor does distribution of the article constitute any endorsement of the information contained or of the views of the authors.

ABC does not authorize the copying or use of the original articles. Reproduction of the reviews is allowed on a limited basis for students, colleagues, employees and/or members. Other uses and distribution require prior approval from ABC.