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File: ■ Ginkgo (*Ginkgo biloba*)
■ Cognition
■ Dementia

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RE: Meta-analysis Shows Ginkgo to Be Effective for Mild Dementia

Wang B-S, Wang H, Song Y-Y, et al. Effectiveness of standardized *Ginkgo biloba* extract on cognitive symptoms of dementia with a six-month treatment: a bivariate random effect meta-analysis. *Pharmacopsychiatry*. May 2010;43(3):86-91.

Dementia is the age-related loss of thinking, reasoning, and remembering skills. There is currently no cure for dementia. Drugs may be helpful in delaying progression of the disease and improving some symptoms, but the benefits are modest, and adverse side effects can be serious. Herbs are being explored as an alternative to drug treatment for people with dementia. Ginkgo (*Ginkgo biloba*) leaf extract is the herb most commonly used to reduce the symptoms of dementia.

More than 30 published placebo-controlled trials have evaluated the effectiveness of ginkgo extract in people with dementia. Some studies found that ginkgo extract was no better than placebo in reducing cognitive symptoms, while other studies found ginkgo extract was superior to placebo. In these studies, the difference between ginkgo and placebo was due to both improvements in the ginkgo-treated group and natural progression of dementia in the untreated placebo group. Systematic reviews should take into account the widely variable cognitive decline that occurs in untreated dementia patients in placebo groups. This variation is called the baseline risk. Short term studies (< 6 months) are insufficient to measure effects and may also contribute to mixed results. The purpose of this article was to review trials with intervention periods of at least 6 months and to conduct a bivariate random effects meta-analysis of the impact of ginkgo extract in people with dementia, taking into account the influence of baseline risk.

The researchers searched PubMed and Cochrane Library databases to identify articles published in English from January 1980 to January 2009. The researchers also searched bibliographies of published trials and systematic review articles for additional trials. Criteria for inclusion were randomized, double-blind, placebo-controlled trials; diagnosis of dementia by prospective criteria; use of standardized ginkgo extract in any dose and dosage form; trial duration of at least 24 weeks, as long as outcomes were reported at 24 ± 2 weeks; clearly stated exclusion criteria; and use of at least one objective assessment of cognitive function as an outcome measure. The Alzheimer's Disease Assessment Scale-cognition (ADAS-cog) and/or

the Syndrom Kurz Test scale (SKT) were used as assessment tools in the trials. In this meta-analysis, SKT scores were converted to ADAS-cog scores in order to directly compare results.

The search identified six trials that met all the inclusion criteria. The duration of the intervention ranged from 22 to 52 weeks, and ginkgo doses ranged from 120 to 240 mg extract daily. The six trials involved a total of 1,838 participants, with 1,004 receiving ginkgo extract and 834 receiving placebo. Mean ages of the participants ranged from 64 to 78 years, and the mean proportion of female participants ranged from 52-72%. The average dementia severity was rated as mild at baseline, using average cognitive scores.

The bivariate random effects meta-analysis of data from the six trials showed a significant difference in ADAS-cog scores between ginkgo and placebo. The estimated difference of change in scores was -2.65 (95% confidence interval [CI], -4.53 to -0.76), which was a significant difference in favor of ginkgo extract. According to the authors, this meta-analysis demonstrated that ginkgo extract given for a period of six months significantly improved cognitive function in people with mild dementia.

The authors explain that progression of dementia is influenced by many factors and the rate of cognitive decline can vary considerably. Variations in baseline risk can lead to conflicting results in clinical trials of dementia treatments. Results of this meta-analysis suggest that direct comparisons of numerical differences between placebo and treatment groups, without taking into account the baseline risk, is not a reliable way to evaluate the efficacy of ginkgo extract in people with mild dementia.

The authors discuss some limitations of this study. Because only six trials met the inclusion criteria, the amount of data was relatively small. Conversion of SKT scores to ADAS-cog scores may not have accurately represented participants' actual ADAS-cog scores. The data came only from published clinical trials in the scientific literature, thereby creating the possibility of publication bias.

The authors did not explain why they chose to limit their analysis to clinical trials published in English. Excluding trials published in other languages reduced the amount of data available for the meta-analysis. It may also have introduced bias and limited the applicability of the results. Two high quality trials in progress at the time of publication will help bring more data to bear in understanding the benefits of ginkgo in the dementia patient.

—Heather S. Oliff, PhD

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