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FILE: ▪Ginkgo (*Ginkgo biloba*)
▪Dementia
▪Ginkgo Evaluation of Memory Study

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RE: Design Information for the Ginkgo Evaluation of Memory Study

DeKosky ST, Fitzpatrick A, Ives DG, et al. The Ginkgo Evaluation of Memory (GEM) study: Design and baseline data of a randomized trial of *Ginkgo biloba* extract in prevention of dementia. *Contemp Clin Trials*. Jun 2006;27(3):238-253.

A meta-analysis of ginkgo (*Ginkgo biloba*) clinical trials suggests that ginkgo is efficacious for the treatment of age-related or disease-caused memory decline. One theory as to the reason Alzheimer's disease (AD) occurs is that the disease is caused by significant oxidative stress. Another theory is the amyloid protein fragments that the brain normally produces accumulate in the brain of people with AD. The accumulated amyloid forms plaques that contribute to the degradation of neurons in the brain. Ginkgo has both antioxidant capabilities and anti-amyloid aggregation affects.

All neurodegenerative dementias have a transitional stage between normalcy and mild cognitive impairment and between mild cognitive impairment and dementia. The goal of a treatment would be to slow the transitional stages. There are only a few prevention trials underway because the trials are expensive, of long duration, and so far have not been successful. This paper describes the design of the Ginkgo Evaluation of Memory (GEM) study, which is currently underway with 3000 participants.

The study is a 5-year, randomized, double-blind, placebo-controlled trial of ginkgo for the prevention of dementia (especially AD). Participants (n = 3072) were recruited from 14603 candidates from the following four clinical sites: University of Pittsburgh/Pittsburgh, PA, University of California Davis/Sacramento, CA; The Johns Hopkins University/Hagerstown, MD; and Wake Forest University/Winston-Salem, MA, from September 2000 to June 2002. All participants were required to have a proxy who agreed to provide an independent assessment of the functional and cognitive abilities of the participant. Assessments are repeated every 6 months. Significant decline at any visit (defined by specific changes in cognitive screening scores) would lead to a repeat battery of detailed neuropsychological tests, neurological and medical evaluation, and MRI scan

of the brain; the final diagnosis of dementia would rest with a panel of experts. The National Center for Complementary and Alternative Medicine (NCCAM) identified manufacturers of ginkgo that might be interested in participating in the study. An independent panel of experts in botany, ethnobotany, pharmacognosy, pharmacology, and medicinal chemistry judged the product from Dr. Willmar Schwabe and Co. GmbH (Karlsruhe, Germany) to be the most acceptable for testing. The product, EGb761, is standardized to 24% ginkgo flavonol glycosides and 6% terpene trilactones, such that 120 mg of dried extract of ginkgo leaves contain 28.8 mg ginkgo-flavonol glycosides and 7.2 mg terpene trilactones. Participants received either placebo or 120 mg EGb761 twice daily. The primary outcome is the incidence rate of all-cause dementia, which was predicted to decrease following ginkgo administration. Secondary outcomes are the rate of cognitive and functional decline, incidence of cardiovascular and cerebrovascular events, and mortality. Participants will be assessed every 6 months for 8.5 years.

People taking cognitive enhancers or vitamin E were excluded. People with normal or mild cognitive impairment, as assessed via a battery of tests were enrolled. Participants are predominately Caucasian, both sexes are equally represented, and 65-70% of the population are between 75-79 years old. Eighty percent of the cohort described themselves as in good or very good health. Hypertension was present in 43% of the participants, and 50% were former smokers. Sixty percent of the participants were judged to have no deficits in cognition and 40% to have some impairment.

For the broadest application to the general population, participants were included regardless of their family history of dementia or if they had an increased genetic risk for dementia. The study is monitoring all hospitalizations, so the data from this study can also be used to analyze other health and disease outcomes. The data will become available over the next couple of years. It is encouraging that American researchers find the results of ginkgo trials, which are mostly conducted overseas, sufficiently compelling that they are persuaded to conduct such a rigorous study. The authors believe that this study will assess definitively the efficacy as well as the safety of ginkgo.

—Heather S. Oliff, PhD

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