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File: ■ Ginkgo (*Ginkgo biloba*)
■ Alzheimer's Disease
■ Dementia

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RE: High-dose Ginkgo Extract Shows Evidence of Benefit in Alzheimer's Disease

Janssen IM, Sturtz S, Skipka G, Zentner A, Garrido MV, Busse R. *Ginkgo biloba* in Alzheimer's disease: a systematic review. *Wien Med Wochenschr*. 2010;160(21-22):539-546.

Alzheimer's disease (AD) is the most common form of dementia, accounting for 50-70%. There is no cure, and symptoms get progressively worse. Symptom management is the goal of current therapies. The purpose of this systematic review was to evaluate the beneficial and harmful effects of long-term ginkgo (*Ginkgo biloba*) leaf extract treatment in patients with AD. The review was commissioned by the German Institute for Quality and Efficiency in Health Care.

The following databases were searched: MEDLINE (1966 to January 2010), EMBASE (1980 to January 2010), The Cochrane Library (Clinical Trials, January 2010), CHID via ADEAR (October 2005), The Cochrane Database of Systematic Reviews (Cochrane Reviews), the Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). Clinical trial registries and study result databases available on the Internet were screened, as were the websites of the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA). The search strategy included the terms dementia (especially AD) and ginkgo (including trade names). Unpublished data on EGb 761 (ginkgo standardized extract) was provided by Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe, Germany. The review included randomized, controlled studies with a follow-up of ≥ 16 weeks. The included studies had to evaluate at least 1 patient-relevant outcome measure (i.e., how patient feels or functions), and the patients had to have a diagnosis confirmed by standard diagnostic testing methods.

Six studies were located that fit all of the criteria. All were double-blind, parallel, multicenter, randomized controlled trials comparing EGb 761 with placebo. Three of the studies used only 240 mg/day ginkgo, and two used only 120 mg/day ginkgo, and one used both ginkgo doses in different subgroups. Treatment duration ranged from 22 to 26 weeks, with one study treating patients for 52 weeks but providing an interim 26-week analysis that was utilized for comparability. The methodological quality of all studies was

rated good to excellent. Cognition was the primary endpoint for all studies, and all studies assessed Activities of Daily Living (ADL). Despite these similarities, statistical testing indicates that the studies were highly heterogeneous; having differences in quality, duration of treatment, dose, inclusion/exclusion criteria, etc. This prevented the data from being pooled. Overall, methodological quality was good.

When considering the 4 high-dose studies, ginkgo was favored for the ADL and cognition outcomes. Three studies evaluated general symptoms, and the two with high doses of ginkgo had a positive effect. Two studies evaluated quality of life; one using 120 mg/day showed no significant benefit with ginkgo whereas the other 240 mg/day study showed a benefit. When evaluating safety, there was no evidence of a harmful effect associated with ginkgo; however, the ginkgo group had significantly more withdrawals due to adverse events (AEs) compared with placebo. Age and psychopathological symptoms modified outcomes, but the data were insufficient to adequately interpret.

The authors conclude that the high dose of ginkgo can be beneficial in AD; however, the conclusion is based on very heterogeneous results. Therefore, no potential effect size could be estimated. Based on the inclusion criteria of the four high-dose studies, the benefit may only occur in patients with accompanying psychopathological symptoms. One problem was the substantial heterogeneity between studies that could not be attributed to a specific factor. The authors conclude that the results on AEs are inconsistent—there were no serious AEs; however, more ginkgo-treated patients discontinued the studies due to AEs.

Other reviews have different conclusions. The authors point out that those other reviews, for example The Cochrane Review, had different inclusion and exclusion criteria, so the reviews cannot be compared. The authors state that, "Although this assessment found beneficial effects of ginkgo for AD patients, a clear recommendation for the use of ginkgo cannot be given" because effect size could not be calculated. Long-term studies comparing ginkgo with other anti-dementia drugs are needed, as are studies of subgroups of patients with AD.

—Heather S. Oliff, PhD

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