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File: ■ Ginkgo (*Ginkgo biloba*, Ginkgoaceae)
■ EGb 761®
■ Dementia
■ Systematic Review/Meta-analysis

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RE: Meta-analysis Demonstrates Safety and Efficacy of Defined Ginkgo Extract EGb 761® for Treating Dementia in the Elderly

Gauthier S, Schlaefke S. Efficacy and tolerability of *Ginkgo biloba* extract EGb 761® in dementia: a systematic review and meta-analysis of randomized placebo-controlled trials. *Clin Interv Aging*. November 28, 2014;9:2065-2077.

Many older adults suffer from Alzheimer's disease (AD) and cerebrovascular disease. The leading clinically-tested proprietary ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaf extract EGb 761® has shown a variety of mechanisms related to treating AD in vivo, including repairing mitochondrial function, modulating neuroplasticity, and increasing dopamine concentrations in only frontal brain areas.

EGb 761 is an acetonic (60% per weight) dry extract of ginkgo leaves standardized to contain 22-27% ginkgo flavonglycosides, 5-7% terpene lactones (2.8-3.4% ginkgolides A, B, and C, and 2.6-3.2% bilobalide), and less than 5 ppm ginkgolic acids. It is produced by Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe, Germany.

Processing methods and bioactive compound content are integral to establishing efficacy and safety in botanicals and may greatly differ among products. This systematic review and meta-analysis investigates clinical trials using the standardized product EGb 761 for the treatment of AD and/or vascular dementia (VaD). The statistical analysis used in this study was funded by Schwabe; one of the authors (Schlaefke) is an employee of the company.

This study searched the databases PubMed (to December 2012), EMBASE (2006-2011), and PASCAL (to December 2011) using the search terms "gingk*," "ginkg*," "clinical trial," "clinical*," "trial," "randomized," "gingko," "ginkgo," "human/ct," "homme/ctfr," "clinical study," "double blind procedure," and "py>2005." Included clinical trials were randomized, placebo-controlled, and double-blind, with a duration of 20 weeks or more. The included trials used EGb 761 for the treatment of AD, VaD, or a combination of the two conditions, according to diagnostic requirements from a variety of internationally recognized sources of criteria. Also, trials must have used two of the three following outcome measures: cognition, activities of daily living (ADL), and clinical global impression. Trials with patients having other mental deficiencies or that incorporated EGb 761 in conjunction with cholinesterase inhibiting drugs (e.g., donepezil [Aricept®] and tacrine [Cognex®]) were excluded.

This study located 15 randomized, placebo-controlled, clinical trials of EGb 761; of these, eight were excluded due to failure to meet inclusion criteria listed above. Patients from the seven included trials took 120 mg (two trials) or 240 mg (six trials) of EGb 761 for 22-26 weeks (one trial tested both dosages). The Jadad Scale, used to evaluate the trial quality (1 to 5, with 5 indicating the highest trial robustness), indicated "appropriate" quality with scores of 3 for two trials and of 5 for five trials. From the trials, 2,625 patients were evaluated, with 1,396 taking EGb 761 and 1,229 taking placebo. Females within studies made up between 50-86% of patients, and the age range of patients was from 63-79 years. Physical metrics such as height, weight, body mass index, and cognitive metrics were not different at baseline between treatment and placebo groups.

The seven included trials used two different but overlapping validated cognitive assessment tools. Five of the trials reported significant beneficial effects on cognition of those taking EGb 761 as compared to those in the placebo group (P=0.03). This was found to be dose dependent, and those taking 240 mg of EGb 761 had significantly better cognitive performance than those in the placebo group (P=0.04). ADL was measured by four different scales. Those taking EGb 761 scored significantly better as compared to those in the placebo group (P<0.001), and those taking 240 mg had a significantly higher ADL "improvement" than those in the placebo group (P=0.001).

Also, in clinical global impression assessments using three different rating scales, those taking EGb 761 rated significantly better than those taking the placebo (P=0.01); this was also observed in those taking 240 mg of EGb 761 as compared to those in the placebo group (P=0.007). In general, the odds ratio for cognitive improvement in those taking EGb 761 as compared to placebo was 2.48 (95% confidence intervals [CI], 1.17, 5.28, P=0.02). The odds ratio for improvement in clinical global impression for EGb 761 treatment as compared to placebo was 3.18 (95% CI, 1.78, 5.67, P<0.0001).

In two of the studies, patients with adverse events (AEs) were "slightly" more numerous in those taking EGb 761 than those taking the placebo; however, in the other five trials, those with AEs were equally distributed between groups. The relative risk (RR) ratio for AEs with EGb 761 was 0.96 (95% CI, 0.90, 1.01). Likewise, serious AEs were comparable in all trials across the treatment groups. In both treatment and placebo groups, AEs included headache, dizziness, hypertension, tinnitus, angina pectoris, and respiratory tract infection. The AEs causing early termination of patient participation in either group were symptoms typical of dementia, including agitation, anxiety, insomnia, or unspecific symptoms such as constipation, nausea, headache, and dizziness.

Overall, the results of this meta-analysis suggest that 240 mg daily intake of EGb 761 is effective in improving cognition, ADL, and clinical global impression in those suffering from AD and/or VaD, with minimal adverse side effects. This phytomedicinal formulation may be a useful adjuvant therapy in those suffering from cognitive decline.

—Amy C. Keller, PhD

Referenced article can be accessed at http://www.dovepress.com/efficacy-and-tolerability-of-ginkgo-biloba-extract-egb-761reg-in-demen-peer-reviewed-article-CIA.