

# Review: *Ginkgo biloba* extract improves cognitive function in mild to moderate Alzheimer's disease

Oken BS, Storzbach DM, Kaye JA. *The efficacy of Ginkgo biloba on cognitive function in Alzheimer disease. Arch Neurol* 1998 Nov;55:1409-15.

## Question

In patients with Alzheimer's disease (AD), is *Ginkgo biloba* extract effective for improving cognitive function?

## Data sources

Studies in all languages were identified by searching Medline, Embase/Excerpta Medica, and PsycLIT using the search terms ginkgo, gingko [sic], Tanakan, Tebonin, Rokan, Ginkoba, and EGb 761. Reference lists of relevant studies, textbooks, and a Cochrane Collaboration review were also used.

## Study selection

Studies were selected if AD was diagnosed by using explicit criteria; exclusion criteria were clearly stated; standardised ginkgo extract (24% or 25% ginkgo-flavone glycosides and 6% terpenoids) in any stated dose and route of administration was used for  $\geq 2$  months; the study was randomised, double blind, and placebo controlled; and  $\geq 1$  outcome measure was an objective assessment of cognitive function. Studies were excluded if they did not state exclusion criteria for depression, other neurological disease, or medication that acted on the central nervous system.

## Data extraction

Data were extracted on patient diagnoses, number of patients analysed, study duration, dropout rate, *G biloba* extract daily dose and formulation, cognitive outcome measures, other outcome measures, and results.

## Main results

5 studies met the inclusion criteria, and 4 studies provided analysable data for 424 patients with mild to moderate AD (range

40 to 207 patients/study). Study duration was 12 weeks in 2 studies, 24 weeks in 1 study, and 26 weeks in 1 study (mean 19 wks). *G biloba* doses were 120 mg/day in 2 studies and 240 mg/day in 2 studies. 2 studies used the Synrom-Kurztest (SKT), 1 study used choice reaction time in addition to the SKT, 1 study used the Alzheimer Disease Assessment Scale—Cognitive subtest, and 1 study used a 10 item battery (which included the Benton Visual Retention Test, Digit Symbol, word list recall, and reaction time) to measure cognitive function. The pooled result showed that *G biloba* extract was better than placebo for improving cognitive function ( $p < 0.001$ ) (table). No substantial adverse events occurred in patients in the *G biloba* extract group.

## Conclusion

In patients with mild to moderate Alzheimer's disease, *Ginkgo biloba* extract improves cognitive function.

### *Ginkgo biloba* extract v placebo in mild to moderate Alzheimer's disease

Outcome at mean follow up of 19 weeks	Weighted mean difference	Controls with a worse outcome than treated*
Cognitive function	0.41 (0.22 to 0.61)	66% (59 to 73)

\*The proportion of control patients with a worse outcome than the average treated patient; calculated from data in article.

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## Commentary

Extracts from the *G biloba* tree have been used for 5000 years in traditional Chinese medicine to treat pulmonary diseases such as asthma and bronchitis. Curiously, the tree was the only plant to survive the bombing of Hiroshima and Nagasaki.<sup>1</sup> Many French and German studies have reported on the efficacy of *G biloba* for treating cerebral insufficiency or neurasthenia; an array of symptoms including memory impairment, depressed mood, confusion, light headed sensation, fatigue, tinnitus, and dizziness; and lack of motivation.

The positive effect of *G biloba* on cognitive function in this review by Oken *et al* is not fully understood. The authors stressed that the 2 chemical components (flavonoid and terpenoid) of *G biloba* have, respectively, an antioxidant profile and an anti-platelet activating factor (PAF) activity. Both mechanisms could be involved in therapeutic effects in AD. It has been claimed that free radicals are responsible for oxidative and peroxidase neuronal damage as well as for the amyloid deposition in AD, which may be

counteracted by *G biloba*. The anti-PAF effect could counteract the pro-inflammatory effects and the extension of any vascular lesion derived by platelet activation, which are possible mechanisms in AD. If these are the underlying mechanisms involved in the beneficial effect of *G biloba*, the action should be limited to the early phases of the disease. Once the anatomical and morphological lesions are established with amyloid and neurofibrillary tangle deposition, no substance can stop the progression of symptoms. The authors did not report on the direct vascular effect of *G biloba* on the arteries and small vessels, which is the reason it is prescribed for intermittent claudication.<sup>2</sup> This may also explain the favourable effect of *G biloba* in AD if, as some believe, there is an overlapping vascular component in this otherwise primary dementia.

Of note, the benefit of *G biloba* in AD in this review is only slightly inferior to that shown in randomised controlled trials for acetylcholinesterase inhibitors, donepezil,<sup>3</sup>

and rivastigmine.<sup>4</sup> These drugs have a totally different mechanism of action because they increase one of the neurotransmitters.

The authors of the primary studies are to be commended for using rigorous evaluation based on randomised controlled trials to understand the efficacy of this old remedy. Future studies on drugs in AD should measure more relevant outcomes, such as functional ones, to better evaluate their efficacy. Meanwhile, *G biloba* is a possible new approach in AD.

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