

# Ginkgo biloba in the treatment of Alzheimer 's disease: A miracle cure?

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## Introduction

Alzheimer's disease (AD) is the most common dementia in the elderly. As the aged population grows, the incidence of AD will increase in the future. AD is a progressive neurodegenerative disorder that affects cognition and behaviour. Loss of cholinergic function, neuronal over-excitation and formation of amyloid plaques or neurofibrillary tangles are hypothesized to cause AD, but no single aetiology has been identified. Current treatments are based on the first two hypotheses using acetylcholinesterase (AChE) inhibitors and NMDA antagonists. Ginkgo biloba (GB) has been used in traditional Chinese medicine for centuries. Its leaf extract is claimed to be effective in AD. This study evaluated the literature evidence for the treatment of AD with GB.

## Methods

The potency of the standardized GB extract, EGb 761, in the treatment of AD was explored by a systematic evaluation of published literature. Evidence from both *in vitro* and *in vivo* studies was critically evaluated.

## Results

The standardized extract EGb 761 is obtained from GB dried leaves and consists primarily of flavone glycosides and terpene lactones. The flavonoid fraction is composed of quercetin, kaempferol and isorhamnetin glycosides; the terpenoid fraction of ginkgolides A, B, C, J and bilobalide<sup>1</sup>. Different constituents account for varying effects of the extract in AD.

The terpenoid fraction increases cerebral blood flow (CBF) and ginkgolide A and B act as platelet activating factor (PAF) antagonists. EGb 761 reduces iNOS and mRNA protein expression and thus NO release, although eNOS mediated NO production is increased by EGb 761, resulting in vasodilatation and increased CBF. The constituents responsible for NO production are not known.<sup>1, 2, 3</sup>

Antioxidative effects are displayed by the flavonoid fraction rather than the terpenoid fraction.<sup>4</sup>

EGb 761 has a positive effect on cholinergic transmission; the extract delays the decrease in acetylcholine receptor density in older rats.<sup>1</sup> No comparative trials with EGb 761 and anti-AChE drugs have been undertaken, but results of placebo controlled trials with EGb 761 (120 mg/day for 52 weeks in 309 patients) and donepezil (10 mg/day for 6-12 weeks in 319 patients) yielded similar results.<sup>5, 6, 7</sup>

Bilobalide increases GABA and prevents neuronal over excitation.<sup>1</sup> EGb 761 decreases neurofibrillary tangles by a seven-fold up-regulation of neuronal tyrosine/threonine phosphatase 1, an enzyme involved in formation/breakdown of neurofibrillary tangles, in the cortex of mice administered 36 mg/kg EGb 761 p.o. for four weeks.<sup>8</sup>

Significant memory and behavioural improvement was seen in mild to moderate AD patients in placebo controlled trials with EGb 761 (120 mg/day, p.o.)<sup>5</sup>, although no significant improvement was seen in healthy adults (120 mg /day, p.o.).<sup>9</sup> Use of different measures of efficacy may explain differences in study outcome.

## Discussion

Ginkgo biloba extract EGb761 may be useful in AD treatment but the mechanisms of its beneficial effects in AD remain to be elucidated. Direct comparative trials with EGb 761 and anti-AChE drugs may show potential benefits in comparison with current treatments. Further studies need to explore appropriate dosage regimens and interactions with herbal products and OTC or prescription drugs.

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Ginkgo biloba may be useful in the treatment of Alzheimer's disease, but further research is needed to identify the specific effects/mechanisms of the various constituents. Appropriate dosage regimens, potential long-term effects and interactions with other herbal products, OTC or prescription drugs need to be explored fully before it is declared a miracle cure in Alzheimer's disease.