

Does Ginkgo *Really* Increase the Risk of Bleeding?

by Michelle Morgan

That Ginkgo increases the risk of bleeding seems to be widely held belief, despite the absence of strong evidence.

Researchers from Germany recently conducted a meta-analysis of randomised clinical trials to assess the effect of standardised Ginkgo extracts compared with placebo on the risk of bleeding. The information was presented at the European Society of Clinical Pharmacy's 39th European Symposium on Clinical Pharmacy held in Lyon, France on October 21–23, 2010 and published in May issue of *Pharmacotherapy* (2011; **31**(5): 490-502). The research was supported by a grant from Dr. Willmar Schwabe Pharmaceuticals, a leading manufacturer of standardised Ginkgo extract.

This is the first time the most rigorous analysis of the data (a meta-analysis) has been conducted.

Eighteen placebo-controlled clinical trials to February 2009 were included, with data for 1985 patients or healthy volunteers. To be included, standardised Ginkgo extract needed to be orally administered for more than one week. Duration of treatment ranged from 1 to 32 weeks (median 12 weeks). The daily dose of standardised Ginkgo extract ranged from 80–480 mg (median 240 mg). In eight of the trials, EGb 761 (50:1 extract; standardised to contain 24% ginkgo flavone glycosides and 6% terpenoids (ginkgolides and bilobalide)) was administered at daily doses of 120-480 mg, equivalent to 6–24 g/day of dried leaf.

For four of the studies, unpublished data was made available to the authors. The effect of Ginkgo on the following parameters was investigated:

- blood flow (3 trials)
- blood viscosity (3 trials)
- platelet function (ADP-induced platelet aggregation; 3 trials)
- fibrinogen concentration (5 trials)
- activated partial thromboplastin time and prothrombin time (7 trials and 8 trials respectively)

Meta-Analysis Results

- There was a large range of effects for some parameters. (A smaller range would indicate more robust results.)
- Standardised Ginkgo extract did not increase blood flow compared with placebo in the three trials investigated.
- Standardised Ginkgo extract reduced blood viscosity, but had no effect on ADP-induced platelet aggregation, fibrinogen concentration, activated partial thromboplastin time or prothrombin time. (Blood viscosity is not a major risk factor for spontaneous bleeding events. Improvement in blood viscosity may be beneficial in conditions such as peripheral artery occlusive disease.)
- There was a reduction in activated partial thromboplastin time for subgroups receiving a high dose of Ginkgo extract (240 mg/day or more) and for studies including only patients (not healthy volunteers) – but both results were not clinically relevant.

The authors concluded that in comparison with placebo, standardised Ginkgo extract was not associated with a higher risk of bleeding.

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