P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

Mariann Garner-Wizard
Heather S Oliff, PhD
Densie Webb, PhD
Shari Henson
Marissa Oppel, MS
Brenda Milot, ELS
Cathleen Rapp, ND

Executive Editor – Mark Blumenthal
Managing Editor – Lori Glenn
Consulting Editors – Dennis Awang, PhD, Steven Foster, Roberta Lee, MD
Funding/Administration – Wayne Silverman, PhD
Production – George Solis

FILE: ▪Ginkgo (*Ginkgo biloba*)
▪Bleeding Risk
▪EGb 761

HC 020665-311

Date: August 31, 2006

RE: Database Evaluation Shows Ginkgo Extract EGb 761 Does Not Cause Risk of Bleeding

Gaus W, Westendorf J, Diebow R, Kieser M. Identification of adverse drug reactions by evaluation of a prescription database, demonstrated for "risk of bleeding". *Methods Inf Med*. 2005;44(5):697-703.

Rare adverse drug reactions are difficult to identify in most study designs. For example, controlled clinical trials and prospective studies often do not have a sample size that is large enough to detect rare adverse drug reactions. Cohort studies often do not include a control or reference cohort. Case reports of spontaneous bleeding associated with some ginkgo (*Ginkgo biloba*) products have raised concerns over its safety. The pre-clinical and clinical trial data that is currently available seem to indicate that these concerns are not warranted. However, the limitations of most studies on ginkgo have made it difficult to confirm if it is indeed associated with a rare increased risk of spontaneous bleeding.

Using the mediplus® database (IMS-Health, Frankfurt/Main, Germany), the authors of this evaluation calculated the relative risk of bleeding episodes associated with ginkgo and conventional antidementia drugs. The mediplus database is a prescription database that includes over five million outpatients and 75 million prescriptions from more than 1,000 medical practices in Germany. The authors used a version of mediplus that includes 320,644 patients observed between July 1, 1999 and June 30, 2002. This large sample size makes it much easier to detect rare adverse drug reactions. The authors focused on the following antidementia treatments: ginkgo special extract EGb 761® (Dr. Willmar Schwabe GmbH, Karlseruhe, Germany), cholinesterase inhibitors, glutamate modulators, and calcium antagonists. Bleeding risk associated with these treatments and possible interactions with anticoagulant and antiplatelet drugs were investigated. This was accomplished by determining the number of bleeding episodes per 100 years of observation for all 320,644 patients in mediplus. By determining the prevalence of bleeding when patients were treated with any type of medication, a baseline was established. This baseline was compared with the prevalence of bleeding episodes when patients were taking the antidementia drugs alone,

when the antidementia drugs were taken along with anticoagulants and antiplatelet drugs, and when patients took no medications.

The prevalence of bleeding for all the patients in mediplus, regardless of whether or not the patients were taking medication, is 2.79 bleeding episodes per 100 years of observation. The prevalence of bleeding while patients were taking any type of medication is 3.51 bleeding episodes per 100 years of observation, and it is 1.63 for times when patients were taking no medications. The cholinesterase inhibitors are associated with the highest risk of bleeding episodes: 1.44, while the ginkgo special extract EGb 761 is associated with a bleeding risk of less than one episode per 100 years of observation. The results indicate that ginkgo special extract EGb 761 does not cause increased risk of bleeding when taken alone. Similarly, the antidementia drugs studied did not raise the risk of bleeding episodes. In addition, when EGb 761was taken along with anticoagulant and antiplatelet drugs, the authors found no increased risk of bleeding episodes. Despite case reports associating ginkgo with an increased risk of bleeding, this observational cross-over study indicates that ginkgo does not cause an increased risk for bleeding and does not interact with anticoagulant and antiplatelet drugs. The authors propose that the observational cross-over design used in this evaluation is a useful tool for determining the prevalence of rare adverse drug reactions.

—Marissa Oppel, MS

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

The American Botanical Council provides this review as an educational service. By providing this service, ABC does not warrant that the data is accurate and correct, nor does distribution of the article constitute any endorsement of the information contained or of the views of the authors.

ABC does not authorize the copying or use of the original articles. Reproduction of the reviews is allowed on a limited basis for students, colleagues, employees and/or members. Other uses and distribution require prior approval from ABC.