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FILE: ■ Ginkgo (*Ginkgo biloba*)

■ **Pregnancy**

■ **Lactation**

HC 120363-330

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RE: Safety and Efficacy of Ginkgo During Pregnancy and Lactation

Dugoua J, Mills E, Perri D, Koren G. Safety and efficacy of ginkgo (*Ginkgo biloba*) during pregnancy and lactation. *Can J Clin Pharmacol*. Fall 2006:e277-e284; November 3, 2006.

Historically, ginkgo (*Ginkgo biloba*) has been used for circulatory disorders, respiratory diseases, urinary tract disorders, and as an antiparasitic. Over the last few years, ginkgo has become the top-selling herbal medicine in the United States.¹ Although its popularity in women's health is for stroke and dementia in the elderly, it is used by women of childbearing age for memory boosting, asthma, mountain sickness, varicose veins, or sometimes for idiopathic cyclic edema.² More recently, it has had a growing popularity in the treatment of sexual dysfunction secondary to the use of selective serotonin reuptake inhibitors,³ and the World Health Organization has recommended the use of ginkgo for Raynaud's disease.⁴ Scientists, clinicians, herbalists, and consumers disagree about the effectiveness and safety of ginkgo during pregnancy and lactation. The authors examine the safety of ginkgo use by pregnant and breastfeeding women by reporting the results of a systematic review of the literature on ginkgo's clinical use. This article is one in a series, with others focusing on the use of black cohosh (*Actaea racemosa* syn. *Cimicifuga racemosa*), St. John's wort (*Hypericum perforatum*), and echinacea (*Echinacea* spp.) during pregnancy and lactation.

Databases searched from inception to June 2005 included AMED, CINAHL, Cochrane CENTRAL, Cochrane Library, MedLine, Natural Database, and Natural Standard. The common and Latin names of the herb were used as keywords, along with pregnancy, lactation, and breastfeeding. The authors also searched the American Botanical Council's Complete German Commission E Monographs.⁵ The nature of the findings and the grade of evidence for efficacy were abstracted and compiled in a final report. The grades for evidence of efficacy and the levels of evidence for harm are presented in the article's accompanying tables. Also included are the herb's constituents, toxicology, pharmacology, and potential drug interactions.

Most of the beneficial therapeutic effects of ginkgo appear to be derived from the leaf. The authors report "very strong evidence" supporting the therapeutic use of ginkgo for intermittent claudication (peripheral vascular disease), dementia (including Alzheimer's disease), cerebrovascular insufficiency, and tinnitus. "Strong evidence" supports its use in age-associated memory impairment, memory enhancement in healthy individuals, altitude sickness, vertigo, and premenstrual syndrome. And, the authors found "good evidence" for ginkgo's use in macular degeneration.

The authors found some "very weak" scientific evidence from animal and in vitro studies that ginkgo leaf has antiplatelet activity, which may be of concern during labor as ginkgo use could prolong bleeding time. The antiplatelet activity is mainly contributed to ginkgolide B. According to recent investigations, this effect, which has been measured so far only in vitro, is of no relevance in vivo.⁶ Also, patients and clinicians should be aware of manufacturers using Good Manufacturing Practices when choosing ginkgo products – the authors cite a case series that reported the presence of colchicine in the placental blood of pregnant women who had taken ginkgo.* One toxicology compendium reported that roasted ginkgo seeds may be potentially safe if eaten as a food during pregnancy and lactation, while another compendium reported that raw seeds may be a concern if used medicinally during pregnancy and lactation. In the evidence-based medicine literature, however, roasted and raw ginkgo seeds were not reported as being either safe or contraindicated in pregnancy.

The authors found no documentation in the literature regarding the safe use of ginkgo during lactation.

The authors conclude that more rigorous and well-controlled research is needed on the use of ginkgo during pregnancy and lactation. "Clinicians and patients should also be concerned about the potential for interactions that may occur between ginkgo and numerous prescription medications, particularly anticoagulant and antiplatelet drugs. This issue has greater significance when the possibility for increased exposure or toxicity to the developing fetus might result from altered drug metabolism due to interaction," they say.

Recent clinical studies did neither show an interaction with anticoagulants and antiplatelet agents nor did they find an interaction potential with certain CYP 450 enzymes for high quality ginkgo extracts.^{7,8} However, the manufacturers of such extracts do not recommend the use of their extracts during pregnancy and lactation.

—Shari Henson

*The article referenced is Petty HR, Fernando M, Kindzelskii AL, et al. Identification of colchicine in placental blood from patients using herbal medicines. *Chem Res Toxicol.* 2001;14:1254-1258. Further research at the University of Illinois in Chicago (Li W, Fitzloff JF, Farnsworth NR, Fong HHS. Evaluation of commercial *Ginkgo biloba* dietary supplements for the presence of colchicine by high-performance liquid chromatography. *Phytomed.* 2002;9:442-446. See HC 120522.233.) determined that colchicine does not naturally occur in ginkgo nor did the researchers find it in the nine commercial ginkgo products they tested. The UIC researchers suggested that the ginkgo product reported to

contain colchicine may have been contaminated with the corms or seeds of autumn crocus (*Colchicum autumnale*) or some other plant in the Liliaceae family. As the Wayne State University researchers would not reveal the identity of the allegedly contaminated ginkgo product, it has also been suggested that the laboratory equipment might have been contaminated.

References

- ¹Blumenthal M. Market report. *HerbalGram*. 1000;No. 51:69.
- ²Sierpina VS, Wollschlaeger B, Blumenthal M. *Ginkgo biloba*. *American Family Physician*. 2003;68.
- ³Cohen AJ, Bartlik B. *Ginkgo biloba* for antidepressant-induced sexual dysfunction. *J Sex Marital Ther*. 1998;24.
- ⁴WHO. WHO monographs on selected medicinal plants. Vol. 1, Ch. 16. Geneva: Folium Ginkgo; 1999.
- ⁵Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, Rister RS, eds. Klein S, Rister RS, trans. *The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines*. Austin, TX: American Botanical Council; Boston: Integrative Medicine Communication; 1998.
- ⁶Koch E. Inhibition of platelet activating factor (PAF)-induced aggregation of human thrombocytes by ginkgolides: considerations on possible bleeding complications after oral intake of *Ginkgo biloba* extracts. *Phytomed*. 2005;12:10-16.
- ⁷Greenblatt D, von Moltke L, Luo Y, et al. *Ginkgo biloba* does not alter clearance of flurbiprofen, a cytochrome P450-2C9 substrate. *J Clin Pharmacol*. 2006;46:214-221.
- ⁸Halil M, Cankurtaran M, Yavuz B, et al. No alteration in the PFA-100 in vitro bleeding time induced by the *Ginkgo biloba* special extract, EGb 761, in elderly patients with mild cognitive impairment. *Blood Coagul Fibrinolysis*. 2005;16:349-353.

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