



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 January 2014
EMA/HMPC/321096/2012
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Ginkgo biloba* L., folium

Draft

The Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.

Ahlemeyer B, Selke D, Schaper C, Kllumpp S, Krieglstein J. Ginkgolic acids induce neuronal death and activate protein phosphatase type-2C. *European Journal of Pharmacology* 2001, 430(1): 1-7

Akiba S, Kawauchi T, Oka T, Hashizume T, Sato T. Inhibitory effect of the leaf extract of *Ginkgo biloba* L. on oxidative stress-induced platelet aggregation. *Biochemistry and Molecular Biology International* 1998, 46(6):1243-1248

Al-Yahya AA, Al-Majed AA, Al-Bekairi AM, Al-Shabanah OA, Qureshi S. Studies on the reproductive, cytological and biochemical toxicity of *Ginkgo biloba* in Swiss albino mice. *Journal of Ethnopharmacology* 2006, 107:222-228

Amin A, Mahmoud-Ghoneim D, Syam MI, Daoud S. Neural network assessment of herbal protection against chemotherapeutic-induced reproductive toxicity. *Theoretical Biology and Medical Modelling* 2012, 9:1

Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. *Jama* 2001, 286(2):208-216

Aruna D, Naidu MU. Pharmacodynamic interaction studies of *Ginkgo biloba* with cilostazol and clopidogrel in healthy human subjects. *British Journal of Clinical Pharmacology* 2007, 63(3):333-338

Ärzte Zeitung Wien 09.03.2009. Available at:

<http://www.aerztezeitung.de/medizin/krankheiten/herzkreislauf/article/536596/ass-erst-drei-tage-op-absetzen-genuegt.html>

Auguet M, DeFeudis FV, Clostre F. Effects of *Ginkgo biloba* on arterial smooth muscle responses to vasoactive stimuli. *General Pharmacology* 1982a, 13:169-171

Auguet M, DeFeudis FV, Clostre F, Deghenghi R. Effects of an extract of *Ginkgo biloba* on rabbit isolated aorta. *Gen Pharmac* 1982b, 13:225-230



- Bachinskaya N, Hoerr R, Ihl R. Alleviating neuropsychiatric symptoms in dementia: the effects of Ginkgo biloba extract EGb 761. Findings from a randomized controlled trial. *Neuropsychiatr Dis Treat* 2011, 7:209-215
- Bäurle P, Suter A, Wormstall H. Safety and effectiveness of a traditional Ginkgo fresh plant extract - Results from a clinical trial. *Forschende Komplementärmedizin* 2009, 16:156-161
- Baron-Ruppert G, Luepke NP. Evidence for toxic effects of alkylphenols from Ginkgo biloba in the hen's egg test (HET). *Phytomedicine* 2001, 8(2):133-138
- Benjamin J, Muir T, Briggs K, Pentland B. *Postgraduate Medical Journal* 2001, 77:112-113
- Bebbington A, Kulkarni R, Roberts P. Persistent bleeding after total hip arthroplasty caused by herbal self-medication. *The Journal of Arthroplasty* 2005, 20(1):125-126
- Bent S, Goldberg H, Padula A, Avins AL. Spontaneous bleeding associated with Ginkgo biloba. *Journal of General Internal Medicine* 2005, 20:657-661
- BfArM, as cited on page 111 in the AR "In Germany currently (June 20, 2012) over 400 adverse reactions reports in nearly all organ systems are labelled according to the Federal Institute for Drugs and Medical devices (BfArM) database for adverse events".
- Biber A. Pharmacokinetics of Ginkgo biloba Extracts. *Pharmacopsychiatry* 2003, 36 Suppl 1:S32-37
- Biggs ML, Sorkin BC, Nahin RL, Kuller LH, Fitzpatrick AL. Ginkgo biloba and risk of cancer: secondary analysis of the Ginkgo Evaluation of Memory (GEM) Study. *Pharmacoepidemiology and Drug Safety* 2010, 19:694-698
- Birks J, Evans JG. Ginkgo biloba for cognitive impairment and dementia (Review). *Cochrane Database of Systematic Reviews* 2009, Issue 2
- Blaschek W, Hilgenfeldt U, Holzgrabe U, Reichling J, Ruth P, Schulz V. HagerROM. Springer Medizin Verlag, Heidelberg 2011
- Blonk M, Colbers A, Poirters A, Schouwenberg B, Burger D. Effect of Ginkgo biloba on the pharmacokinetics of raltegravir in healthy volunteers. *Antimicrobial Agents and Chemotherapy* 2012, 56(10):5070-5075
- Bradley P in the British Herbal Compendium. Vol 2. British Herbal Medicine Association, 2006
- Brautigam MR, Blommaert FA, Verleye G, Castermans J, Jansen Steur EN, Kleijnen J. Treatment of age-related memory complaints with Ginkgo biloba extract: a randomized double blind placebo-controlled study. *Phytomedicine* 1998, 5(6):425-434
- Bressler R. Interactions between Ginkgo biloba and prescription medications. *Geriatrics* 2005, 60(4):30-33
- Brinkley TE et al.; for the Ginkgo Evaluation of Memory (GEM) Study Investigators. Effect of Ginkgo biloba on blood pressure and incidence of hypertension in elderly men and women. *American Journal of Hypertension* 2010, 23(5):528-533
- Brunello N, Racagni G, Clostre F, Drieu K, Braquet P. Effects of an extract of Ginkgo biloba on noradrenergic systems of rat cerebral cortex. *Pharmacological Research Communications* 1985, 17(11):1063-1072
- Cala S, Crismon ML, Baumgartner J. A survey of herbal use in children with attention-deficit-hyperactivity disorder or depression. *Pharmacotherapy* 2003, 23(2):222-230

- Chan P, Xia Q, Fu PP. Ginkgo biloba leave extract: Biological, medicinal, and toxicological effects. *Journal of Environmental Science and Health, Part C* 2007, 25:211-244
- Chan WH. Ginkgolides induce apoptosis and decrease cell numbers in mouse blastocysts. *Biochemical and Biophysical Research Communications* 2005, 338:1263–1267
- Chang TK, Chen J, Yeung EY. Effect of Ginkgo biloba extract on procarcinogen-bioactivating human CYP1 enzymes: identification of isorhamnetin, kaempferol, and quercetin as potent inhibitors of CYP1B1. *Toxicology and Applied Pharmacology* 2006, 213:18-26
- Chatterjee SS, Doelman CJ, Nöldner M, Biber A, Koch E. Influence of the Ginkgo extract EGb 761 on rat liver cytochrome P450 and steroid metabolism and excretion in rats and man. *Journal of Pharmacy and Pharmacology* 2005, 57:641-650
- Commission E (Germany) monograph. Ginkgo biloba leaf. *Bundesanzeiger* Nr. 133, 19 July 1994
- Commission E (Germany) monograph. Ginkgo biloba leaf extract. *Bundesanzeiger* Nr. 133, 19 Jul 1994
- Corrao S, Scaglione R, Calvo L, Licata G. Methodological matters on an Alzheimer's dementia trial: Is a double-blind randomized controlled study design sufficient to draw strong conclusions on treatment? Reply to Dr. Mazza and Colleagues. *European Journal of Neurology* 2007, 14:e11
- DeFeudis FV. Ginkgo biloba extract EGb 761: from chemistry to the clinic. Ullstein Medical, Wiesbaden 1998
- DeFeudis FV, Papadopoulos V, Drieu K. Ginkgo biloba extracts and cancer : a research area in its infancy. *Fundamental and Clinical Pharmacology* 2003, 17:405-417
- DeKosky ST et al.; for the Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for prevention of dementia: a randomized controlled trial. *JAMA* 2008, 300(19):2253-2262
- Dementia - Supporting people with dementia and their carers in health and social care. National Institute for Health and Clinical Excellence, 2012. Available at: <http://www.nice.org.uk/nicemedia/live/10998/30318/30318.pdf>. Accessed 16/12/2013
- Dodge HH, Zitzelberger T, Oken BS, Howieson D, Kaye J. A randomized placebo-controlled trial of Ginkgo biloba for the prevention of cognitive decline. *Neurology* 2008, 70:1809-1817
- Donfrancesco R, Ferrante L. Ginkgo biloba in dyslexia: A pilot study. *Phytomedicine* 2007, 14:367-370
- Drew S, Davies E. Effectiveness of Ginkgo biloba in treating tinnitus: double blind, placebo controlled trial. *British Medical Journal* 2001, 322:1-6
- Duche JC, Barre J, Guinot P, Duchier J, Cournot A, Tillement JP. Effect of Ginkgo biloba extract on microsomal enzyme induction. *International Journal of Clinical Pharmacology Research* 1989, 9(3):165-168
- Dugoua JJ, Mills E, Perri D, Koren G. Safety and efficacy of Ginkgo (Ginkgo biloba) during pregnancy and lactation. *The Canadian Journal of Clinical Pharmacology* 2006, 13(3):e277-e284
- Eckmann F. Hirnleistungsstörungen-Behandlung mit Ginkgo-biloba Extrakt. [Treatment of cerebral insufficiency with Ginkgo-biloba extract. Time of onset of the effect in a double-blind study involving 60 inpatients]. *Fortschritte der Medizin* 1990, 108(29):557-560
- Eimazoudy RH, Attia AA. Efficacy of Ginkgo biloba on vaginal estrous and ovarian histological alterations for evaluating anti-implantation and abortifacient potentials in albino female mice. *Birth Defects Research (Part B)* 2012, 95:444-459

- Elsabagh S, Hartley DE, Ali O, Williamson EM, File SE. Differential cognitive effects of Ginkgo biloba after acute and chronic treatment in healthy young volunteers. *Psychopharmacology* 2005, 179:437-446
- ESCOP Monographs 2nd ed. Ginkgo folium – Ginkgo leaf. European Scientific Cooperative on Phytotherapy, editor. Thieme, Stuttgart 2003, 178-210
- Esposito M, Carotenuto M. Ginkgolide B complex efficacy for brief prophylaxis of migraine in school-aged children: an open-label study. *Neurological Sciences* 2011, 32:79-81
- Fan L et al. Effect of Schisandra chinensis extract and Ginkgo biloba extract on the pharmacokinetics of talinolol in healthy volunteers. *Xenobiotica* 2009a, 39(3):249-254
- Fan L et al. Effects of Ginkgo biloba extract ingestion on the pharmacokinetics of talinolol in healthy Chinese volunteers. *Annals of Pharmacotherapy* 2009b, 43:944-949
- Fernandes ES, Pinto RM, de Paula Reis JE, de Oliveira Guerra M, Peters VM. Effects of Ginkgo biloba extract on the embryo-fetal development in Wistar rats. *Birth Defects Research (Part B)* 2010, 89(2):133-138
- Fessenden JM, Wittenborn W, Clarke L. Ginkgo biloba: A case report of herbal medicine and bleeding postoperatively from a laparoscopic cholecystectomy. *The American Surgeon* 2001, 67:33-35
- Floissac M, Chopin S. Ginkgo biloba extract is embryotoxic to chick embryos. *FASEB J Abst* 1999, 13(5):A1031
- Fong KC, Kinnear PE. Retrobulbar haemorrhage associated with chronic Ginkgo biloba ingestion. *Postgraduate Medical Journal* 2003, 79:531-532
- Fourtillan JB et al. [Pharmacokinetics of Bilobalide, Ginkgolide A and Ginkgolide B in healthy volunteers following oral and intravenous administrations of Ginkgo biloba extract (EGb 761)]. *Therapie* 1995, 50:137-144
- Galduróz JC, Antunes HK, Santos RF. Gender- and age-related variations in blood viscosity in normal volunteers: a study of the effects of extract of Allium sativum and Ginkgo biloba. *Phytomedicine* 2007, 14:447-451
- Gardner CD, Taylor-Piliae RE, Kiazand A, Nicholus J, Rigby AJ, Farquhar JW. Effect of Ginkgo biloba (EGb 761) on treadmill walking time among adults with peripheral artery disease: a randomized clinical trial. *J Cardiopulm Rehabil Prev* 2008, 28:258-265
- Gardner CD, Zehnder JL, Rigby AJ, Nicholus JR, Farquhar JW. Effect of Ginkgo biloba (EGb 761) and aspirin on platelet aggregation and platelet function analysis among older adults at risk of cardiovascular disease: a randomized clinical trial. *Blood Coagulation and Fibrinolysis* 2007, 18:787-793
- Gaudineau C, Beckerman R, Welbourn S, Auclair K. Inhibition of human P450 enzymes by multiple constituents of the Ginkgo biloba extract. *Biochemical and Biophysical Research Communications* 2004, 318:1072-1078
- Gertz HJ, Kiefer M. Review about Ginkgo biloba special extract EGb 761 (Ginkgo). *Current Pharmaceutical Design* 2004, 10(3):261-264
- Geßner B, Voelp A, Klasser M. Study of the long-term action of a Ginkgo biloba extract on vigilance and mental performance as determined by means of quantitative pharmaco-EEG and psychometric measurements. *Arzneimittelforschung* 1985, 35(9):1459-1465

- Getov I, Tzenova ATV, Ristoff M, Todorov T, Petrova G. Safety assessment of newly marketed herbal medicines – Methodological approach (Ginkgo biloba example in Bulgaria). *Journal of Herbal Pharmacotherapy* 2007, 7(3-4):239-257
- Gilbert GJ. Ginkgo biloba. *Neurology* 1997, 48:1137
- Granger AS. Ginkgo biloba precipitating epileptic seizures. *Age and Ageing* 2001, 30:523-525
- Grass-Kapanke B, Busmane A, Lasmanis A, Hoerr R, Kaschel R: Effects of Ginkgo Biloba Special Extract EGb 761® in Very Mild Cognitive Impairment (vMCI). *Neuroscience & Medicine* 2011, 2:48-56
- Greenblatt DJ et al. Ginkgo biloba does not alter clearance of flurbiprofen, a cytochrome P450-2C9 substrate. *Journal of Clinical Pharmacology* 2006, 46:214-221
- Guideline on medicinal products for the treatment of Alzheimer's disease and other dementias from Committee for medicinal products for human use (CHMP). Doc. Ref. CPMP/EWP/553/95 Rev. 1. European Medicines Agency, London 2009. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003562.pdf. Accessed 16/12/2013
- Guinot P, Caffrey E, Lambe R, Darragh A. Tanakan inhibits platelet-activating-factor-induced platelet aggregation in healthy male volunteers. *Haemostasis* 1989, 19:219-223
- Gurley BJ et al. Clinical assessment of effects of botanical supplementation on cytochrome P450 phenotypes in the elderly: St John's wort, garlic oil, Panax ginseng and Ginkgo biloba. *Drugs Aging* 2005, 22(6):525-539
- Haguenauer JP, Cantenot F, Koskas H, Pierart H. [Treatment of disturbances of equilibrium with Ginkgo biloba extract. A multicenter double-blind, drug vs. placebo study]. *Presse Médicale* 1986, 15(31):1569-1572
- Halama P, Bartsch G, Meng G. Hirnleistungsstörungen vaskulärer Genese. [Cerebrovascular Insufficiency – Placebo-controlled, randomised, double-blind trial on the effect of Ginkgo biloba-extract]. *Fortschritte der Medizin* 1988, 106(19):408-412
- Halil M 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 Coagulation and Fibrinolysis* 2005, 16:349-353
- Hamann KF. Ginkgo-Spezialextrakt bei Schwindel. Ein systematischer Review randomisierter, doppelblinder, placebokontrollierter klinischer Prüfungen. [Special ginkgo extract in cases of vertigo. A systematic review of randomised, double-blind and placebo controlled clinical examinations.] *HNO* 2007, 55:258-263
- Hauser D, Gayowski T, Singh N. Bleeding complications precipitated by unrecognized Ginkgo biloba use after liver transplantation. *Transplant International* 2002, 15:377-379
- Hecker H, Johannisson R, Koch E, Siegers CP. *In vitro* evaluation of the cytotoxic potential of alkylphenols from Ginkgo biloba L. *Toxicology* 2002, 177:167-177
- Heinen-Kammerer T et al. Versorgungssituation von Demenzkranken kann durch Ginkgo biloba verbessert werden. Ergebnisse einer Studie zur Versorgungsforschung hinsichtlich der Leistungsfähigkeit der Demenzkranken, der Lebensqualität der Pflegenden und der Gesamtkosten der Behandlung. [The situation of Patients with Dementia may be rectified by Ginkgo biloba. Results of a Health Services Research Study Concerning the Ability of Patients with Dementia, Quality of Life of the Nursing Family Members and Total treatment Costs.] *MMW Fortschritte der Medizin* 2005, 147:127-133

- Hellegouarch A, Baranès J, Clostre F, Drieu K, Braquet P, DeFeudis FV. Comparison of the contractile effects of an extract of *Ginkgo biloba* and some neurotransmitters on rabbit isolated vena cava. *General Pharmacy* 1985, 16(2):129-132
- Hellum BH, Nilsen OG. *In vitro* inhibition of CYP3A4 metabolism and P-glycoprotein-mediated transport by trade herbal products. *Basic & Clinical Pharmacology & Toxicology* 2008, 102:466-475
- Herrschaft H, Nacu A, Likhachev S, Sholomov I, Hoerr R, Schlaefke S. *Ginkgo biloba* extract EGb 761 in dementia with neuropsychiatric features: A randomised, placebo-controlled trial to confirm the efficacy and safety of a daily dose of 240 mg. *Journal of Psychiatric Research* 2012, 46:716-723
- Hilton MP, Stuart EL. *Ginkgo biloba* for tinnitus (Review). Cochrane Database of Systematic Reviews 2010, Issue 3
- Hofferberth B. Einfluss von *Ginkgo biloba*-Extrakt auf neurophysiologische und psychometrische Messergebnisse bei Patienten mit hirnorganischem Psychosyndrom. [Effect of *Ginkgo biloba* extract on neurophysiological and psychometric measurement results in patients with cerebro-organic syndrome/ a double-blind study versus placebo.] *Arzneimittelforschung* 1989, 39(8):918-922
- Hofferberth B. The efficacy of EGb 761 in patients with senile dementia of the Alzheimer type, a double-blind, placebo-controlled study on different levels of investigations. *Human Psychopharmacology* 1994, 9:215-222
- Holgers KM, Axelsson A, Pringle I. *Ginkgo biloba* extract for the treatment of tinnitus. *Audiology* 1994, 33:85-92
- Horsch S, Walther C. *Ginkgo biloba* special extract EGb 761 in the treatment of peripheral arterial occlusive disease (PAOD) - a review based on randomized, controlled studies. *Int J Clin Pharmacol Ther* 2004, 42(2):63-72
- Ihl R, Tribanek M, Bachinskaya N. Baseline neuropsychiatric symptoms are effect modifiers in *Ginkgo biloba* extract (EGb 761®) treatment of dementia with neuropsychiatric features. Retrospective data analyses of a randomized controlled trial. *Journal of Neurological Sciences* 2010b, 299:184-187
- Ihl R et al.; on behalf of the GOTADAY Study Group. Efficacy and safety of a once-daily formulation of *Ginkgo biloba* extract EGb 761 in dementia with neuropsychiatric features: a randomized controlled trial. *International Journal of Geriatric Psychiatry* 2010a. Available at: wileyonlinelibrary.com. doi: 10.1002/gps.2662
- Ihl R, Tribanek M, Bachinskaya N, for the GOTADAY Study Group. Efficacy and Tolerability of a Once Daily Formulation of *Ginkgo biloba* Extract EGb 761® in Alzheimer's disease and Vascular Dementia: Results from a Randomised Controlled Trial. *Pharmacopsychiatry* 2011, [Epub ahead of print]
- Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG). *Ginkgo* in Alzheimer's disease. IQWiG Reports - Commission No. A05-19B. Cologne: IQWiG, 2008
- Issing W, Klein P, Weiser M. The homeopathic preparation Vertigoheel versus *Ginkgo biloba* in the treatment of vertigo in an elderly population: a double-blinded, randomized, controlled clinical trial. *Journal of Alternative and Complementary Medicine* 2005, 11(1):155-160
- Jiang X, Blair EY, McLachlan AJ. Investigations of the effects of herbal medicines on warfarin response in healthy subjects: A population pharmacokinetic-pharmacodynamic modeling approach. *Journal of Clinical Pharmacology* 2006, 46:1370-1378
- Jiang X et al. Effect of *ginkgo* and *ginger* on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. *British Journal of Clinical Pharmacology* 2005, 59(4):425-432

Jung F, Mrowietz C, Kiesewetter H, Wenzel E. Effect of Ginkgo biloba on fluidity of blood and peripheral microcirculation in volunteers. *Arzneimittelforschung* 1990, 40(5):589-593

Kanowski S, Herrmann WM, Stephan K, Wierich W, Hörr R. Proof of efficacy of the *Ginkgo biloba* special extract EGb 761 in outpatients suffering from mild to moderate primary degenerative dementia of the Alzheimer type or multi-infarct dementia. *Pharmacopsychiatry* 1996, 29:47-56

Kanowski S, Herrmann WM, Stephan K, Wierich W, Hörr R. Proof of efficacy of the *Ginkgo biloba* special extract EGb 761 in outpatients suffering from mild to moderate primary degenerative dementia of the Alzheimer type or multi-infarct dementia. *Phytomedicine* 1997, 4(1):3-13

Kanowski S, Hoerr R. Ginkgo biloba extract EGb 761 in dementia: intent-to-treat analyses of a 24-week, multi-center, double-blind, placebo-controlled, randomized trial. *Pharmacopsychiatry* 2003, 36:297-303

Kaschel R. Ginkgo biloba: Specificity of neuropsychological improvement – A selective review in search of differential effects. *Human Psychopharmacology* 2009, 24:345-370

Kaschel R. Specific memory effects of Ginkgo biloba extract EGb 761 in middle-aged healthy volunteers. *Phytomedicine* 2011, 18(14):1202-1207. doi 10.1016/j.phymed.2011.06.021. Epub 2011 Jul 30.

Keheyang G, Dunn LA, Hall WL. Acute effects of Ginkgo biloba extract on vascular function and blood pressure. *Plant Foods Hum Nutr* 2011, 66(3):209-211

Kehr J, Yoshitake S, Ijiri S, Koch E, Nöldner M, Yoshitake T. Ginkgo biloba leaf extract (EGb 761®) and its specific acylated flavonol constituents increase dopamine and acetylcholine levels in the rat medial prefrontal cortex: possible implications for the cognitive enhancing properties of EGb 761®. *Int Psychogeriatr* 2012, 24 Suppl 1:S25-34

Kellermann AJ, Kloft C. Is there a risk of bleeding associated with standardised Ginkgo biloba extract therapy? A systematic review and meta-analysis. *Pharmacotherapy* 2011, 31(5):490-502

Kim BH et al. Influence of Ginkgo biloba extract on the pharmacodynamic effects and pharmacokinetic properties of ticlopidine: an open-label, randomized, two-period, two-treatment, two-sequence, single-dose crossover study in healthy Korean male volunteers. *Clin Ther* 2010, 32(2):380-390

Koch 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. *Phytomedicine* 2005, 12:10-16

Köhler S, Funk P, Kieser M. Influence of a 7-day treatment with Ginkgo biloba special extract EGb 761 on bleeding time and coagulation: a randomized, placebo-controlled, double-blind study in healthy volunteers. *Blood Coagul Fibrinolysis* 2004, 15(4):303-309

Korczyn AD. Comments on the article by Mazza et al. concerning Ginkgo biloba and donepezil: A comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study [5]. *European Journal of Neurology* 2007, 14:e9

Kressmann S, Biber A, Wonnemann M, Schug B, Blume HH, Mueller WE. Influence of pharmaceutical quality on the bioavailability of active components from Ginkgo biloba preparations. *Journal of pharmacy and pharmacology* 2002, 54:1507-1514

Kudolo GB, Wang W, Barrientos J, Elrod R, Blodgett J. The ingestion of Ginkgo biloba extract (EGb 761) inhibits arachidonic acid-mediated platelet aggregation and thromboxane B2 production in healthy volunteers. *Journal of Herbal Pharmacotherapy* 2004, 4(4):13-26

- Kudolo GB, Wang W, Javors M, Blodgett J. The effect of the ingestion of Ginkgo biloba extract (EGb 761) on the pharmacokinetics of metformin in non-diabetic and type 2 diabetic subjects-a double blind placebo-controlled, crossover study. *Clinical Nutrition* 2006, 25:606-616
- Kuller LH, Ives DG, Fitzpatrick AL, Carlson MC, Mercado C, Lopez OL, Burke GL, Furberg CD, DeKosky ST; Ginkgo Evaluation of Memory Study Investigators. Does Ginkgo biloba reduce the risk of cardiovascular events? *Circulation. Cardiovascular Quality and Outcomes* 2010, 3:41-47
- Kupiec T, Raj V. Fatal seizures due to potential herb-drug interactions with Ginkgo biloba. *Journal of Analytical Toxicology* 2005, 29:755-758
- Le Bars PL, Katz MM, Berman N, Itil TM, Freedman AM, Schatzberg AF; for the North American EGb Study Group. A placebo-controlled, double-blind, randomized trial of an extract of Ginkgo biloba for dementia. *JAMA* 1997, 278(16):1327-1332
- Lei HP et al. Effects of Ginkgo biloba extract on the pharmacokinetics of bupropion in healthy volunteers. *British Journal of Clinical Pharmacology* 2009a, 68(2):201-206
- Lei HP, Wang G, Wang LS, Ou-yang DS, Chen H, Li Q, Zhang W, Tan ZR, Fan L, He YJ, Zhou HH. Lack of effect of Ginkgo biloba on voriconazole pharmacokinetics in Chinese volunteers identified as CYP2C19 poor and extensive metabolizers. *Annals of Pharmacotherapy* 2009b, 43:726-731
- Leistner E, Drewke C. Ginkgo biloba and ginkgotoxin. *Journal of Natural Products* 2010, 73(1):86-92
- Letzel H, Schoop W. Ginkgo-biloba-Extrakt EGb 761 und Pentoxifyllin bei Claudicatio intermittens. Sekundäranalyse zur klinischen Wirksamkeit. *VASA* 1992, 21(4):403-410
- Li W, Trovero F, Cordier J, Wang Y, Drieu K, Papadopoulos V. Prenatal exposure of rats to Ginkgo biloba extract (EGb 761) increases neuronal survival/growth and alters gene expression in the developing fetal hippocampus. *Brain Research. Developmental Brain Research* 2003, 144(2):169-180
- Lin CC, Cheng WL, Hsu SH, Chang CM. The effects of Ginkgo biloba extracts on the memory and motor functions of rats with chronic cerebral insufficiency. *Neuropsychobiology* 2003, 47:47-51
- Liu ZH, Zeng S. Cytotoxicity of ginkgolic acid in HepG2 cells and primary rat hepatocytes. *Toxicology Letters* 2009, 187(3):131-136
- Lu WJ, Huang JD, Lai ML. The effects of ergoloid mesylates and ginkgo biloba on the pharmacokinetics of ticlopidine. *Journal of Clinical Pharmacology* 2006, 46:628-634
- Lüders S, Stöve S, Schrader J. Prävention der vaskulären Demenz. Evidenz und Praxis. [Prevention of vascular dementia. Evidence and practice.] *Internist* 2012, 53:223-231
- Mahadevan S, Park Y. Multifaceted therapeutic benefits of Ginkgo biloba L.: Chemistry, Efficacy Safety, and Uses. *JFS* 2008, 73(1):R14-R19
- Markowitz JS, Donovan JL, DeVane L, Sipkes L, Chavin KD. Multiple-dose administration of Ginkgo biloba did not affect cytochrome P-450 2D6 or 3A4 activity in normal volunteers. *Journal of Clinical Psychopharmacology* 2003, 23(6):576-581
- Matthews MK. Association of Ginkgo biloba with intracerebral hemorrhage. *Neurology* 1998, 50:1933-1934
- Mauro VF, Mauro LS, Kleshinski JF, Khuder SA, Wang Y, Erhardt PW. Impact of ginkgo biloba on the pharmacokinetics of digoxin. *American Journal of Therapeutics* 2003, 10(4):247-251

- Mazza M, Capuano A, Bria P, Mazza S. Ginkgo biloba and donepezil: a comparison in the treatment of Alzheimer's dementia in a randomized placebo-controlled double-blind study. *European Journal of Neurology* 2006, 13:981-985
- Mazza M, Capuano A, Bria P, Mazza S. Reply to Dr. Corrao and Colleagues [8]. *European Journal of Neurology* 2007, 14:e12
- Mazza M, Capuano A, Bria P, Mazza S. Reply to Dr. Korczyn [6]. *European Journal of Neurology* 2007, 14:e10
- McCarney R et al. Ginkgo biloba for mild to moderate dementia in a community setting: a pragmatic, randomised, parallel-group, double-blind, placebo-controlled trial. *International Journal of Geriatric Psychiatry* 2008, doi: 10.1002/gps.2055
- McKenna DJ, Jones K, Hughes K. Efficacy, safety, and use of Ginkgo biloba in clinical and preclinical applications. *Alternative therapies* 2001, 7(5):70-90
- Mehlsen J, Drabaek H, Wiinberg N, Winther K. Effects of a Ginkgo biloba extract on forearm haemodynamics in healthy volunteers. *Clinical Physiology & Functional Imaging* 2002, 22(6):375-378
- Meisel C, Johne A, Roots I. Fatal intracerebral mass bleeding associated with Ginkgo biloba and ibuprofen. *Atherosclerosis* 2003, 167:367
- Miller LG, Freeman B. Possible subdural hematoma associated with Ginkgo biloba. *Journal of Herbal Pharmacotherapy* 2002, 2(2):57-63
- Mohutsky MA, Anderson GD, Miller JW, Elmer GW. Ginkgo biloba: evaluation of CYP2C9 drug interactions in vitro and in vivo. *American Journal of Therapeutics* 2006, 13(1):24-31
- Moreau JP, Eck CR, Mc Cabe J, Skinner S. Absorption, distribution et élimination de l'extrait marqué de feuilles de Ginkgo biloba chez le rat. [Absorption, distribution and elimination of radiolabelled Ginkgo biloba leaves extract in the rat.] *La Presse Médicale* 1986, 15(31):1458-1461
- Morgenstern C, Biermann E. The efficacy of Ginkgo special extract EGb 761 in patients with tinnitus. *International Journal of Clinical Pharmacology and Therapeutics* 2002, 40(5):188-197
- Naccarato M, Yoong D, Gough K. A potential drug-herbal interaction between Ginkgo biloba and efavirenz. *Journal of the International Association of Physicians in AIDS Care* 2012, 11(2):98-100
- Napryeyenko O, Borzenko I, for the GINDEM-NP Study Group. Ginkgo biloba special extract in dementia with neuropsychiatric features. A randomised, placebo-controlled, double-blind clinical trial. *Arzneimittelforschung* 2007, 57(1):4-11
- Napryeyenko O, Sonnik G, Tartakovsky I. Efficacy and tolerability of Ginkgo biloba extract EGb 761 by type of dementia: analyses of a randomised controlled trial. *Journal of the Neurological Sciences* 2009, doi: 10.1016/j.jns.2009.02.353
- Nicolaï SPA, Kruidenier LM, Bendermacher BLW, Prins MH, Teijink JAW. Ginkgo biloba for intermittent claudication. *Cochrane Database of Systematic Reviews* 2009, Issue 2
- Norred CL, Finlayson CA. Hemorrhage after the preoperative use of complementary and alternative medicines. *AANA Journal* 2000, 68(3):217-220
- NTP technical report on the toxicology and carcinogenesis studies of Ginkgo biloba extract (CAS No. 90045-36-6) in F344/N rats and B6C3F1/N mice (gavage studies). National toxicology program, Research triangle park, North Carolina 2013

Oberpichler-Schwenk H. Überdosierung von Ginkgopräparaten? [Overdose with Ginkgo preparations?] *Medizinische Monatsschrift für Pharmazeuten* 1995, 18(4):100-101

Ohnishi N et al. Studies on interactions between functional foods or dietary supplements and medicines. I. Effects of Ginkgo biloba leaf extract on the pharmacokinetics of diltiazem in rats. *Biological & Pharmaceutical Bulletin* 2003, 26(9):1315-1320

Ondrizek RR, Chan PJ, Patton WC, King A. An alternative medicine study of herbal effects on the penetration of zona-free hamster oocytes and the integrity of sperm deoxyribonucleic acid. *Fertility and Sterility* 1999a, 71(3):517-522

Ondrizek RR, Chan PJ, Patton WC, King A. Inhibition of human sperm motility by specific herbs used in alternative medicine. *Journal of Assisted Reproduction and Genetics* 1999b, 16(2):87-91

Patterson CJ et al. The recognition, assessment and management of dementing disorders: conclusion from the Canadian Consensus Conference on Dementia. *Canadian Medical Association Journal* 1999, 160(12 Suppl):S1-S15

Peter H, Fisel J, Weisser W. Zur Pharmakologie der Wirkstoffe aus Ginkgo biloba. *Arzneimittel Forschung* 1966, 16(6):719-725

Pinto RM, Fernandes ES, Reis JE, Peters VM, Guerra MDE O. Intra-uterine growth retardation after prenatal administration of Ginkgo biloba to rats. *Reproductive Toxicology* 2007, 23:480-485

Pittler MH, Ernst E. Ginkgo Biloba extract for the treatment of intermittent claudication: A meta-analysis of randomized trials. *The American Journal of Medicine* 2000, 108:276-281

Rejali D, Sivakumar A, Balaji N. Ginkgo biloba does not benefit patients with tinnitus: a randomized placebo-controlled double-blind trial and meta-analysis of randomized trials. *Clinical Otolaryngology and Allied Sciences* 2004, 29:226-231

Robertson SM, Davey RT, Voell J, Formentini E, Alfaro RM, Penzak SR. Effect of Ginkgo biloba extract on lopinavir, midazolam and fexofenadine pharmacokinetics in healthy subjects. *Current Medical Research and Opinion* 2008, 24(2):591-599

Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of Ginkgo biloba extract. *N Engl J Med* 1997, 336(15):1108

Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic Ginkgo biloba ingestion. *Neurology* 1996, 46:1775-1776

Rudge MV, Damasceno DC, Volpato GT, Almeida FC, Calderon IM, Lemonica IP. Effect of Ginkgo biloba on the reproductive outcome and oxidative stress biomarkers of streptozotocin-induced diabetic rats. *Brazilian Journal of Medical Biological Research* 2007, 40(8):1095-1099

S3-Leitlinie "Demenzen". German association for psychiatry, psychotherapy and neurology (DGPPN) and the German association for neurology (DGN), Bonn 2009. Available at: <http://www.dgppn.de/documents/s3-leitlinie-demenz-kf.pdf>. Accessed: 16/12/2013

Salehi B et al. Ginkgo biloba for Attention-Deficit/Hyperactivity Disorder in children and adolescents: A double blind, randomized controlled trial. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 2010, 34:76-80

Salvador RL. Ginkgo. *CPJ* 1995, 39-41+52

- Santos RF, Galduróz JC, Barbieri A, Castiglioni ML, Ytaya LY, Bueno OF. Cognitive performance, SPECT, and blood viscosity in elderly non-demented people using Ginkgo biloba. *Pharmacopsychiatry* 2003, 36:127-133
- Schneider C, Bord C, Misse P, Arnaud B, Schmitt-Bernard CF. Hyphéma spontané provoqué par l'extrait de Ginkgo biloba. [Spontaneous hyphema caused by Ginkgo biloba extract.] *Journal Français d'ophtalmologie* 2002, 25(7):731-732
- Schneider LS, DeKosky ST, Farlow MR, Tariot PN, Hoerr R, Kieser M. A randomized, double-blind, placebo-controlled trial of two doses of Ginkgo biloba extract in dementia of the Alzheimer's type. *Current Alzheimer Research* 2005, 2(5):541-551
- Scottish Intercollegiate Guidelines Network, Management of patients with dementia. Edinburgh 2006. Available at: <http://www.sign.ac.uk/pdf/sign86.pdf>. Accessed: 16/12/2013
- Scripnikov A, Khomenko A, Napryeyenko O; for the GINDEM-NP Study Group. Effects of Ginkgo biloba extract EGb 761 on neuropsychiatric symptoms of dementia: findings from a randomised controlled trial. *Wiener medizinische Wochenschrift* 2007, 157(13-14):295-300
- Shiao NH, Chan WH. Injury effects of ginkgolide B on maturation of mouse oocytes, fertilization, and fetal development in vitro and in vivo. *Toxicology Letters* 2009, 188:63-69
- Smith PF, Zheng Y, Darlington CL. Ginkgo biloba extracts for tinnitus: More hype than hope? *Journal of Ethnopharmacology* 2005, 100:95-99
- Snitz BE et al.; for the Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for preventing cognitive decline in older adults: a randomized trial. *JAMA* 2009, 302(24):2663-2670
- Solomon PR, Michalczuk DE. Toward establishing guidelines for evaluating cognitive enhancement with complementary and alternative medicines. *Evaluation & the Health Professions* 2009, 32(4):370-392
- Szczurko O, Shear N, Taddio A, Boon H. Ginkgo biloba for the treatment of vitiligo vulgaris: an open label pilot clinical trial. *BMC Complementary and Alternative Medicine* 2011, 11(21):1-9
- Thomson GJ, Vohra RK, Carr MH, Walker MG. A clinical trial of Ginkgo biloba extract in patients with intermittent claudication. *International Angiology* 1990, 9(2):75-78
- Trick L, Boyle J, Hindmarch I. The effects of Ginkgo biloba extract (LI 1370) supplementation and discontinuation on activities of daily living and mood in free living older volunteers. *Phytotherapy Research* 2004, 18:531-537
- Uchida S et al. Effects of Ginkgo biloba extract on pharmacokinetics and pharmacodynamics of tolbutamide and midazolam in healthy volunteers. *J Clin Pharmacol* 2006, 46:1290-1298
- Usai S, Grazi L, Bussone G. Ginkgolide B as migraine preventive treatment in young age: results at 1-year follow-up. *Neurological Sciences* 2011, 32 (Suppl 1):S197-S199
- Vale S. Subarachnoid haemorrhage associated with Ginkgo biloba. *The Lancet* 1998, 352:63
- Van Beek TA. Ginkgo biloba. Harwood Academic Publishers, Amsterdam 2000
- Van Dongen M, van Rossum E, Kessels A, Sielhorst H, Knipschild P. Ginkgo for elderly people with dementia and age-associated memory impairment: a randomized clinical trial. *Journal of Clinical Epidemiology* 2003, 56:367-376
- Van Dongen MC, van Rossum E, Kessels AG, Sielhorst HJ, Knipschild PG. The efficacy of ginkgo for elderly people with dementia and age-associated memory impairment: new results of a randomized clinical trial. *Journal of the American Geriatrics Society* 2000, 48(10):1183-1194

Vellas B et al. Long-term use of standardised ginkgo biloba extract for the prevention of Alzheimer's disease (GuidAge): a randomised placebo-controlled trial. *Lancet Neurology* 2012, Sep 5 [Epub ahead of print]

Vilain B, DeFeudis FV, Clostre F. Effect of an extract of Ginkgo biloba on the isolated ileum of the guinea-pig. *General Pharmacology* 1982, 13:401-405

Von Boetticher A. Ginkgo biloba extract in the treatment of tinnitus: a systematic review. *Neuropsychiatric Disease and Treatment* 2011, 7:441-447

Von Moltke et al. Inhibition of human cytochrome P450 by components of Ginkgo biloba. *JPP* 2004, 56:1039-1044

Wang BS et al. Effectiveness of standardised ginkgo biloba extract on cognitive symptoms of dementia with a six-month treatment: A bivariate random effect meta-analysis. *Pharmacopsychiatry* 2010, 43:86-91

Wang J, Zhou S, Bronks R, Graham J, Myers S. Supervised exercise training combined with ginkgo biloba treatment for patients with peripheral arterial disease. *Clinical Rehabilitation* 2007, 21:579-586

Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN. Effects of Ginkgo biloba in dementia: systematic review and meta-analysis. *BMC Geriatrics* 2010, 10(14)

WHO monographs on selected medicinal plants. Vol. 1. Folium ginkgo. World Health Organization. Geneva 1999, 154-167

Winter JC, The effects of an extract of Ginkgo biloba, EGb 761, on cognitive behaviour and longevity in the rat. *Physiology and Behavior* 1998, 63(3):425-433

Woelkart K, Feizlmayr E, Dittrich P, Beubler E, Pinl F, Suter A, Bauer R. Pharmacokinetics of bilobalide, ginkgolide A and B after administration of three different Ginkgo biloba L. preparations in humans. *Phytotherapy Research* 2010, 24(3):445-450

Wójcicki J et al. Comparative pharmacokinetics and bioavailability of flavonoid glycosides of Ginkgo biloba after a single oral administration of three formulations to healthy volunteers. *Materia Medica Polona* 1995, 27(4):141-146

Wolf HR. Does Ginkgo biloba special extract EGb 761 provide additional effects on coagulation and bleeding when added to acetylsalicylic acid 500 mg daily? *Drugs R D* 2006, 7(3):163-172

Wu Y, Li S, Cui W, Zu X, Du J, Wang F. Ginkgo biloba extract improves coronary blood flow in healthy elderly adults: role of endothelium-dependent vasodilation. *Phytomedicine* 2008, 15:164-169

Wu Y, Li S, Cui W, Zu X, Wang F, Du J. Ginkgo biloba extract improves coronary blood flow in patients with coronary artery disease: role of endothelium-dependent vasodilation. *Planta Medica* 2007, 73:624-628

Yagmur E, Piatkowski A, Gröger A, Pallua N, Gressner AM, Kiefer P. Bleeding complication under Ginkgo biloba medication. *American Journal of Hematology* 2005, 79:343-345

Yancheva S, Ihl R, Nikolova G, Panayotov P, Schlaefke S, Hoerr R; GINDON Study Group. Ginkgo biloba extract EGb 761(R), donepezil or both combined in the treatment of Alzheimer's disease with neuropsychiatric features: a randomised, double-blind, exploratory trial. *Aging and Mental Health* 2009, 13(2):183-190

Yang Z, Li WJ, Huang T, Chen JM, Zhang X. Meta-analysis of Ginkgo biloba extract for the treatment of Alzheimer's disease. *Neural Regeneration Research* 2011, 6(15):1125-1129

- Yasui-Furukori N, Furukori H, Kaneda A, Kaneko S, Tateishi T. The effects of Ginkgo biloba extracts on the pharmacokinetics and pharmacodynamics of donepezil. *Journal of Clinical Pharmacology* 2004, 44: 538-542
- Yin OQ, Tomlinson B, Waye MM, Chow AH, Chow MS. Pharmacogenetics and herb-drug interactions: experience with Ginkgo biloba and omeprazole. *Pharmacogenetics* 2004, 14(12): 841-850
- Yoshikawa T, Naito Y, Kondo M. Ginkgo biloba leaf extract: Review of biological actions and clinical applications. *Antioxidants and Redox Signaling* 1999, 1(4):469-480
- Yoshioka M et al. Studies on interactions between functional foods or dietary supplements and medicines. III. Effects of ginkgo biloba leaf extract on the pharmacokinetics of nifedipine in rats. *Biological & Pharmaceutical Bulletin* 2004a, 27(12): 2042-2045
- Yoshioka M et al. Studies on interactions between functional foods or dietary supplements and medicines. IV. Effects of ginkgo biloba leaf extract on the pharmacokinetics and pharmacodynamics of nifedipine in healthy volunteers. *Biological & Pharmaceutical Bulletin* 2004b, 27(12): 2006-2009
- Zadayan G et al. Effect of Ginkgo biloba special extract EGb 761® on human cytochrome P450 activity: a cocktail interaction study in healthy volunteers. *European Journal of Clinical Pharmacology* 2011, doi: 10.1007/s00228-011-1174-5
- Zagermann-Muncke P. Wenn Arzneistoffe Transportproteine beeinflussen. *Pharmazeutische Zeitung online* 2006, 50
- Zehra U, Tahir M, Lone KP. Ginkgo biloba induced malformations in mice. *Journal of the College of Physicians and Surgeons Pakistan* 2010, 20(2):117-121
- Zuo Xia-Cong, Zhang Bi-Kui, Jia Su-Jie, Liu Shi-Kun, Zhou Ling-Yun, Jing Li, Jie Zhang, Ling-Ling Dai, Chen Ben-Mei, Yang Guo-Ping, Hong Yuan. Effects of Ginkgo biloba extracts on diazepam metabolism: a pharmacokinetic study in healthy Chinese male subjects. *European Journal of Clinical Pharmacology* 2010, 66: 503-509