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Committee on Herbal Medicinal Products (HMPC)

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

Final

**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, Kriegstein 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(2):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. *Journal of the American Medical Association* 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-guenegt.html>. Accessed 02/08/2014

Auguet M, DeFeudis FV, Clostre F. Effects of *Ginkgo biloba* on arterial smooth muscle responses to vasoactive stimuli. *General Pharmacology* 1982a, 13(2):169-171

Auguet M, DeFeudis FV, Clostre F, Deghenghi R. Effects of an extract of *Ginkgo biloba* on rabbit isolated aorta. *General Pharmacology* 1982b, 13(3):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. *Neuropsychiatric Disease and Treatment* 2011, 7:209-215

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

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(3):156-161

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

Benjamin J, Muir T, Briggs K, Pentland B. A case of cerebral haemorrhage – can *Ginkgo biloba* be implicated? *Postgraduate Medical Journal* 2001, 77(904):112-113

Bent S, Goldberg H, Padula A, Avins AL. Spontaneous bleeding associated with *Ginkgo biloba*. *Journal of General Internal Medicine* 2005, 20(7):657-661

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(7):694-698

Birks J, Grimley Evans J. *Ginkgo biloba* for cognitive impairment and dementia (Review). *Cochrane Database of Systematic Reviews* 2009, 1:CD003120

Blaschek W, Hilgenfeldt U, Holzgrabe U, Reichling J, Ruth P, Schulz V, editors. HagerROM 2011: Hagers Enzyklopädie der Arzneistoffe und Drogen. 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 PR, editor. British Herbal Compendium. Vol 2. British Herbal Medicine Association, Bournemouth 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, Lovato JF, Arnold AM, Furberg CD, Kuller LH, Burke GL, et al.. 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 PC, Xia Q, Fu PP. *Ginkgo biloba* leave extract: Biological, medicinal, and toxicological effects. *Journal of Environmental Science and Health, Part C* 2007, 25(3):211-244

Chan WH. Ginkgolides induce apoptosis and decrease cell numbers in mouse blastocysts. *Biochemical and Biophysical Research Communications* 2005, 338(2):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(1):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(5):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(9):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(4):405-417

DeKosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA, Ives DG, Saxton JA, et al. *Ginkgo biloba* for prevention of dementia: a randomized controlled trial. *Journal of the American Medical Association* 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(6):367-370

Drew S, Davies E. Effectiveness of *Ginkgo biloba* in treating tinnitus: double blind, placebo controlled trial. *British Medical Journal* 2001, 322(7278):73

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(6):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(2):437-446

ESCOP Monographs 2<sup>nd</sup> 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(1):79-81

Fan L, Mao XQ, Tao GY, Wang G, Jiang F, Chen Y, 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, Tao GY, Wang G, Chen Y, Zhang W, He YJ, et al. Effects of *Ginkgo biloba* extract ingestion on the pharmacokinetics of talinolol in healthy Chinese volunteers. *Annals of Pharmacotherapy* 2009b, 43(5):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(1):33-35

Floissac M, Chopin S. *Ginkgo biloba* extract is embryotoxic to chick embryos. *The Journal of the Federation of American Societies for Experimental Biology Suppl* 1999, 13(5):A1031

Fong KC, Kinnear PE. Retrobulbar haemorrhage associated with chronic *Ginkgo biloba* ingestion. *Postgraduate Medical Journal* 2003, 79(935):531-532

Fourtillan JB, Brisson AM, Girault J, Ingrand I, Decourt JP, Drieu K, et al. [Pharmacokinetic properties of Bilobalide, Ginkgolide A and Ginkgolide B in healthy subjects after intravenous and oral administration of *Ginkgo biloba* extract (EGb 761)]. *Therapie* 1995, 50(2):137-144 [French]

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(7-8):447-451

Gardner CD, Taylor-Piliae RE, Kiazzand 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. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2008, 28(4):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(8):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(4):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(4):1137

Granger AS. *Ginkgo biloba* precipitating epileptic seizures. *Age and Ageing* 2001, 30(6):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(1):48-56

Greenblatt DJ, von Moltke LL, Luo Y, Perloff ES, Horan KA, Bruce A, et al. *Ginkgo biloba* does not alter clearance of flurbiprofen, a cytochrome P450-2C9 substrate. *Journal of Clinical Pharmacology* 2006, 46(2):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](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(4):219-223

Gurley BJ, Gardner SF, Hubbard MA, Williams DK, Gentry WB, Cui Y, 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 equilibrium disorders with *Ginkgo biloba* extract. A multicenter double-blind drug vs. placebo study.] *Presse Médicale* 1986, 15(31):1569-1572 [French]

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, Cankurtaran M, Yavuz BB, Ozkayar N, Ulger Z, Dede DS, 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(5):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, 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(7):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(2-3):167-177

Heinen-Kammerer T, Motzkat K, Daniel D, Gertz HJ, Koller M, Lorenz W, 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 (Suppl 3):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(5):466-475

Herrschart 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(6):716-723

Hilton MP, Stuart EL. *Ginkgo biloba* for tinnitus (Review). Cochrane Database of Systematic Reviews 2010, 3:CD003852

Hitzenberger G. [The effect of *Ginkgo biloba* special extract.] *Wiener Medizinische Wochenschrift* 1992, 142(17):371-379 [German]

Hofferberth B. Einfluss von *Ginkgo biloba*-Extrakt auf neurophysiologische und psychometrische Messergebnisse bei Patienten mit hirnorganischem Psychosyndrom. [The effect of *Ginkgo biloba* extract on neurophysiological and psychometric measurement results in patients with psychotic organic brain syndrome. A double-blind study against 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(3):215-222

Holgers KM, Axelsson A, Pringle I. *Ginkgo biloba* extract for the treatment of tinnitus. *Audiology* 1994, 33(2):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. *International Journal of Clinical Pharmacology and Therapeutics* 2004, 42(2):63-72

Ihl R, Bachinskaya N, Korczyn AD, Vakhapova V, Tribanek M, Hoerr R, et al.; 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* 2011, 26(11):1186-1194

Ihl R, Tribanek M, Bachinskaya N. Baseline neuropsychiatric symptoms are effect modifiers in *Ginkgo biloba* extract (EGb 761<sup>®</sup>) treatment of dementia with neuropsychiatric features. Retrospective data analyses of a randomized controlled trial. *Journal of Neurological Sciences* 2010, 299(1-2):184-187

Ihl R, Tribanek M, Bachinskaya N, 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* 2012, 45(2):41-46

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG). Ginkgo in Alzheimer's disease. IQWiG Reports - Commission No. A05-19B. IQWiG, Cologne 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(11):1370-1378

Jiang X, Williams KM, Liauw WS, Ammit AJ, Roufogalis BD, Duke CC, 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(2):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(6):297-303

Kaschel R. *Ginkgo biloba*: Specificity of neuropsychological improvement – A selective review in search of differential effects. *Human Psychopharmacology* 2009, 24(5):345-370

Kaschel R. Specific memory effects of *Ginkgo biloba* extract EGb 761 in middle-aged healthy volunteers. *Phytomedicine* 2011, 18(14):1202-1207

Keheyen G, Dunn LA, Hall WL. Acute effects of *Ginkgo biloba* extract on vascular function and blood pressure. *Plant Foods for Human Nutrition* 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®. *International Psychogeriatrics* 2012, 24 (Suppl 1):25-34

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, Kim KP, Lim KS, Kim JR, Yoon SH, Cho JY, 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. *Clinical Therapeutics* 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(1-2):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. *European Journal of Neurology* 2007, 14(9):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(11):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, *et al.* T; Ginkgo Evaluation of Memory Study Investigators. Does *Ginkgo biloba* reduce the risk of cardiovascular events? *Circulation. Cardiovascular Quality and Outcomes* 2010, 3(1):41-47

Kupiec T, Raj V. Fatal seizures due to potential herb-drug interactions with *Ginkgo biloba*. *Journal of Analytical Toxicology* 2005, 29(7):755-758

Le Bars PL, Katz MM, Berman N, Itil TM, Freedman AM, Schatzberg AF; North American EGb Study Group. A placebo-controlled, double-blind, randomized trial of an extract of *Ginkgo biloba* for dementia. *Journal of the American Medical Association* 1997, 278(16):1327-1332

Lei HP, Ji W, Lin J, Chen H, Tan ZR, Hu DL, *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, *et al.* Lack of effect of *Ginkgo biloba* on voriconazole pharmacokinetics in Chinese volunteers identified as CYP2C19 poor and extensive metabolizers. *Annals of Pharmacotherapy* 2009b, 43(4):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. [Ginkgo biloba extract EGb 761 and pentoxifylline in intermittent claudication. Secondary analysis of the clinical effectiveness.] *VASA Zeitschrift für Gefässkrankheiten* 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(1):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.] *The Internist* 2012, 53(2):223-231

Maeda J, Kijima A, Inoue K, Ishii Y, Ichimura R, Takasu S, et al. *In vivo* genotoxicity of *Ginkgo biloba* extract in gpt delta mice and constitutive androstane receptor knockout mice. *Toxicological Sciences* 2014, 140(2):298-306

Mahadevan S, Park Y. Multifaceted therapeutic benefits of *Ginkgo biloba* L.: Chemistry, Efficacy Safety, and Uses. *Journal of Food Sciences* 2008, 73(1):14-19

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(6):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(9):981-985

Mazza M, Capuano A, Bria P, Mazza S. Reply to Dr. Corrao and Colleagues. *European Journal of Neurology* 2007a, 14:e12

Mazza M, Capuano A, Bria P, Mazza S. Reply to Dr. Korczyn. *European Journal of Neurology* 2007b, 14:e10

McCarney R, Fischer P, Iliffe S, van Haselen R, Griffin M, van der Meulen, 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, 23(12):1222-1230

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(2):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; 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, 283(1-2):224-229

Nicolai SP, Kruidenier LM, Bendermacher BL, Prins MH, Teijink JA. *Ginkgo biloba* for intermittent claudication. *Cochrane Database of Systematic Reviews* 2009, 2:CD006888

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, Kusuhara M, Yoshioka M, Kuroda K, Soga A, Nishikawa M, 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

Ondracek 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

Ondracek 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, Gauthier S, Bergman H, Cohen C, Feightner JW, Feldman H, 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(Suppl 12):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(4):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(4):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(3):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. *The New England Journal of Medicine* 1997, 336(15):1108

Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic *Ginkgo biloba* ingestion. *Neurology* 1996, 46(6):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.dggpp.de/documents/s3-leitlinie-demenz-kf.pdf>. Accessed: 16/12/2013

Salehi B, Imani R, Mohammadi MR, Fallah J, Mohammadi M, Ghanizadeh A, 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(1):76-80

Salvador RL. Herbal medicine - *Ginkgo*. *Canadian Pharmaceutical Journal* 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(4):127-133

Schneider C, Bord C, Misso 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; 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(1):63-69

Smith PF, Zheng Y, Darlington CL. *Ginkgo biloba* extracts for tinnitus: More hype than hope? *Journal of Ethnopharmacology* 2005, 100(1-2):95-99

Snitz BE, O'Meara ES, Carlson MC, Arnold AM, Ives DG, Rapp SR, et al.; Ginkgo Evaluation of Memory (GEM) Study Investigators. *Ginkgo biloba* for preventing cognitive decline in older adults: a randomized trial. *Journal of the American Medical Association* 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(7):531-537

Uchida S, Yamada H, Li XD, Maruyama S, Ohmori Y, Oki T, et al. Effects of *Ginkgo biloba* extract on pharmacokinetics and pharmacodynamics of tolbutamide and midazolam in healthy volunteers. *Journal of Clinical Pharmacology* 2006, 46:1290-1298

Usai S, Grazzi L, Bussone G. Ginkgolide B as migraine preventive treatment in young age: results at 1-year follow-up. *Neurological Sciences* 2011, 32 (Suppl 1):197-199

Vale S. Subarachnoid haemorrhage associated with *Ginkgo biloba*. *The Lancet* 1998, 352(9121):36

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(4):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, Coley N, Ousset PJ, Berrut G, Dartigues JF, Dubois B, et al. Long-term use of standardised *Ginkgo biloba* extract for the prevention of Alzheimer's disease (GuidAge): a randomised placebo-controlled trial. *The Lancet Neurology* 2012, 11(10):851-859

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(5):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, Weemhoff JL, Bedir E, Khan IA, Harmatz JS, Goldman P, et al. Inhibition of human cytochrome P450 by components of *Ginkgo biloba*. *Journal of Plant Pathology* 2004, 56(8):1039-1044

Wang BS, Wang H, Song YY, Qi H, Rong ZX, 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(3):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(7):579-586

Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN. Effects of *Ginkgo biloba* in dementia: systematic review and meta-analysis. *BioMed Central 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, et al. 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, Gawrońska-Szklarz B, Bieganowski W, Patalan M, Smulski HK, Samochowiec L, 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 in 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(3):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(7):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(4):343-344

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(5):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, Ohnishi N, Koishi T, Obata Y, Nakagawa M, Matsumoto T, 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

Yoshioka M, Ohnishi N, Sone N, Egami S, Takara K, Yokoyama T, 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

Zadayan G, Rokitta D, Klement S, Dienel A, Hoerr R, Gramatté T, 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, 68(5):553-560

Zagermann-Muncke P. Wenn Arzneistoffe Transportproteine beeinflussen. *Pharmazeutische Zeitung online* 2006, 50. Available at: <http://www.pharmazeutische-zeitung.de/index.php?id=2381>. Accessed 23/11/2014

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 XC, Zhang BK, Jia SJ, Liu SK, Zhou LY, Li J, et al. Effects of *Ginkgo biloba* extracts on diazepam metabolism: a pharmacokinetic study in healthy Chinese male subjects. *European Journal of Clinical Pharmacology* 2010, 66(5):503-509