Ginkgo

Other common names: Maidenhair tree

Botanical family: Ginkgoaceae.

Medicinal parts: The leaves are used medicinally in western phytotherapy, but the “seed” or ovule is used both for cooking and medicine in many countries of the Orient (Schulz et al., 2004; Wichtl, 2004; Samuelsson, 1999).

History

Ginkgo is a gymnosperm tree that is considered a living fossil, since all of its relatives died out during the last glacial period (Zhou et al., 2004; Zhou and Zheng, 2003; Libster, 2002; Mahdavi and Cupp, 2000). This tree is the only existing species of its genus. Some living specimens of this plant may be as much as 3,000 years old. (Spinella, 2001; Foster and Tyler, 2000).

The Ginkgo tree does not reproduce until it is about 20 years old and continues to do so after it has reached 1000 years of age. There are ginkgo plantations in the U.S. and France that contain an estimated 50 million trees (Spinella, 2001).

Ginkgo has been a part of traditional Chinese and Japanese medicine for many centuries (Evans, 2002; Samuelsson, 1999). The Ginkgo tree has also proven to be very resistant to environmental pollution and some pathogens (Libster, 2002).

The medicinal use of the leaves is of relatively recent origin and more common in western phytotherapy (Wichtl, 2004; Weiss and Fintelmann, 2000), in comparison to the culinary and
medicinal use of the seed (ovule), by the Oriental herbal tradition, which presumably dates back to the year 2800 BC (Schulz et al., 2004; Hoffmann, 2003; Evans, 2002; Mills and Bone, 2000).

**Active Principles**

- Bioflavonoids (amentoflavone, bilobetin, ginkgetin)
- Flavonoids (quercetin, isorhamnetins, kaempferol)
- Proanthocyanidins
- Trilactonic diterpenes: Ginkgolides A,B,C
- Trilactonic sesquiterpene bilabolids (Bilobalide) (Barrett, 2004; Kraft and Hobbs, 2004; Deng and Zito, 2003; Evans, 2002; McKenna et al., 2001; Bruneton 2000; Samuelsson, 1999).

- Most Ginkgo extracts available on the European market are standardized to 24% flavone glycosides and 6% terpene lactones (Mahady et al., 2001; Ahlemeyer and Krieglstein, 1998; Cott, 1995).

- Although some ginkgo preparations have also been applied parenterally, the great majority are ingested as tablets, capsules or extracts (Koltringer et al., 1989).

**Applications in Herbal Therapy**

- For the treatment of bronchial asthma (Rottblatt and Ziment 2002; Mahmoud et al., 2000; Weiss and Fintelmann, 2000; Li et al., 1997).

- For the treatment of cerebral insufficiency, cognitive performance and memory loss (Cieza et al., 2003 1,2; Kennedy et al., 2002; Rottblatt and Ziment, 2002; Hansel et al., 2001; Wesnes et al., 2000; Rigney et al., 1999; Brautigam et al., 1998; Kleijnen and Knipschild, 1992; Rai et al., 1991), especially in the elderly (Dongen et al., 2003, 2000; Tesch, 2003).

- For the treatment of Alzheimer’s disease or senile dementia (Andrieu et al., 2003; Schulz, 2003; Smith and Luo, 2003; Loew, 2002; Luo et al., 2002; Keltner et al., 2001; Mc Kenna et al., 2001; Spinella 2001; Ernst, 1999; Oken et al., 1998; Haase et al., 1996; Halama et al., 1988), although the exact therapeutic mechanism by which ginkgo may be effective is not yet known (Colciaghi et al., 2004).

- Anxiety and depression (Rottblatt and Ziment 2002; Ahlemeyer and Krieglstein, 1998).

- Attention deficit–hyperactivity (ADHA) disorder (Cala et al., 2003; Lyon et al., 2001).

- Against diabetes and related circulatory disorders (Kudolo et al., 2002; Savickiene et al., 2002; Kudolo, 2001; Mahdavi and Cupp, 2000).

- Glaucoma and macular degeneration (Bartlett and Eperjesi, 2004; Fies and Dienel, 2002; Head, 2001).
• Intermittent claudication (Hansel et al. 2001; Pittler and Ernst, 2000; Ahlemeyer and Krieglstein, 1998; Draebeck et al., 1996).

• Impotence or erectile dysfunction of vascular origin (Moyad et al., 2004; Sohn and Sikora, 2001; Mahdavi and Cupp 2000) or due to secondary effects of antidepressant therapy (McKay, 2004; Ashton et al., 2000; Cohen and Bartlik, 1998).

• Tinnitus of vascular origin (Gruenwald, 2004; Rottblatt and Ziment, 2002; Spinella, 2001; Ahlemeyer and Krieglstein, 1998; Von Wedel et al., 1995).

• Some components in ginkgo leaves have antioxidant and free radical scavenging properties (Ferrari, 2004; Ellnaina-Wojtasek et al., 2003; Ikeda et al., 2003; Woo et al., 2003; Firenzuoli et al., 2004; Naidu et al., 2002; Mc Kenna et al., 2001; Yao et al., 2001; DeFeudis and Drieu, 2000; Mills and Bone, 2000; Marcocci et al., 1998).

• Ginkgo may offer a good option for the prevention and treatment of high altitude sickness (hypoxia) and related ailments (Basnyat and Murdoch, 2003; Gertsch et al., 2002; Leadbetter et al., 2001; Dumont et al., 2000; Roncin et al., 1996).

• For the treatment of slowly spreading vitiligo (Parsad et al., 2003).

• Against Raynaud’s syndrome (Muir et al., 2003).

• For the treatment of depression (Fugh-Berman and Cott, 1999; Schubert and Halama, 1993).

• Ginkgo extracts may also have a role in the prevention and treatment of circulatory system/heart disease (Zhou et al., 2004; Mahady, 2002; Pietri et al., 1997; Mouren et al., 1994).

• The numerous active principles (26 or more) contained in ginkgo leaf affect various components of the circulatory system including arteries, veins, capillaries, red and white blood cells, capillary perfusion and venous toniciry (Hoffmann, 2003; McKenna et al., 2002; Mills and Bone, 2000).

• The compounds known as ginkolides A, B and C have shown to be inhibitors of platelet activation factors (PAF). This action is important in the coagulation of blood, as well as in the potential treatment of hypertension (Chang and Chang, 1997; Braquet and Hosford, 2001). For this reason, caution should be exercised when using Ginkgo and other herbs or pharmaceuticals that have anticoagulant action (Mi see section on safety and precautions below).

• The active principles in ginkgo reduce blood viscosity, antioxidant, vasodilator, stimulates neuronal activity. Ginkgo inhibits platelet function by lowering fibrinogen levels and decreasing plasma viscosity due to the action of flavonoids and terpenoids (gingkolide B) that inhibit platelet activating factor. Terpene compounds, such as the ginkolides, appear to inhibit platelet activating factor, decrease vascular resistance and improve circulatory flow without affecting blood pressure (Evans, 2002; Maclennan et al., 2002).

• A procedure known as coronary artery bypass grafting (CABG) could be a risk factor for a subtle decrease in cognitive functions. Preparations including ginkgo may be of value in
improving cognitive function in patients who have undergone this procedure, but further research is needed to prove their efficacy (Raja et al., 2004).

Clinical Studies Using Ginkgo

- Various ginkgo biloba extracts, especially EGb 761 have been studied in depth, both in animal and human trials, especially in Europe (Ulbricht and Basch, 2005; Barrett, 2004; Gertz and Kiefer, 2004; Wichtl, 2004; Anonymous, 2003; Blumenthal, 2003; Christen and Maixent, 2002; Ahlemeyer and Krieglstein, 1998).

- Ginkgo leaf extracts such as Egb 761 and LI 1370, for example, are licensed in Germany for the treatment of various ailments, including cerebral dysfunction, intermittent claudication, tinnitus, anxiety, erectile dysfunction, macular degeneration and vertigo (Anonymous, 2003; Fies and Dienel, 2002; Horr and Kieser, 2002; Loew, 2002; Luo et al., 2002; Mclennan et al., 2002).

- Various reviews have evaluated evidence-based information related to the use of Ginkgo biloba, for the treatment of various conditions including dementia, intermittent claudication, tinnitus, and macular degeneration. Some of the reviewers criticized a number of the articles as having various flaws in methodology. With regard to the articles that did meet their selection criteria for adequate methodology (double-blind, placebo–controlled studies), the results indicated that ginkgo, in some instances, can be superior to placebo and may be useful in the treatment of some ailments, although, according to available evidence, a definitive conclusion as to its efficacy could not be made (Linde et al. 2003; Birks et al., 2002; Diamond et al., 2000; Pittler and Ernst, 2000; Kleijnen and Knipschild, 1992).

- In a review of based on meta-analyses of clinical trials using various products containing ginkgo, Kurz and Van Baeln (2004), concluded that ginkgo showed only a modest health benefit compared to cholinesterase inhibitors, in the treatment of patients suffering from dementia.

- It is important to note that ginkgo’s purported activity is possibly due to a positive or synergistic interaction among its many components, rather than to any particular active ingredient. For example, a flavonoid-free Egb 761 extract had no neuromodulating effect on mice cerebral cortex synaptosomes (Ramassamy et al., 1992).

- In a study evaluating the hemodynamic and electrocardiographic effects of short-term Ginkgo use in young, healthy volunteers, Kalus and collaborators (2003), noted no immediate or short-term effects on blood pressure, heart rate, or electrocardiographic variables.

- In mice, at the behavioral level, these potent in vivo effects of Egb 761, ginkgolide B, and bilobalide, resemble those of certain antidepressants (Brochet et al., 1999).

- Studies in rats and humans have shown that ginkgo extracts may have a restorative action on 5-HT 1A receptor binding in the cerebral cortex (McKenna et al., 2002).
• Studies undertaken in vitro show that ginkgo extract EGb 761 possesses antioxidant activity, anti-ischemic activity on the central nervous system (CNS). Flavonoids reduce capillary permeability and fragility, and act as free radical scavengers, inhibiting lipid peroxidation and also cause the blood vessels to relax (McKenna et al., 2001).

• Two studies report possible beneficial effects of ginkgo in improving sleep patterns in patients with depressive illness (Hemmeter et al., 2001; Holsboer-Trachsler, 2000).

• Both in vivo and in vitro experiments have shown that ginko biloba extracts possess neuroprotective effects, which may have therapeutic applications for various nervous system disorders (Beal, 2003; Lin et al., 2003; Batianetto and Quirion, 2002; Chandrasekaran et al., 2002; Maclennan et al., 2002; Pierr et al., 2002; Roman, 2002; Sastre et al., 2002; Ternaux and Portalier, 2002; Zimmermann et al., 2002; Zhang et al., 2000; Ahlemeyer and Krieglstein, 1998).

• In a review of clinical trials comparing the efficacy of cholinesterase inhibitors and ginkgo on cognitive function in patients suffering from dementia or Alzheimer’s disease, the data from the trials for cholinesterase inhibiting drugs were more consistent than those for ginkgo, especially with relation to the patient populations and outcome measures. The significant benefits on cognition compared to placebo were seen with the drugs donepezil, galantamine, and rivastigmine, for example. The preparations containing ginkgo were significant compared to placebo only when all doses were pooled (Evans et al., 2004; Kurz and Van Baelen, 2004).

• A review of a recent large trial with Ginkgo biloba showed that a product containing this plant was not effective in preventing acute mountain sickness (AMS) compared to the drug acetazolamide in a low dose of 2 x 125 mg. According to the reviewers, acetazolamide remains the drug of choice for prevention of this malady (Bartsch et al., 2004).

• According to some authors, ginkgo biloba extract, provides symptom relief comparable to pentoxifylline for the treatment of intermittent claudication (Jacoby and Mohler, 2004).

• In a review of results from clinical trials using a ginkgo biloba standardized extract (Egb 761) for the treatment of stage II peripheral arterial occlusive disease (PAOD), the majority of the studies (7 out of 9), showed that there was an advantage of Egb 761 in the increase of pain-free walking distance compared to placebo (Horsch and Walther, 2004).

• A review of clinical trials employing ginkgo for the treatment of tinnitus showed that there is little evidence that this plant can be useful for that condition (DeBisschop, 2003).

• Ginkgo biloba leaf extracts could have anticancer (chemopreventive) properties due to their antioxidant, anti-angiogenic and gene-regulatory effects. Both the antioxidant and associated anti-lipoperoxidative effects of Ginkgo biloba extracts seem to be due to their flavonoid and terpenoid constituents (De Feudis et al., 2003).

• In vitro studies have shown that ginkgo biloba extract (EGB761) significantly suppressed the proliferation and increased cytotoxicity in HepG2 and Hep3B in human cancer cells. Additionally, Ginkgo biloba extract decreased PCNA and increased p53 expression in HepG2 cells (Chao and Chu, 2004).
• Experimentally, ginkgo biloba exocarp polysaccharides (GBEP) can inhibit proliferation and induce apoptosis and differentiation of human gastric tumor cells (Xu et al., 2004).

Table 1. Selected Clinical Trials Employing Ginkgo*

<table>
<thead>
<tr>
<th>Reference</th>
<th>Plant part / herbal product</th>
<th>Purpose of study</th>
<th>Number of subjects</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gertsch et al., 2004</td>
<td>Ginkgo supplement</td>
<td>Comparison of ginkgo biloba and acetazolamide for prevention of acute mountain sickness</td>
<td>614</td>
<td>Not effective</td>
</tr>
<tr>
<td>Mattes and Pawlik, 2004</td>
<td>Ginkgo extract</td>
<td>To assess the effects of Ginkgo biloba on alertness and chemosensory function in healthy adults</td>
<td>39</td>
<td>Not effective</td>
</tr>
<tr>
<td>Nathan et al., 2004</td>
<td>An extract containing Ginkgo biloba (120 mg) and Bacopa monniera (300 mg)</td>
<td>To evaluate the effects of a combined extract of Ginkgo biloba and Bacopa monniera on cognitive function in healthy subjects</td>
<td>85</td>
<td>Not effective</td>
</tr>
<tr>
<td>Rejali et al., 2004</td>
<td>Ginkgo biloba tablets</td>
<td>To evaluate the efficacy of ginkgo for the treatment of tinnitus</td>
<td>66</td>
<td>Not effective</td>
</tr>
<tr>
<td>Singh et al., 2004</td>
<td>Capsules containing a combination of 75mg of Codonopsis pilosula total glycosides and 40 mg of ginkgo biloba extract</td>
<td>To test whether ginkgo biloba extract in combination with Codonopsis pilosula (dangshen) or ginkgo alone could enhance memory acquisition and retention of normal human subjects, better</td>
<td>60</td>
<td>The combination of Codonopsis and ginkgo extract was more effective than ginkgo extract alone in improving the cognitive function and overall health</td>
</tr>
<tr>
<td>Authors</td>
<td>Treatment</td>
<td>Objective</td>
<td>Participants</td>
<td>Outcome</td>
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<tr>
<td>Sumboonnanonda and Lertsithichai, 2004</td>
<td>Ginko biloba-Troxerutin-Heptaminol Hce</td>
<td>To assess the clinical efficacy, and safety of Ginko biloba-Troxerutin-Heptaminol Hce in the treatment of patients with acute hemorrhoid attacks</td>
<td>22</td>
<td>Effective</td>
</tr>
<tr>
<td>Trick et al., 2004</td>
<td>Ginkgo biloba extract (120 mg/day)</td>
<td>To investigate the effects of continuing treatment with ginkgo on the activities of daily living (ADL), as well as improving various aspects of mood and sleep</td>
<td>1570</td>
<td>Effective</td>
</tr>
<tr>
<td>Chen et al., 2003</td>
<td>Ginkgo biloba exocarp polysaccharides (GBEP) capsule preparation taken orally</td>
<td>To observe the clinical efficacy of (GBEP capsule preparation in treating upper digestive tract malignant tumors of middle and late stage</td>
<td>86</td>
<td>The GBEP capsule preparation had positive therapeutic effects on upper digestive tract malignant tumors of middle and late stages</td>
</tr>
<tr>
<td>Cieza et al., 2003</td>
<td>EGb 761 standardized extract</td>
<td>To evaluate the effects of ginkgo biloba extract on mental functioning and quality of life in healthy subjects</td>
<td>66</td>
<td>Effective</td>
</tr>
<tr>
<td>Reference</td>
<td>Extract/Formulaation Type</td>
<td>Treatment/Condition</td>
<td>Outcome</td>
<td>Notes</td>
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<tr>
<td>Kanowski and Hoerr, 2003</td>
<td>EGB 761 standardized extract</td>
<td>Use of ginkgo biloba extract for the treatment of dementia</td>
<td>Not available</td>
<td>Effective</td>
</tr>
<tr>
<td>Muir et al., 2003</td>
<td>Seredrin® (standardized Ginkgo biloba extract)</td>
<td>Treatment for Raynaud’s syndrome</td>
<td>Not available</td>
<td>Effective</td>
</tr>
<tr>
<td>Prasad et al., 2003</td>
<td>Ginkocer® (Ginkgo biloba extract)</td>
<td>Treatment for vitiligo</td>
<td>47</td>
<td>Effective</td>
</tr>
<tr>
<td>Van Dongen et al., 2003</td>
<td>EGB 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>214</td>
<td>Not effective</td>
</tr>
<tr>
<td>Gertsch et al., 2002</td>
<td>Ginkgo biloba extract</td>
<td>Treatment for acute mountain sickness</td>
<td>26</td>
<td>Effective (as pretreatment)</td>
</tr>
<tr>
<td>Kang et al., 2002</td>
<td>Ginkgo biloba extract</td>
<td>Treatment for antidepressant-induced sexual dysfunction</td>
<td>19</td>
<td>Not effective</td>
</tr>
<tr>
<td>Kennedy et al., 2002</td>
<td>Ginkgo biloba extract alone, Panax ginseng extract alone and a combination of ginkgo and ginseng extracts</td>
<td>Treatment for secondary memory performance and mood improvement</td>
<td>20</td>
<td>Effective</td>
</tr>
<tr>
<td>Le Bars, et al., 2002</td>
<td>EGB 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>Not available</td>
<td>Effective</td>
</tr>
<tr>
<td>Nathan et al., 2002</td>
<td>EGB 761 standardized extract</td>
<td>To test acute effects on memory functioning in healthy older human subjects</td>
<td>Not available</td>
<td>Not effective</td>
</tr>
<tr>
<td>Burschka et al., 2001</td>
<td>EGB 761 standardized extract</td>
<td>Treatment for sudden unilateral hearing loss</td>
<td>106</td>
<td>Effective</td>
</tr>
<tr>
<td>Drew and Davies, 2001</td>
<td>LI 1370 standardized extract</td>
<td>Treatment for tinnitus</td>
<td>956</td>
<td>Not effective</td>
</tr>
<tr>
<td>Leadbetter et al., 2001</td>
<td>Ginkgo biloba</td>
<td>Treatment for</td>
<td>40</td>
<td>Effective (as</td>
</tr>
<tr>
<td>Year</td>
<td>Product</td>
<td>Treatment</td>
<td>Effectiveness</td>
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<tr>
<td>2001</td>
<td>extract</td>
<td>acute mountain sickness pretreatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stough et al., 2001</td>
<td>EGb 761 standardized extract</td>
<td>Memory enhancement</td>
<td>61 Effective</td>
<td></td>
</tr>
<tr>
<td>Kennedy et al., 2000</td>
<td>GK 501 (Ginkgo biloba extract)</td>
<td>Cognitive enhancement</td>
<td>20 Effective</td>
<td></td>
</tr>
<tr>
<td>Le Bars et al., 2000</td>
<td>EGb 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>309 Effective</td>
<td></td>
</tr>
<tr>
<td>Van Dongen et al., 2000</td>
<td>EGb 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>196 Not effective</td>
<td></td>
</tr>
<tr>
<td>Wesnes et al., 2000</td>
<td>Ginkgo biloba extract (GK501) combined with Panax ginseng extract (G115)</td>
<td>Cognitive function in healthy volunteers</td>
<td>256 Effective</td>
<td></td>
</tr>
<tr>
<td>Rigney et al., 1999</td>
<td>Kaveri®</td>
<td>Memory enhancement</td>
<td>31 Not effective</td>
<td></td>
</tr>
<tr>
<td>Brautigam et al., 1998</td>
<td>Geriaforce® (liquid extract)</td>
<td>Treatment for cerebral insufficiency</td>
<td>197 Effective (improvement of short term visual memory)</td>
<td></td>
</tr>
<tr>
<td>Cohen and Bartlik, 1998</td>
<td>Ginkgo biloba standardized extract</td>
<td>Treatment for sexual dysfunction related to SSRI antidepressants</td>
<td>63 Effective</td>
<td></td>
</tr>
<tr>
<td>Kanowski et al., 1997</td>
<td>EGb 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>156 Effective</td>
<td></td>
</tr>
<tr>
<td>Le Bars et al., 1997</td>
<td>Ginkgold® (EGb 761 tablets)</td>
<td>Treatment for dementia</td>
<td>202 Effective</td>
<td></td>
</tr>
<tr>
<td>Li et al., 1997</td>
<td>Concentrated leaf liquid (Chinese product)</td>
<td>Treatment for asthma</td>
<td>61 Effective</td>
<td></td>
</tr>
<tr>
<td>Haase et al., 1996</td>
<td>EGb 761 standardized extract</td>
<td>Treatment for dementia</td>
<td>40 Effective</td>
<td></td>
</tr>
<tr>
<td>Roncin et al., 1996</td>
<td>Tanakan® (EGb 761 tablet)</td>
<td>Treatment for mountain altitude sickness</td>
<td>44 Effective</td>
<td></td>
</tr>
<tr>
<td>Brochet et al., 1995</td>
<td>Intravenous application of ginkgolide B</td>
<td>Treatment for exacerbations of multiple sclerosis</td>
<td>104 Not effective</td>
<td></td>
</tr>
<tr>
<td>Von Wedel et al., 1995</td>
<td>Soft-laser/Ginkgo therapy</td>
<td>Treatment for chronic tinnitus</td>
<td>Not available Effective</td>
<td></td>
</tr>
<tr>
<td>Hofferberth, 1994</td>
<td>Tebonin® forte</td>
<td>Treatment for</td>
<td>40 Effective</td>
<td></td>
</tr>
<tr>
<td>Study Authors</td>
<td>Product</td>
<td>Condition</td>
<td>Number</td>
<td>Result</td>
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<tr>
<td>Mouren, et al., 1994</td>
<td>EGb 761 standardized extract</td>
<td>Treatment of peripheral arterial occlusive disease</td>
<td>20</td>
<td>Effective</td>
</tr>
<tr>
<td>Vesper and Hansgen, 1994</td>
<td>Kaveri® LI 1370</td>
<td>Treatment for cerebral insufficiency</td>
<td>86</td>
<td>Effective</td>
</tr>
<tr>
<td>Allain et al., 1993</td>
<td>Kaveri® LI 1370</td>
<td>Dual coding test for memory</td>
<td>19</td>
<td>Effective</td>
</tr>
<tr>
<td>Grassel, 1992</td>
<td>Rokan ® (EGb 761)</td>
<td>Treatment for cerebral insufficiency</td>
<td>53</td>
<td>Effective</td>
</tr>
<tr>
<td>Bruchert et al., 1991</td>
<td>Kaveri® LI 1370</td>
<td>Treatment for cerebral insufficiency</td>
<td>209</td>
<td>Effective</td>
</tr>
<tr>
<td>Halama, 1991</td>
<td>Kaveri® LI 1370</td>
<td>Treatment for dementia of vascular origin</td>
<td>42</td>
<td>Effective</td>
</tr>
<tr>
<td>Rai et al., 1991</td>
<td>Tanakan®</td>
<td>Improvement of memory dysfunction</td>
<td>27</td>
<td>Effective</td>
</tr>
<tr>
<td>Schmidt et al., 1991</td>
<td>Kaveri® LI 1370</td>
<td>Treatment for Cerebral insufficiency</td>
<td>99</td>
<td>Effective</td>
</tr>
<tr>
<td>Eckmann, 1990</td>
<td>LI 1370 (standardized liquid extract)</td>
<td>Treatment for cerebral insufficiency</td>
<td>58</td>
<td>Effective</td>
</tr>
</tbody>
</table>

• Standardized ginkgo leaf extracts are usually regarded as being safe (Mills and Bone, 2005; Gertz and Kiefer, 2004; Kraft and Hobbs, 2004; Rottblatt and Ziment 2002; Mc Kenna et al., 2001; Le Bars and Kastelan, 2000; Brinker, 2001; Mills and Bone, 2000).

• There may be great variability in the content and quality of ginkgo’s active principles in herbal extracts available on the market today (Ganzera et al., 2001).

• Although with normal therapeutic dosages, the risk of bleeding is uncommon (Rottblatt and Ziment 2002), ginkgo preparations should be used with caution in patients with known bleeding disorders (Mills and Bone, 2005; Schneider et al., 2002; Harkness and Bratman, 2003; Purroy-Garica et al., 2001; Brinker, 2001; Smolinske, 1999).

• Avoid during pregnancy and lactation. (Gruenwald, 2004; Herr 2002; Libster, 2002).

• Cardiac patients should consult with their health care provider before taking this plant, due to possible ventricular arrhythmia associated with Ginkgo use (Cianfrocca et al., 2002).

• Patients who are at risk for intracranial hemorrhage should avoid using Ginkgo preparations due their inhibition of Platelet Activating Factors (PAF) (Harkness and Bratman, 2003).

• There is one report that mentions the presence of the toxic alkaloid, colchicine, in a commercial herbal preparation containing Ginkgo (Petty et al., 2001), but after subsequent chemical analyses, that statement was later refuted (Li et al., 2002 a, b).

• Avoid using the ovule (seed) for medicinal or culinary purposes, due to its potential toxicity (Burrows and Tyrl, 2001; Brinker, 2000) Ingestion of the ovules (seeds) is associated with intoxication, known as Gin-nan poisoning, which has occurred primarily in children in the Orient, where the ovules are employed both for culinary and medicinal purposes (Mills and Bone, 2005; Rottblatt and Ziment, 2002; Mahdavi and Cupp, 2000; Samuelsson, 1999).

• The commercial extracts do not contain the poisonous principles contained in the ovules or “seeds” (Mills and Bone, 2005; Rottblatt and Ziment, 2002; Mahdavi and Cupp, 2000).

• Ginkgo may cause allergic reactions in susceptible people (Mossabeb et al., 2001).

• Parenteral use may be related to blood pressure problems, phlebitis and allergic reactions (Gruenwald, 2004).

• Due to the fact that Ginkgo preparations delay blood clotting, suspend ingestion of this herb product at least 36 hours before you plan to undergo surgery (Herr, 2002; Skogh, 1998).
Potential Herb/Drug Interactions

- Although some authors mention that ginkgo preparations may potentially interfere with certain anticancer medications (Sparreboom et al., 2004), other researchers have found that ginkgo does not seem to possess significant effect on CYP activity (Markowitz et al., 2003; Gurley et al., 2002).

- The anti inflammatory effect present in extract of ginkgo biloba has been used therapeutically, since it is a known inhibitor of platelet activating factor (PAF), which is important in the pathogenesis of asthma. This effect could be synergistic with cyclosporin A, in order to inhibit pathogenic immune activation in asthmatic patients (Mahmoud et al., 2000).

- The scientific literature on herb-drug interactions usually warns that ginkgo may increase the blood-thinning effects of warfarin (Collins and Dufresne, 2002; Herr 2002; Boniel and Dannon, 2001; Brinker, 2001; Izzo and Ernst, 2001; Argento et al., 2000; Evans, 2000; Heck et al., 2000; Miller, 1998), although evidence of this particular interaction may not always be conclusive (Vaes and Chyka, 2000).

- A double-blind, placebo-controlled clinical trial employing Coenzyme Q-10, Ginkgo and warfarin was conducted. The results showed no interactions between ginkgo’s components and warfarin. (Engelsen et al., 2003).

- A single case of spontaneous hyphema was associated with the concomitant ingestion of aspirin and ginkgo (Rosenblatt and Mondel, 1997), however, a controlled trial investigating the possible interactions between aspirin and ginkgo failed to produce any negative effects (Schwabe, 2001, cited by Blumenthal, 2003).

- A fatal case of cerebral hemorrhage associated with an interaction between ibuprofen and Ginkgo has been reported (Meisel et al., 2003).

- Ginkgo extract (EGb 761) enhanced the antithrombotic activity of ticlopidine in animal experiments (Kim et al., 1998).

- One case of an interaction between thiazide diuretics and ginkgo has been reported, which presumably caused an increase in blood pressure. However, the ginkgo preparation had been injected, which is an unusual way of administering this herb (Izzo et al., 2005; Izzo and Ernst, 2001).

- Avoid using together with therapeutic amounts of other herbs that could theoretically interfere with blood coagulation, such as garlic, uña de gato (“cat’s claw”), dong quai (Chinese Angelica) or ginger (Brinker, 2001).

- In studies with rats, EGb 761 standardized extract was regarded as a facilitating drug for the development of amikacin ototoxicity. Although the effects of this combination in humans is unknown at this time, the results of the study warn against concomitant use of aminoglycosides,
specifically amikacin, together with EGb 761, without medical supervision (Miman et al., 2002).

**Literature Cited**


Kennedy DO, Scholey AB, Wesnes KA. Modulation of cognition and mood following administration of single doses of Ginkgo biloba, ginseng, and a ginkgo/ginseng combination to healthy young adults. Physiol Behav. 2002; 75(5):739-751.


