**Ginkgo biloba/common ginkgo**

What is Ginkgo biloba?

Ginkgo biloba or common ginkgo is one of the oldest types of trees in the world. Ginkgo is been cultivated all over the world but only can be found in the wild in China. (Royer)

According to Charles Darwin Ginkgo is a living fossil. It is the oldest living tree species in the world. After the ice age it was thought that it hadn’t survived. In 1691 Englebert Kaempfer, a German Physician and Botanist, discovered in China a ginkgo biloba tree. It was not the same tree as its ancient ancestors due to environmental changes. (Nelson)

The tree normally reaches a height of 20–35 m, some specimens in China are known being over 50 m. The tree has an angular shaped crown and long, somewhat erratic branches, and is usually deep rooted and resistant to wind and snow damage. A combination of resistance to disease, insect-resistant wood and the ability to form aerial roots and sprouts makes ginkgo long-lived, with some specimens claimed to be more than 2,500 years old. (Royer)

Ginkgo’s are also popular subjects for growing as bonsai. It takes 20-35 years for trees to reach maturity and start bearing seeds. Male and female trees are separate; male trees have pollen-producing catkins while female trees, once fertilised, bear rounded and yellowish seeds with a fleshy outer coat. (Simmonds)

Ginkgo biloba as plant food supplement

Ginkgo seeds have been used in traditional Chinese medicine for thousands of years, and cooked seeds are occasionally eaten. The seeds, known as ginkgo nuts, are eaten roasted or in birds’ nest soup. (Simmonds) In food supplements the leaves are more commonly used instead of seeds or other parts
Use

Ginkgo extracts are commonly used pharmaceutically for (Ginkgo, 2009):

- Enhancement of memory and concentration
- Treatment for dementia (Alzheimer’s disease)
- Improving blood flow to most tissues and organs
- Protection against anti-oxidative cell damage from free radicals
- Relief symptoms premenstrual symptoms
- ...

Intake

The daily dose suggested varies between 40 - 120 mg of Ginkgo extract depending on the product/supplement and the intention. The amount of Ginkgo per capsule or tables varies between 40 – 120 mg. (NIH, 2014) The amount of intake can be raised to 240mg/day in case of more serious cases of dementia of Alzheimer’s. (Ginkgo biloba, 2014) Besides tablets and capsules ginkgo is also available as tea, tincture or as a cold drink.

Contaminant information

Table 1 summarizes contaminant information on Ginkgo biloba plant parts. This information comes from the ePlantLIBRA database which used MoniQA for determination of the contaminants.

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>Regulatory plant classification</th>
<th>MRL: max residue level</th>
<th>Unit</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxin B1 (seed)</td>
<td>2.1.4. Tree nuts, other than the tree nuts listed in 2.1.2 and 2.1.3, to be subjected to sorting, or other physical treatment, before human consumption or use as an ingredient in foodstuffs</td>
<td>5</td>
<td>µg/kg</td>
<td>Regulation (EC) 401/2006</td>
</tr>
<tr>
<td>Aflatoxin B1+B2+G1+G2 (seed)</td>
<td>2.1.4. Tree nuts, other than the tree nuts listed in 2.1.2 and 2.1.3, to be subjected to sorting, or other physical treatment, before human consumption or use as an ingredient in foodstuffs</td>
<td>10</td>
<td>µg/kg</td>
<td>Regulation (EC) 401/2006</td>
</tr>
<tr>
<td>Pesticides (leaves)</td>
<td>063. Herbal infusions from (b) leaves and herbs</td>
<td>MRLs for mate (0632030) apply</td>
<td>mg/kg</td>
<td>Regulation (EC) No 396/2005 and its Annex amendments</td>
</tr>
<tr>
<td>Pesticides (seed)</td>
<td>012. Tree nuts</td>
<td>MRLs for tree nuts - other (0120990) apply</td>
<td>mg/kg</td>
<td>Regulation (EC) No 396/2005 and its Annex amendments</td>
</tr>
</tbody>
</table>

Table 1 Contaminant information on Ginkgo biloba (EuroFIR AISBL PlantLIBRA, 2014)

1 The ePlantLIBRA database (http://ePlantLIBRA.eurofir.eu/) contains quality evaluated compositional, beneficial and adverse effects data on bioactive composition in Plant Food Supplements.

2 International Association for Monitoring and Quality Assurance in the Total Food Supply Chain
According ePlantLIBRA following compounds occur are unique to Ginkgo biloba:

- Bilobalide
- Ginkgolide A
- Ginkgolide B
- Ginkgolide C
- Ginkgolide J
- Ginkgotoxin
- Terpene trilactones

The following tables and charts report the amount of the above described compounds in Ginkgo biloba plant parts and in plant food supplements obtained from scientific publications.

**Figure 3** structure of bilobalide  
**Figure 4** Structure of ginkgolide  
**Figure 5** structure of terpene trilactones

**Chart 1** Bilobalide in Ginkgo biloba leaves  
**Chart 2** Ginkgo compounds in Ginkgo biloba leaves

Chart 1 shows that the documented quantity of bilobalide in leaves varies between 1040 and 6200 mg/kg DW. The reason for this can be the sample date or season or the place where the trees grow. The same applies for chart 2; average composition of the most important compounds in Ginkgo biloba leaves. Although the average level of ginkgolide A is 1170 mg/kg DW the range covers 200 and 3000 mg/kg DW. The amount of ginkgotoxin in the leaves has not reported in any publications. However table 1 shows levels in other plant parts.

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See appendix for detailed chart

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Finglas Paul, Plumb Jenny, Segers Tom  
Version 2: April 2014
### Table 2 Ginkgotoxin in Ginkgo biloba plants

<table>
<thead>
<tr>
<th>Ginkgotoxin in seed or kernel (mg/kg DW)</th>
<th>Ginkgotoxin in skin or bran (mg/kg DW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>171</td>
<td>7.15</td>
</tr>
<tr>
<td>177</td>
<td></td>
</tr>
<tr>
<td>179</td>
<td></td>
</tr>
</tbody>
</table>

The amount of ginkgotoxin is the highest in the seeds or kernels (average 175.6 mg/kg DW) of Ginkgo biloba; the amount in the skin (7.15 mg/kg DW) or other parts is around 24 times lower. Ginkgotoxin is also found in smaller amounts in Plant Food Supplements.

**Chart 3 Amount TTT in Ginkgo biloba leaves**

Chart 3 shows the amount of total terpene trilactones in leaves, the large differences in measured values can be explained by the origin, age and the growing altitude of the trees.

**Chart 4 Amount of Bilobalide in Ginkgo tablets**

Chart 4 shows the amount of Bilobalide in Ginkgo biloba tablets. A comparison with the amount in dried leaves can’t be made because there is insufficient data on the weight of tablets or capsules used or quantity of leaf in the products. The diversity of the amount bilobalide recovered is again large mostly due to different tablets with different concentrations that are used.
Table 3 Average amount of ginkgolides, ginkgotoxin and total terpene trilactones in dried, liquid and tablet samples

Table 2 shows the average amount of the most important Ginkgo biloba compounds analysed in different types of plant food supplements. There are no results of the amount of ginkgotoxin expressed in mg/tablet. The higher amount of ginkgotoxin expressed in mg/kg DW is caused by the amount found in capsules and tablets (3 references in EPlantLIBRA) which lies between 32 and 86 mg/kg DW. The other values are lower and are from analysis of boiled or canned Ginkgo seeds; they vary between 0.8 and 25 mg/kg DW. All the used samples except for determination of ginkgotoxin (expressed in mg/kg DW) are made from leaves or leaves extracts.

### Beneficial effects (EuroFIR AISBL PlantLIBRA, 2014)

3 Papers have been reported in EPlantLIBRA with clinical trials on beneficial effects of Ginkgo biloba supplements.

<table>
<thead>
<tr>
<th></th>
<th>Ginkgolide A</th>
<th>Ginkgolide B</th>
<th>Ginkgolide C</th>
<th>Ginkgolide J</th>
<th>Ginkgotoxin</th>
<th>Terpene trilactones total</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/kg DW</td>
<td>11882.57</td>
<td>7474.52</td>
<td>7989.69</td>
<td>3231.89</td>
<td>17.6</td>
<td>44174.09</td>
</tr>
<tr>
<td>mg/l</td>
<td>57.79</td>
<td>18.32</td>
<td>37.53</td>
<td>37.22</td>
<td>3.33</td>
<td>216.28</td>
</tr>
<tr>
<td>mg/tablet</td>
<td>94.18</td>
<td>57.53</td>
<td>31.34</td>
<td>30.29</td>
<td>/</td>
<td>3.08</td>
</tr>
</tbody>
</table>

#### 1. Does Ginkgo biloba reduce the risk of cardiovascular events? (Kuller, 2009)

This randomised, double-blind, placebo controlled study investigated the effects of Ginkgo biloba extract (EGb 761) on incidence of fatal and non-fatal cardiovascular events in men and women aged >75 years.

**Amount:**
- 120mg Ginkgo biloba extract (containing 28.8mg flavone glycosides and 7.2mg terpene lactones) twice daily. Ginkgo biloba extract was supplied by Schwabe Pharmaceuticals, Germany.

**Result:**
- There was no significant difference in CHD/CVD mortality between Ginkgo biloba and placebo groups.
- There was no significant difference in hospitalisations for cardiovascular events between groups (among those with no self-reported history of CVD at baseline).
- There was a significant reduction in peripheral vascular disease (PVD) events in subjects taking Ginkgo biloba supplement compared with placebo.

**Conclusion:**
- The data do not support the use of Ginkgo biloba to reduce the risk of cardiovascular events.
- However, further study may be indicated on the effects of Ginkgo biloba on risk of PVD.

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4 See appendix for detailed table and charts

This double-blind, randomized, placebo controlled study investigated the clinical efficacy of Ginkgo biloba extract for the treatment of RP (Raynaud’s phenomenon).

Amount:
- 360 mg Seredrin (Ginkgo biloba extract) per day.

Result:
- There was a significant decrease in attacks per day compared to placebo group.
- There was a reduction of 56% in number of attacks per week in treatment group, compared to a 27% reduction in placebo.
- There were no significant differences in haemorrheology (blood rheology) between the two groups.

Conclusion:
- A significant reduction in the number of Raynaud’s attacks per day has been observed, however a small sample size was included in this study and it should be seen as a pilot study.

3. Short-term oral ingestion of Ginkgo biloba extract (EGb 761) reduces malondialdehyde levels in washed platelets of type 2 diabetic subjects (Kudolo G, 2005)

This study was designed to examine the efficacy of EGb 761 as a free radical scavenger in platelets harvested from Type 2 Diabetes Mellitus subjects with and without hypercholesterolemia.

Amount:
- 120 mg daily for 3 months (containing 24% Ginkgo flavone glycosides and 6% terpenes).

Result:
- There was a significantly reduced platelet thiobarbituric acid reacting substances (TBARS) in both the normal and hypercholesterolemic subjects.

Conclusion:
- The ingestion of EGB 76 for 3 months by Type 2 Diabetes Mellitus subjects significantly inhibits platelet MDA (malondialdehyde) accumulation. No dose response effect studied.
Adverse effects (EuroFIR AISBL PlantLIBRA, 2014)

3 papers have been reported in EPlantLIBRA with Adverse effects of Ginkgo biloba seeds, 31 have been reported from Plant Food Supplements.


Type patient:
- 2 children (2 years old) and 1 37 year old woman

Amount:
- 50-80 Ginkgo biloba nuts/seeds (result of 3 reports)

Adverse effect:
- Generalized tonic convulsion, with eyes deviation and symmetric extremities extention
- Vomiting and diarrhea
- epileptic seizure

Diagnose:
- A high concentration of 4'-O-methylpyridoxine (ginkgotoxin) was present in the patient's serum and urine.
- Ginkgo nut poisoning

2. Ginkgo biloba supplement

Type patient:
- Men and women age between 33 and 83 years old.
- Different types of prehistory or no significant prehistory.

Amount:
- 40mg – 240mg from 1-4 times a day.
- 29% of the papers didn’t report any intake amount.
Adverse effect:

- (Spontaneous intracerebral) haemorrhage mostly in combination with anticoagulants. In some cases death has been reported
- Nose bleeds, ecchymosis on hands and arms after minor trauma
- Bilateral subdural hematomas
- Severe apraxia, change from mild to moderate cognitive deficits
- Hematoma
- Erythematous eruption
- Possible severe hepatitis and multiacinex dropout, no proof if it’s due Ginkgo or other product in supplement
- Frequent ventricular arrhythmia
- Paroxysmal atrial fibrillation

Diagnose:

- Inhibiting erythrocyte and platelet aggregation which cause bleeding.
- Sinus rhythm with frequent ventricular premature beats.

Causality assessment

Chart 5 Causality assessment adverse effect data

Chart 5 shows the amount of possible and probable interactions of Ginkgo biloba in the observed adverse effects. In 4 papers no classification was given due to lack of information or that no good judgement could be made.

Conclusions

There is scientific evidence that Ginkgo biloba extract/supplement can be used to reduce the number of Raynaud’s attacks per day, it can reduce platelet thiobarbituric acid reacting substances (TBARS) and it inhibits platelet MDA accumulation in normal and hypercholesterolemic Type 2 Diabetes Mellitus subjects.

There is also scientific evidence that Ginkgo biloba seeds and supplements can cause adverse effects in children and adults. In case of nut ingestion there is proof that the adverse effects are been caused by ginkgotoxin. In the other cases it has not been linked to a specific compound.
Bibliography


References EPlantLIBRA database


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Appendix

Chart 6 Amount of ginkgolides in Ginkgo leaves

![Chart 6 Amount of ginkgolides in Ginkgo leaves](image)

Chart 7 Amount of ginkgotoxin in processed Ginkgo seeds

![Chart 7 Amount of ginkgotoxin in processed Ginkgo seeds](image)
Table 4 Amount of ginkgotoxin in selected liquid Ginkgo supplements

<table>
<thead>
<tr>
<th></th>
<th>Ginkgo toxin (mg/l)</th>
<th>Ginkgo toxin (mg/l)</th>
<th>Ginkgo toxin (mg/l)</th>
<th>Ginkgo toxin (mg/l)</th>
<th>Ginkgo toxin (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo biloba allopathic medication</td>
<td>3.8</td>
<td>7.18</td>
<td>8.13</td>
<td>9.77</td>
<td>/</td>
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<tr>
<td>Ginkgo biloba homeopathic medication</td>
<td>0.008</td>
<td>0.015</td>
<td>0.301</td>
<td>0.589</td>
<td>1.5</td>
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<td></td>
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<td>1.995</td>
</tr>
</tbody>
</table>

Table 3 shows the amount of ginkgotoxin (4’-O-Methylpyridoxine) expressed in mg/l. 2 different types of supplements have been analysed; an allopathic type which contain higher amounts of ginkgotoxin then in comparison with the homeopathic type.