

# Monograph



## Ginkgo Biloba

**Common Name: Ginkgo, Maidenhair Tree**

### Description and Constituents

Extracts of the dried leaves of *Ginkgo biloba* [Family Ginkgoaceae] are used therapeutically. The extracts utilized in clinical trials (EGb761 and LI1370) are standardized in a multi-step procedure designed to concentrate the desired active principles from the plant. These extracts contain approximately 24% flavone glycosides (primarily composed of quercetin, kaempferol, and isorhamnetin) and 6% terpene lactones (2.8-3.4% ginkgolides A, B, and C, and 2.6-3.2% bilobalide). Other constituents include proanthocyanadins, glucose, rhamnose, organic acids (hydroxykinurenic, kynurenic, protocatechic, vanillic, shikimic), D-glucaric acid and ginkgolic acid, and related alkylphenols (at most 5 ppm ginkgolic acids).

### Mechanisms of Action

*Ginkgo biloba* is an antioxidant<sup>1-4</sup> with the ability to reduce clastogenic activity of the plasma.<sup>5</sup> Ginkgo extracts are capable, *in vitro*, of scavenging various reactive oxygen species,<sup>6</sup> and inhibiting or reducing the functional and morphological impairments observed after lipoperoxide release.<sup>7-8</sup> It is possible that a large part of its anti-ischemic effect involves an inhibition of free radical formation.<sup>9</sup>

One of the components of *Ginkgo biloba*, ginkgolide B, is a potent platelet-activating factor antagonist. It is also likely that the flavonoid fraction, containing free radical scavengers, is important in this respect.<sup>10</sup> Extracts from the leaves of *Ginkgo biloba* are reported to be effective at increasing vascular relaxation via a nitrous oxide pathway.<sup>11</sup> Ginkgo extracts (specifically the bilobalide component) can suppress hypoxia-induced membrane breakdown (release of choline from phospholipids) in the brain.<sup>12</sup> Oral administration can prevent the decline in muscarinic (cholinergic) receptor density in the hippocampus of rats,<sup>13</sup> and might have ability to inhibit the degradation of acetylcholine by acetylcholinesterase.<sup>14</sup>

Experimental evidence indicates Ginkgo's effect on the central adrenergic system might also be involved in its therapeutic actions,<sup>15</sup> since the extract appears to reactivate noradrenergic activity,<sup>16</sup> particularly in aged animals.<sup>17</sup> Extracts of *Ginkgo biloba* leaves produce reversible inhibition of rat brain monoamine (MAO). Both MAO-A and -B types were inhibited to a similar extent.<sup>18</sup> The antistress and neuroprotective effects of *Ginkgo biloba* extract might also be related to its effect on glucocorticoid biosynthesis. Ginkgo extract, and specifically its components ginkgolide A and B, decrease corticosteroid synthesis.<sup>19</sup> *Ex vivo* treatment with Ginkgo extract has resulted in 50% reduction of ACTH-stimulated corticosterone production by adrenocortical cells.<sup>20</sup>

### Clinical Uses

Research indicates ginkgo extract may be efficacious in the treatment of a wide array of conditions associated with age-related physical and mental deterioration. These include:

- 1) Alzheimer's Disease/senile dementia: Ginkgo extracts appear to be capable of stabilizing and, in some cases, improving the cognitive performance and the social functioning of patients with dementia.<sup>21-22</sup>
- 2) Cardiovascular Disease: Treatment with *Ginkgo biloba* extract lowers fibrinogen levels and decreases

plasma viscosity.<sup>23</sup> Ginkgo administration might improve the clinical outcome following cardiopulmonary bypass by limiting oxidative stress.<sup>24</sup>

3) Cerebral vascular insufficiency and impaired cerebral performance:<sup>25-26</sup> Administration of *Ginkgo biloba* extracts has been shown to improve a variety of conditions associated with cerebral insufficiency, including visual field disturbances associated with chronic lack of bloodflow,<sup>27</sup> oculomotor and complex choice reaction,<sup>28</sup> vigilance and reaction times,<sup>29</sup> depressive mood,<sup>30</sup> memory and mental performance,<sup>31-32</sup> dizziness,<sup>32</sup> and decreased blood flow.<sup>33</sup>

Other therapeutic applications include:

- 1) Congestive symptoms of premenstrual syndrome: Ginkgo extract was effective for the treatment of the congestive (particularly breast symptoms) and neuropsychological symptoms of PMS,<sup>34</sup> and in the alleviation of idiopathic cyclic oedema.<sup>35</sup>
- 2) Diabetes: Although human clinical trials have not been conducted, in experimental models, *Ginkgo biloba* extract appears to positively modify some complications associated with diabetes.<sup>36-37</sup>
- 3) Impotence<sup>38</sup>
- 4) Intermittent Claudication<sup>39-40</sup>
- 5) Liver Fibrosis: *Ginkgo biloba* was shown to be effective in arresting the development of liver fibrosis associated with chronic hepatitis B.<sup>41</sup>
- 6) Macular degeneration: In spite of the small population sample, a statistically significant improvement in long distance visual acuity was observed in patients with macular degeneration after treatment with *Ginkgo biloba* extract.<sup>42</sup>
- 7) Tinnitus: Studies have shown contradictory results in the treatment of tinnitus, which might be due to the diverse etiology of this condition.<sup>43-46</sup>
- 8) Vertigo/Equilibrium Disorders<sup>47-48</sup>

## Dosage

Generally recommended daily dosage is 40-80 mg of standardized extract two to three times daily. 120-160 mg of the standardized extract bid or tid. Recommended dosage for Alzheimer's Disease is at the higher end of this range or around 240 mg daily. In chronic conditions the extract should be administered for at least 6-8 weeks before evaluation of efficacy.

## Contraindications

*Ginkgo biloba* should be avoided in patients with known hypersensitivity to the plant. The use of Ginkgo preparations during pregnancy and lactation has not been studied in humans.

## Side Effects

Side effects are uncommon; however, gastrointestinal disturbances (nausea, vomiting, increased salivation, loss of appetite), headaches, dizziness, tinnitus, peripheral visual shimmering and hypersensitivity reactions, such as skin rash, have been reported to occur in some individuals.

## Drug/Nutrient Interactions

The combined use of aspirin and *Ginkgo biloba* extracts has been reported to cause subdural hematomas in some individuals.<sup>49</sup> Although the bleeding has resolved after discontinuation of the *Ginkgo biloba* extract, this combination, or the use of *Ginkgo biloba* extract with other blood thinners should be avoided, or, if used, done with caution.<sup>49</sup> At least one case of retinal hemorrhage associated with Ginkgo and aspirin use has been reported.

## Toxicity Data

The LD<sub>50</sub> of *Ginkgo biloba* extract is 15.3 g/kg. No mutagenicity has been detected for the extract. The administration of the extract does not promote the effect of other mutagenic substances studied.

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