Ginkgo-Eco

BOTANY

Ginkgo biloba L. (= Salisburia adiantifolia Sm, Salisburia biloba Hoffm). Dioecious tree from the Ginkgoaceae family; common name ginkgo or maidenhair tree. This plant grows slowly: 15cm during the first year, 30cm during the second year, and reaches its normal height (13-17m) by the age of 30-40.

The leaves are bilobate and green. In the autumn, all the leaves turn bright-yellow and fall in a very short space of time. The fruits are fleshy, greenish-yellow, with a characteristic unpleasant smell when they fall.

Ginkgo biloba is native to Asia (China, Korea, Japan). This is the unique species in the Ginkgoaceae family, which makes its classification difficult; the plant is an intermediate type between Pteridophyta (ferns) and conifers. This is a very long-living tree, which can live some 1000 years. No cultivations of this plant exist, except for a mountain region in the east of China.

Ginkgo-Eco extract is produced from the leaves of Ginkgo biloba.

CHEMISTRY

Basically, ginkgo leaves contain two main groups of compounds: flavonoids and terpenes (diterpenes and sesquiterpenes). These compounds are the basis for its therapeutic actions.

Flavonoids
Flavonoids account for up to 1% of the dry material. Ginkgo leaves contain flavonoids called flavonoid glycosides. Flavonoids may be found as aglycones or as mono- di- or tri-glycosides, some of them esterified with coumaric acid.

Ginkgo leaves also contain biflavones, which are dimeric flavonoid structures. Main biflavones in ginkgo are: ginkgetin, isoginkgetin, amentoflavone, sciadopitysin and bilobetin.
Diterpenes in ginkgo are known as ginkgolides. Gingko leaves contain ginkgolides A, B, C, and J; all ginkgolides in a proportion of 0.50%.

Sesquiterpenes in ginkgo – called bilobalides – are present in proportions of 0.005-0.40%.
Other active principles
6-hydroxykinuretic acid, 2-hexanal (main volatile component), sterols (sitosterol, stigmasterol), polyphenols, simple organic acids (shikimic, chlorogenic, vanillic, protocatechic, quinic, ascorbic and p-coumaric), long chain alkylphenols (ginkgolic acids, cardanols and uroshiols), carbohydrates (glucose, fructose, saccharose), alkali-soluble polysaccharides, cyclitols (pinitol, sequoyitol), β-lecithin, carotenoids.

TRADITIONAL USES
Ginkgo fossils older than 200 million years have been found, which make these trees – commonly observed in our parks and gardens – the oldest tree species in the World. Ancient Chinese medicinal writings document the use of Ginkgo biloba since 5000 years. The earliest applications were to treat chilblains, asthma, age-related memory loss, headache, dizziness and trauma with severe edema-related consequences. At present, ginkgo leaf extracts, mainly oral administrations, are the most often prescribed plant-drug.

COSMETIC PROPERTIES

Antioxidant activity
Ginkgo extract acts as an antioxidant by scavenging free radicals and inhibiting the generation of reactive oxygen species. The antioxidant compounds identified in ginkgo are mainly flavonoids (Tiedtke J., et al., 2006).

In vitro studies have shown that standardized solutions of Ginkgo biloba (EGb761) inhibit the formation of hydroxyl radical by 65% and adriamycin radical by 50%, thus reducing lipid peroxidation. Additionally, antioxidant activity against superoxide anion, nitric oxide and diphenyl-picrylhydrazyl has also been observed. Studies carried out with healthy volunteers showed that ginkgo extracts were more effective than β-carotene and vitamin E to reduce UV-induced oxidative stress in epidermal cells. The action mechanism seems to involve the group of flavonoids (Alonso, J, 2004).

Thus, ginkgo-eco extract is recommendable to formulate cosmetic products for the protection of skin and hair integrity against oxidative agents.

Anti-inflammatory activity
This activity is due to flavonoids and terpenes in ginkgo leaves.

Kwak W-J et al. (2002) studied the anti-inflammatory actions of ginkgetin, a biflavone from Ginkgo biloba leaves. Previous research had revealed that ginkgetin was a phospholipase A2 inhibitor with potent anti-arthritic activity in rats and analgesic activity. The authors investigated possible effects of ginkgetin on the cyclooxygenases COX-1 and COX-2 including its possible in vivo effects. The results suggested that ginkgetin from G. biloba leaves had anti-inflammatory activity based on its capacity to down-regulate COX-2 induction.

Cheon B.S. et al. (2000) studied the inhibitory activity of bilobetin and ginkgetin on nitric oxide (NO) production in lipopolysaccharide-induced macrophage cell lines (RAW 264.7). Nitric oxide (NO) produced by inducible NO synthase (iNOS) is known to play an important role in inflammatory disorders. The results showed that bilobetin and ginkgetin inhibited NO production from lipopolysaccharide-induced RAW 264.7 cells at concentrations higher than 10 μM. Such inhibition was mediated by suppression of iNOS enzyme induction but not by direct inhibition of iNOS enzyme activity.
Ginkgolides have shown a potent platelet activating factor (PAF) antagonistic activity. PAF stimulates the conversion of cell phospholipids into arachidonic acid, which is metabolized to prostaglandins and leukotrienes, both associated to blood coagulation and inflammation processes. In recent years, a number of studies have demonstrated that ginkgolides reduce platelet aggregation, allergic reactions and general inflammatory responses, probably due to their PAF antagonistic activity (Houghton P, 1994).

Therefore, ginkgo-eco extract is useful to formulate cosmetic products with anti-irritation activity.

**Vessel-protection activity**

In 1965, Dr. Willmar Schwabe standardized a ginkgo leaf extract, called EGb 761, in which 24% flavonoid glycosides were quantified. This extract was found to improve blood flow to the brain on the basis of its antioxidant activity, platelet activating factor (PAF) inhibitory activity and hemorrheologic activity. PAF and free radicals erode blood vessel membranes and increase permeability, consequently impairing blood flow to the brain, neuronal metabolism and neurotransmitters actions. Ginkgo flavonoids were found to act as free radical scavengers, while terpenes (especially ginkgolide B) inhibited PAF (Alonso, J., 2004).

Ginkgo has been observed to reduce the number of circulating endothelial cells, which is an indicator of vascular endothelium damage in patients with chronic venous insufficiency. In patients treated with EGb, the number of circulating endothelial cells was reduced by 14.5% after 4 weeks treatment, while in a placebo group, an average 8.4% reduction was observed. This study confirmed the importance of endothelial alterations in the development of varicose veins and suggested potential benefits of this plant-drug on vein walls (Morales Segura, M. et al., 2000).

Thus, ginkgo-eco extract is useful to formulate cosmetic products, which stimulate blood circulation.

**Lipolysis stimulating activity**

Cellulite is a condition associated to venous stasis and chronic venous insufficiency. Symptoms may be relieved by applying substances, which promote blood micro-circulation and lipolysis in the adipose tissue. Since lipolysis is regulated by the cAMP levels, the use of compounds, which stimulate the adenylate cyclase enzyme or inhibit the cAMP phosphodiesterase enzyme could promote lipolysis.

Several studies suggest that a dimeric flavonoid-rich fraction of Ginkgo biloba has anti-inflammatory and vasokinetic properties. This fraction contains amentoflavones and biflavonoids, such as bilobetin, ginkgetin, isoginkgetin and sciadopitysin, all of them with different number and position of methylated hydroxyl groups.

In laboratory assays, this fraction inhibited cAMP phosphodiesterase in rat adipose tissue. The inhibition degree of each compound was inversely proportional to the number of methoxyl groups in the compound, with sciadopitysin showing the weakest anti-phosphodiesterase activity and amentoflavone and bilobetin showing the strongest activity (Dell'Agli M & Bosisio E, 2002).

Therefore, ginkgo-eco extract is recommendable to formulate anti-cellulite cosmetic products.
Cell regeneration stimulating activity
Kim SJ et al (1997) evaluated the stimulating effects of ginkgo extracts, especially the flavonoid fractions, on the proliferation of normal human skin fibroblasts in vitro measured by MTT assay and direct hemocytometer cell count. Furthermore, they observed increased production of collagen and extra-cellular fibronectin by radioisotope incorporated collagen assay, procollagen type I C-peptide assay and by immunoturbidimetric assay.

Thus, this activity makes ginkgo-eco extract recommendable to formulate cosmetic products with re-epithelizing and/or wound-healing activity.

BIBLIOGRAPHIC EFFICACCY TEST

1. Materials
Extract of Ginkgo biloba (EGb). EGb is a standardized mixture of different compounds containing two major groups of substances: flavonoid glycosides and terpenoids. Flavonoids have been reported to be effective scavengers of superoxide, hydroxyl radicals and inhibitors of lipid peroxidation. The antioxidant activity of the flavonoid constituents of EGb was tested in rat brain neurons dissociated.

2. Experimental method
Oyama T et al (1994) made a study to examine the efficacy of the flavonoid constituents of EGb, rutin, kaempferol, quercetin and myricetin in reducing oxidative metabolism in both resting and Ca$^{2+}$ loaded brain neurons using the fluorescent dye, 2',7'-dichlorofluorescin diacetate (DCFH), which is retained within the neuron and then is oxidized by cellular hydrogen peroxide to be highly fluorescent.

3. Results and discussion
Incubation with myricetin or quercetin reduced the oxidation of DCFH in resting brain neurons more profoundly than EGb, rutin and kaempferol. Myricetin decreased the oxidative metabolism at concentration of 3 nM or more. It was 10 nM or more for the case of quercetin. Table 1 shows the effects of myricetin and quercetin on the DCF fluorescence of resting brain neurons.

Table 1. Comparison of the action of EGb on mean intensity of DCF fluorescence with that of the constituents of EGb. Asterisks indicate the significant difference from the control column. * P<0.05, ** P<0.01 and ***P<0.005.
Ionomycin, Ca$^{2+}$ ionophore, greatly increases the oxidation of DCFH which is thought to be oxidized by cellular hydrogen peroxide in mammalian brain neurons. Thus, excessive Ca$^{2+}$ influx into the brain neuron may result in an increased formation of reactive oxygen species. In this study it was observed that incubation with each EGb flavonoid constituent also reduced the Ca$^{2+}$-induced increase in the oxidative metabolism without affecting the cellular content of DCFH or the intracellular concentrations of Ca$^{2+}$.

Such an antioxidant action of myricetin and quercetin may be responsible for a part of beneficial effects of EGb (Oyama Y et al, 1994).

**COSMETIC APPLICATIONS**

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**RECOMMENDED DOSE**

The recommended dose is between 0.1% and 3.0%.

**BIBLIOGRAPHY**

Oyama Y, Fuchs PA, Katayama N, Noda K. Myricetin and quercetin, the flavonoid constituents of Ginkgo biloba extract, greatly reduce oxidative metabolism in both resting and Ca\(^{2+}\)-loaded brain neurons. Brain research, 1994; 635: 125-129.


Web sites: