



AMERICAN
BOTANICAL
COUNCIL

Post Office Box 144345
Austin, Texas 78714-4345
Phone 512/926-4900
Fax 512/926-2345
Email: abc@herbalgram.org
www.herbalgram.org

Mark Blumenthal
Editor

Wayne Silverman, PhD
Underwriting Coordinator

Betsy Levy
Densie Webb, PhD
Leela Devi, MSN, RN
Summary Writers

Karen Newton
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Susan McFarland
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Co-coordinators

Dawnelle Malone
Research Assistant

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HERBCLIP

FILE: •Ginkgo (*Ginkgo biloba*)

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RE: **Ginkgo Monograph**

Van Beek, T.A., E. Bombardelli, P. Morazzoni and F. Peterlongo.
Ginkgo biloba L. *Fitoterapia*, 1998, Vol. 49 (3) pp. 195-244.

This extensive review of 203 published papers covers the chemistry, analysis, pharmacology and clinical applications of extracts of the maidenhair tree (*Ginkgo biloba*). The genus *Ginkgo* probably originated 200 million years ago and *G. biloba* is considered a "living fossil." It is believed to be native to China. The name of the genus comes from an incorrect transcription of the Japanese name Yin-Kwo, meaning "silver fruit." The species name *biloba* is based on the bilobed shape of the leaves. In China and Japan, ginkgo is held sacred and is cultivated in temple gardens. It was introduced into Europe around 1730 and is now widely cultivated as an ornamental tree in streets and parks in Western countries, and as a medicinal plant particularly in China, Korea, France, Germany and the United States.

History

The ginkgo tree was first cited in Chinese herbals around the 14th century CE, for its "fruit," that was consumed raw or cooked. The medicinal properties of ginkgo seeds were reported in traditional Chinese medicine. Ginkgo seeds are prescribed as a remedy against asthma, cough, bladder inflammation, blenorrhagia (gonorrhoea), leukorrhoea, and alcohol abuse. Only ginkgo seed are officially mentioned in the Chinese Pharmacopoeia. Nevertheless, the medicinal use of ginkgo leaves in cardiovascular disorders and asthma dates back to 1550 CE. Ginkgo leaves are used in popular Chinese medicine for the treatment of asthma, pneumonic tuberculosis, leukorrhoea and disturbed spermatogenesis. They also are believed to stimulate blood circulation and have pain-relieving properties. *G. biloba* is rarely mentioned in European herbals until the mid 19th century. Contrary to traditional Chinese medicine, which uses mainly seed preparations, in Europe only leaf extracts are used in the treatment of peripheral and cerebral circulation disorders. The seed and leaf of ginkgo, in spite of their medicinal properties, also contain some toxic principles. Potent allergens such as ginkgolic acids are present in the seed. Contact with the fresh seed pulp may cause dermatitis and other allergic reactions. Ginkgo leaves also contain allergens that are present in the full extract, but are removed during the preparation of standardized extracts. When excessive amounts of edible ginkgo *nuts* are consumed, convulsions,

loss of consciousness and even death may occur. Children are particularly sensitive.

Chemistry

This monograph contains an extensively detailed section on ginkgo chemistry and recent analytical methods. *G. biloba* leaf extract is a well-defined and complex product for which a draft United States Pharmacopeia monograph has been recently published. A series of analytical methods by HPLC, GC, GC-MS and other methods have been developed and are routinely applied to *G. biloba* and its leaf preparations.

Commercially successful ginkgo extracts are not total extracts, but well-elaborated standardized extracts from which certain compounds have been removed, while others have been enriched. The industrial extraction procedures set up for their production have been patented. These extracts are standardized for the contents of flavonoid glycosides (24%) and total terpene trilactones (6%). The authors provide a detailed background on the methods used for chemical analysis of ginkgo.

Two groups of compounds are of great importance: flavonoids and terpene trilactones (ginkgolides and bilobalide). Generally, the extracts are standardized for their flavonoid content and several are also standardized for their terpene trilactone content. The intense pharmacological interest in ginkgolides and the need for quality control of drugs containing them have led to an increased demand for pure ginkgolides. However, only partially pure ginkgolides are present in ginkgo leaves in very small amounts (<0.1%). Several research groups have been involved in the isolation and synthesis of these compounds. The synthesis of ginkgolides represents a challenge for the chemist due to their unique structures.

Different classes of flavonoid compounds have been isolated from ginkgo leaves. In the extracts of therapeutic interest, the dimeric flavonoids, as well as the monoglycosides, are present only in small amounts. Besides these two groups of compounds, other minor components are present in ginkgo leaves, among them organic acids, alkylphenols and proanthocyanidins.

Pharmacology

In 1965, extracts of *G. biloba* leaves were introduced into medical practice in Germany. The earliest pharmacological and clinical studies concerned the activity of an extract of leaves that was initially defined as a complex mixture containing flavonoid glycosides and several other natural products. The initial pharmacological and clinical results led to the development of a product for the treatment of cerebral and peripheral disorders of blood flow or cerebral insufficiency in the elderly. The result of numerous *in vitro* and *in vivo* pharmacological studies and several clinical trials indicate that the actions of *G. biloba* may be classified on the one hand as vaso- and tissue-protective, which explains the peripheral and central effects of the extract, and on the other hand as a cognition-enhancing action, which contributes to the beneficial effects on subjects with cognitive decline.

The vaso- and tissue-protective action includes:

- a relaxing effect on blood vessels in spastic condition
- a contractile action, probably mediated by the catecholaminergic system, that results in an increase in the tone of abnormally relaxed vessels;
- a protective action against increase in capillary permeability;
- inhibition of platelet aggregation and antithrombotic activity;
- anti-ischemic and antiedema properties.

The cognition-enhancing action could be partially related to the flavonoids present in the extract:

- enhancement of the release of catecholamines and other inhibition of biogenic amine uptake;
- inhibition of catechol-O-methyl transferase and/or monoamine oxidase;
- protection of endothelial derived relaxing factor (EDRF) mechanisms at the brain level;
- inhibition of proteases (which regulate the metabolism of some peptides with behavioral effects, such as enkephalins and angiotensins.)

Clinical Applications

The major therapeutic indications for the extract are: disturbances of cerebral function and peripheral vascular insufficiency. *G. biloba* extract is authorized in Germany and in France for the treatment of cerebral dysfunctions including difficulties of memory, dizziness, tinnitus, headache and emotional disturbances. In 1994, the German Commission E approved ginkgo standardized extract for the treatment of the symptoms of dementia.

Safety

Standardized extract of *G. biloba* leaves was well tolerated in the most recent clinical trials. The most frequent adverse effects were gastrointestinal disorders, headache and allergic skin reactions.

The authors conclude that the pharmacological and clinical studies in the review confirm the therapeutic value and tolerability of the standardized extract of *G. biloba* leaves in the treatment of disorders of cerebral function and peripheral vascular insufficiency. While they found the existing chemical, pharmacological and clinical literature on the standardized extract impressive, the authors also called for more ginkgo research. —*Densie Webb, Ph.D.*

In the interest of conserving resources, the American Botanical Council has chosen not to include the original 48-page *FITOTERAPIA* monograph with this HerbClip summary. The monograph is now available through our Herbal Education Catalog as part of a new *FITOTERAPIA* monograph series: order item #425B (\$10) for the ginkgo monograph, or item #425K (\$89) for the complete series of 10 monographs.