“BioGinkgo 27/7 Extra Strength is a dietary supplement being sold by Pharmanex as an advanced concentration and memory formula, to stimulate memory and concentration, and to promote circulation to the brain, arms, and legs. This is an educational publication provided to help licensed healthcare practitioners understand the science upon which BioGinkgo 27/7 is based and the mechanism of action by which BioGinkgo 27/7 works. This pamphlet should not be used to sell BioGinkgo 27/7, and it should be distributed only to licensed healthcare practitioners.”

“The only claims that can be made for BioGinkgo are those that have been approved by the Company.”

**Memory and Circulation Enhancer**

**STANDARDIZED GINKGO BILOBA EXTRACT**

A Scientific Product Review
by Michael Chang, Ph.D.
Summary

As modern medicine enhances its ability to fight disease, the human population is expected to live longer. The quality of life, however, may be compromised with age if mental acuity and physical well being decrease sharply. As baby boomers age and approach retirement, there is a growing need for products that counteract the decline in mental acuity often seen during aging.

Recently, there is scientific evidence to suggest that herbal medicines and dietary supplements can improve cognitive functions and conserve mental sharpness. One of the best-studied herbal extracts is *Ginkgo biloba*.

This review surveys the published scientific work that pertains to this intriguing herb. It also provides the scientific rationale behind the formulation of BioGinkgo 27/7. This product has been formulated by Pharmanex, Inc. to provide the maximal benefits that can be derived from *Ginkgo biloba* extract while complying with guidelines defined by European health authorities.

What is BioGinkgo 27/7

*Ginkgo biloba* extract (GBE), with its beneficial effects on cognitive functions, has become one of the most widely used of the traditional supplements. Extracts from the leaves of the *Ginkgo biloba* tree (the maidenhair tree) have been medicinally for thousands of years and *Ginkgo biloba* is still one of the most widely used herbal products in China for breathing problems. In the West, *Ginkgo biloba* extract is increasingly prescribed in Europe and has recently been approved by the German Commission E, Europe's most respected herbal standards authority, for treating a variety of symptoms often found in the aging population.

Perhaps the most important age-related condition affected by GBE is a group of symptoms usually referred to as cerebral insufficiency. These symptoms include: difficulties in concentration and memory, absent-mindedness, confusion, lack of energy, tiredness and decreased physical performance. GBE, therefore, has the potential to greatly improve the quality of life during aging.

German Commission E Monograph

The use of phytomedicines in Germany is well integrated into conventional medicine and pharmacy. The German government has established a regulatory mechanism whereby herbs and phytomedicines are reviewed for their safety and efficacy for approval as over-the-counter (OTC) therapies. The German Federal Health Agency established the Commission E, which consists of physicians, pharmacists, toxicologists, pharmacognosists, and others who are familiar with medicinal plant research.

The Commission E has published 410 monographs covering 324 herbs and combinations. Of these, more than 200 herbs are approved for OTC use, including GBE. The Commission E Monograph for GBE describes, in detail, its health-related benefits, pharmacology, toxicology, active component composition, manufacturing requirements, and quality control standards.

The Monograph defines the two key active components of *Ginkgo biloba* 50:1 extract as:

- 22% to 27% flavonoid glycosides, determined as quercetin and kaempferol including isorhamnetin (via HPLC).
- 5 to 7% terpene lactones, as measured by the percentage of ginkgolides A, B and C, as well as bilobalide content.

Constituents of Ginkgo biloba Extracts

The most important bioactive ingredients in GBE are the terpene lactones (ginkgolides and bilobalide) and the ginkgo flavone glycosides. The ginkgo flavone glycosides are a group of small molecules that are derived from flavone (2-phenyl-benzopyrene); the major flavonoid glycosides are kaempferol, quercetin and isorhamnetin linked to sugar residues. The terpene lactone ginkgolides are unique to the ginkgo tree and are not found elsewhere in nature. They are diterpenes and are divided into types A, B, C, and J, which differ slightly in structure; ginkgolide B has the greatest PAF bioactivity. The terpene lactone bilobalide has a sesquiterpenoid structure.

The amounts of flavone glycosides and terpene lactones in GBE, and thus their health promoting properties, vary according to the source of the ginkgo leaves and the extraction and enrichment procedures used to prepare the extract. Therefore, the extracts are usually standardized in terms of their flavone glycoside and terpene lactone content.
content and typically contain from 22% to 27% w/w (weight of active compound/total weight of extract) flavone glycosides and from 5% to 7% w/w terpene lactones.

BioGinkgo® 27/7, the Pharmanex version of GBE, contains significant concentrations of ginkgolides, especially ginkgolide B, the most potent and long-acting PAF (platelet activating factor) antagonist. A recent bioavailability study7 in rabbits has shown that after a single dose, a higher concentration of ginkgolides was maintained for a longer duration time with BioGinkgo 27/7 than with another commercially available Ginkgo biloba 24/6 extract.

**Mechanism of Action**

The effects of GBE are due to the sum of its bioactive components since the flavone glycosides and terpene lactones act in different ways. Each bioactive constituent alone would not be as effective nor can explain the total health related effect of GBE. Many studies suggest that the health promoting effects of the ginkgo flavone glycosides result mainly from their antioxidant properties, particularly their ability to act as scavengers of oxygen free-radicals.* The accumulation of oxygen free-radicals (which are highly reactive and harmful, and damage many types of biomolecules by a process called peroxidation) is an important contributor to several age-related ailments. Ginkgo flavone glycosides have also been shown to protect against the deleterious peroxidation of lipids, which are important components of cell membranes and are essential for maintaining membrane fluidity.* Importantly, the radical scavenging potency of GBE is comparable to other well-known antioxidants such as vitamin E and vitamin C.*

The pharmacology of GBE, particularly the terpene lactones, the ginkgolides and bilobalide, may also be related to antagonism of the actions of platelet activating factor (PAF)* PAF, a small molecule that binds to specific receptors on platelet surfaces, initiates platelet aggregation, one of the first steps in blood clotting. Studies have shown that ginkgolides, by inhibiting binding of PAF to its receptors, improve blood flow to the brain and other tissues.* Ginkgolide B has been shown to be the most potent PAF-inhibitor (ten times more potent) with the longest duration of action in comparison to all the other ginkgolides. Current scientific evidence supports the notion that the antioxidant properties of the flavone glycosides and the antagonism of PAF by ginkgo extracts, particularly terpene lactones, act in concert to produce a health related effect.

**Clinical Studies**

GBE is primarily used to affect the relatively slow decline in cognitive functions, a condition referred to as cerebral insufficiency in Europe.* There have been several controlled clinical trials using different extracts of Ginkgo biloba to test the effectiveness of ginkgo extracts in mitigating symptoms characteristic of cerebral insufficiency, i.e., difficulties of concentration and memory, absent mindedness, confusion, lack of energy, tiredness and decreased physical performance. These symptoms are also often found in people suffering from age-associated memory impairment (AAMI), a condition that may also be alleviated by GBE.*

One double-blinded, placebo-controlled trial involved 99 patients with an average age of 59 years who had shown symptoms of cerebral insufficiency for an average of 26 months; 50 patients received GBE and 49 received placebo for 12 weeks. The overall effect on the well-being of the patients and on the severity of each of the symptoms listed above were rated by both the patients and their doctors on a four-point scale. After treatment, significant improvement was reported in a majority of the symptoms listed above. By patient self-assessment, 70% of the GBE group felt improvement compared to 14% of the placebo group. The doctor’s assessment showed similar results: 72% of the GBE group showed improvement compared with 8% of the placebo group.

In another study, 110 patients received GBE for 12 weeks and 99 were treated with placebo. These patients had an average age of 69 years and had experienced symptoms of cerebral insufficiency for an average of 46 months. After treatment, significant improvements in 8 of the 12 symptoms were reported on a four-point or three-point scale by patients and doctors, respectively. By patient self-assessment, 83% of the GBE group reported improved cognitive functions compared with 8% of the placebo group.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.
concentrations of active components in Ginkgo biloba leaves can vary by as much as 300% depending on location, season and method of harvest. To ensure the best quality and consistency of finished product, Pharmanex employs on-site harvest management and testing so that only fresh, clean leaves of the highest quality are procured. BioGinkgo 27/7 is manufactured to GMP’s (Good Manufacturing Practice’s) standards using a proprietary 23-step extraction and washing process requiring approximately 50 pounds of leaves to yield just one pound of extract.

Active components of each batch are stringently analyzed by HPLC to control the concentrations of flavonoid glycosides (as measured by the percentage of kaempferol, quercetin and isorhamnetin content) and terpene lactones (as measured by the percentage of ginkgolide A, B, C, and bilobalide content). Furthermore, each batch is then tested against fifteen additional quality criteria including heavy metal and residue solvent, ginkgolic acid and microbial content.

**Health Benefits**

*Tissue damage.* Because of its radical-scavenging ability, GBE may protect both nerve and heart cells against damage by free radicals. GBE may also enhance the ability of the body to repair free radical tissue damage.*

*Cognitive Function.* Important neuro-transmitters such as dopamine and 5-hydroxytryptamine are key players in central nervous system activity. Since ginkgo flavonoids protect against membrane damage, GBE can maintain the normal interaction of nerve cells with these neurotransmitters.* By inhibiting PAF-induced platelet aggregation and reducing the resulting viscosity or stickiness of the blood, the ginkgolides may increase cerebral blood flow and contribute to the improvement in cognitive function seen after GBE treatment.*

*Circulatory Benefits.* Peripheral circulation is improved after GBE treatment, resulting in an increased supply of oxygen to the muscles. GBE has been demonstrated to help with leg problems often experienced by the elderly when walking.* GBE has also been shown to improve peripheral blood circulation (e.g., hands, feet, inner ear, eyes).*

*Lung Function.* In addition to platelets, PAF binds to cells involved in maintaining the healthy functioning of the airways. PAF is believed to narrow airways, and the antagonism of the action of PAF by the ginkgolides may, therefore, improve lung function in those individuals where breathing is hindered.*

**Vision Benefits.** The macular area of the retina is responsible for fine reading and is particularly sensitive to damage by lipid free-radicals. GBE may help promote eye health in the elderly through its antioxidant properties.*

**BioGinkgo® 27/7 Proprietary Processing**

Research conducted by Pharmanex reveals that concentrations of active components in Ginkgo biloba leaves can vary by as much as 300% depending on location, season and method of harvest. To ensure the best quality and consistency of finished product, Pharmanex employs on-site harvest management and testing so that only fresh, clean leaves of the highest quality are procured. BioGinkgo 27/7 is manufactured to GMP’s (Good Manufacturing Practice’s) standards using a proprietary 23-step extraction and washing process requiring approximately 50 pounds of leaves to yield just one pound of extract.

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**Side Effects**

An important finding with GBE is that no serious side effects have been reported in any GBE trials and the frequency of side-effects is low. Mild gastrointestinal disorders, headache, and allergic skin reactions are the only side effects that have been reported!
Drug Interactions
No drug interactions have been identified, even in reports where elderly patients are taking multiple medications simultaneously. Due to Ginkgo’s mechanisms of actions, persons taking anticoagulants that affect platelet aggregation should consult with a physician.

Directions for Use
As a dietary supplement, take one tablet two times per day (morning and evening) with food and drink. Do not chew tablet. Tablet is coated for ease of swallowing.

How Supplied
BioGinkgo® 27/7 tablets (60 mg each) are supplied in a one-month supply of 60 tablets.

Storage
Store in dry, cool place. Avoid excessive heat. Protect from light.

Shelf Life
Expiration date and lot code numbers are imprinted on the bottom of the box or bottle.

Warnings
Keep out of reach of children. If you are pregnant or lactating, please consult your physician before taking this product. Contact your physician if you are taking a prescription medication. Persons taking anticoagulants that affect platelet aggregation should consult their physician before using a GBE product.

Do not use if...
- You are taking anticoagulants;
- You are taking aspirin on a daily basis;
- You are taking monoamine oxidase (MAO) inhibitors;
- You are allergic to the Ginkgo biloba plant or its products.

Note: If you have a known medical condition or are taking a medication stated above, please consult with a doctor before taking BioGinkgo®.

About the Author
Michael Chang, Ph.D., Senior Vice President of Research and Development and Chief Scientific Officer, leads Pharmagen’s R&D team efforts. Dr. Chang has a strong pharmaceutical background, with more than 15 years in the industry, first as Deputy Director of Medicinal Chemistry at Merck Sharpe and Dohme and then as Director of Medicinal Chemistry at Rhone Poulenc Rorer.
All Pharmagen Research and Development efforts are coordinated at our state-of-the-art facilities in the United States and China under Dr. Chang’s leadership.

Key References


The Pharmanex 6S Quality Process™
Central to the Pharmanex mission of transforming time-honored, traditional preparations into health-promoting botanical products with known content and consistent activity is the Pharmanex 6S Quality Process.

| Selection   | • Exhaustive scientific review of research and databases is conducted.  
|            | • Authenticity, usefulness, and safety standards are determined. |
| Sourcing    | • Teams of experts investigate potential sources and evaluate quality.  
|            | • Comprehensive botanical and chemical evaluations are completed. |
| Structure   | • Structural analyses of natural compounds are determined.  
|            | • Active ingredients are isolated and studied. |
| Standardization | • Strict standardization to at least one relevant marker molecule is required.  
|            | • Proprietary processing methods to increase consistency and ensure measured dose effectiveness are developed. |
| Safety      | • Safety is assessed from available research.  
|            | • Microbial test, chemical, toxin, and heavy metal analyses are conducted. |
| Substantiation | • Documented pre-clinical and clinical studies are reviewed.  
|            | • Pharmanex sponsored studies are initiated when appropriate. |

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