

## The lowdown on Ginkgo Biloba

Gold, PE at al.

- Use of Ginkgo Biloba can be traced back centuries in Chinese traditional medicine
- Most widely-used herbal treatment for cognitive functions – memory, learning, alertness
- Approved in Germany for dementia treatment

- Typical dose (used in many experiments) is 120 milligrams of dried extract in two or three oral doses.
- Extract in German product is named EGb 761, manufactured by Schwabe Pharmaceuticals.
- The extract contains
  - flavonoids and biflavonoids, a large group of natural plant products
  - terpenes (active ingredients in catnip and marijuana)

- Dozens of clinical trials have examined the cognitive effects of ginkgo in humans.
- Great majority of studies have involved subjects with mild to moderate impairment, usually an early diagnosis of Alzheimer's.
- Most experiments test learning and memory; less often attention, motivation or anxiety.

- Most subjects were selected and tested long after they began using ginkgo, typically several months, so their cognitive level before using ginkgo is unknown.
- This may introduce a bias, if those with better cognitive abilities are more likely to take ginkgo.
- For example, higher scores on the memory and learning tests may come from subjects who could read and understood articles suggesting ginkgo might help them, or who were better able remember to take the drug.
- Researchers need to give tests both before and after the patients start taking ginkgo, or else the experiment results are suspect.

- Barry Oken at Oregon Health Sciences University looked at more than 50 trials involving subjects with mental impairment and found four that met criteria:
  - sufficient characterization of Alzheimer's diagnosis
  - standardized ginkgo extract
  - placebo controlled, double-blind study (neither patients nor doctors knew who got drug and who got placebo)

- Each of these studies showed that the Alzheimer's patients who received ginkgo performed better on various cognitive tests than did patients who received a placebo
- Improvements were shown in standardized tests of attention, short term memory and reaction time.
- Average improvement from ginkgo was 10 to 20 percent.
- In some cases, ginkgo slowed the cognitive decline (compared to placebo) and in some cases it actually improved performance.

- Effects were comparable to those of the drug donepezil, which is currently the drug most used for Alzheimer's.
- Donepezil works by inhibiting the breakdown of the neurotransmitter acetylcholine.

- Another recent, large, well-controlled clinical trial of EGb 761 sponsored by its manufacturer involved patients with mild or moderate dementia.
- The results showed no "systematic and clinically meaningful effect of ginkgo" on any of the cognitive tests used.

### Studies in healthy subjects

- Fewer studies have examined the effects of ginkgo on healthy young adults.
- In one small study during the mid-1980's Ian Hindmarch from the University of Leeds, U.K., gave a battery of tests to eight healthy subjects, aged 25 to 40, after they took ginkgo EGb 761..
- The highest dose (600 milligrams) improved performance in only a short-term memory test.

### Two more recent studies from Cognitive Drug Research

- One study reported that subjects who took ginkgo performed better on tasks involving attention than did subjects on placebo.
- Second study showed improvement in memory among subjects aged 38 to 66 who were treated with a combination of ginkgo and ginseng.

### Note:

- Gold claims that the effects of Ginkgo did not increase with the dosage, which would be expected of a truly effective substance.
- This statement is not true in general for drugs that affect cognitive function
- Usually an inverted-U shaped response curve.

- Later in the article, Gold states
  - "Like most treatments that improve memory, glucose's effects follow a dose-response curve in the shape of an inverted U. Only intermediate doses improve memory; low doses are ineffective, and high doses may actually impair memory."

### Relatively few reports examine ginkgo in animals

- 1991 study of young adult mice trained to press a lever to receive food
- Mice treated with ginkgo for four to eight weeks learned the task slightly more quickly than control mice.
- Some researchers report that ginkgo reduced stress in rats, which may influence learning.

### Is ginkgo safe?

- Few health risks at typical doses (120 to 240 milligrams per day)
- Some complications have occurred in people taking ginkgo:
  - subdural hematomas (blood clots between skull and brain)
  - gastrointestinal problems
  - nausea and vomiting

### Some users experience:

- increased salivation
- decreased appetite
- headaches
- dizziness
- tinnitus
- skin rash

- Large doses may lead to orthostatic hypotension (low blood pressure on standing)
- Incidence of serious adverse reactions to ginkgo is relatively low

### Is ginkgo as effective as glucose or donepezil?

- Differences in experiment design makes comparison difficult
- Glucose enhances performance in a short-term memory test in young adults and healthy elderly subjects by 30% to 40%.
- In patients with Alzheimer's, improvement on similar test is near 100%.
- These results are much greater than the 10% to 20% reported for ginkgo.

- But the experiments using glucose are short-term memory treatments, while the ginkgo tests are longer term.
- Glucose experiments compare patients before and after, ginkgo don't

- One study in rats directly compared ginkgo to other treatments, found effect was about half of that seen with other drugs.
- What about combinations? Different mechanisms, different safety profiles?
- More direct comparisons in animals and humans are needed.