

Ginkgo for Memory Enhancement

A Randomized Controlled Trial

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SOME OVER-THE-COUNTER TREATMENTS are marketed as having the ability to improve memory, attention, and related cognitive functions. These claims are generally not supported by well-controlled clinical studies. Ginkgo claims to “enhance mental focus and improve memory and concentration.”¹ Several published studies reported beneficial effects of ginkgo on cognition. These studies, however, either report cognitive improvement in only 1 of many memory tests administered^{2,3} or report cognitive enhancement in cognitively impaired clinical populations such as patients with cerebrovascular or Alzheimer disease.^{4,5} In contrast, advertising claims imply that the compound is broadly beneficial to those both with and without clinically significant cognitive impairments. Specific advertising claims cite more than 50 clinical trials that demonstrate benefit centered around concentration and memory. These studies were conducted for periods ranging from 14 days to 2 months. The manufacturer claims benefit with “at least 4 weeks of uninterrupted use.”⁶

The purpose of the present study was to evaluate ginkgo in healthy elderly volunteers in a randomized, double-blind, placebo-controlled trial using standardized tests of memory, learning, attention and concentration, and expressive language as well as subjective ratings by participants and family.

Context Several over-the-counter treatments are marketed as having the ability to improve memory, attention, and related cognitive functions in as little as 4 weeks. These claims, however, are generally not supported by well-controlled clinical studies.

Objective To evaluate whether ginkgo, an over-the-counter agent marketed as enhancing memory, improves memory in elderly adults as measured by objective neuropsychological tests and subjective ratings.

Design Six-week randomized, double-blind, placebo-controlled, parallel-group trial.

Setting and Participants Community-dwelling volunteer men (n=98) and women (n=132) older than 60 years with Mini-Mental State Examination scores greater than 26 and in generally good health were recruited by a US academic center via newspaper advertisements and enrolled over a 26-month period from July 1996 to September 1998.

Intervention Participants were randomly assigned to receive ginkgo, 40 mg 3 times per day (n=115), or matching placebo (n=115).

Main Outcome Measures Standardized neuropsychological tests of verbal and non-verbal learning and memory, attention and concentration, naming and expressive language, participant self-report on a memory questionnaire, and caregiver clinical global impression of change as completed by a companion.

Results Two hundred three participants (88%) completed the protocol. Analysis of the modified intent-to-treat population (all 219 participants returning for evaluation) indicated that there were no significant differences between treatment groups on any outcome measure. Analysis of the fully evaluable population (the 203 who complied with treatment and returned for evaluation) also indicated no significant differences for any outcome measure.

Conclusions The results of this 6-week study indicate that ginkgo did not facilitate performance on standard neuropsychological tests of learning, memory, attention, and concentration or naming and verbal fluency in elderly adults without cognitive impairment. The ginkgo group also did not differ from the control group in terms of self-reported memory function or global rating by spouses, friends, and relatives. These data suggest that when taken following the manufacturer's instructions, ginkgo provides no measurable benefit in memory or related cognitive function to adults with healthy cognitive function.

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METHODS

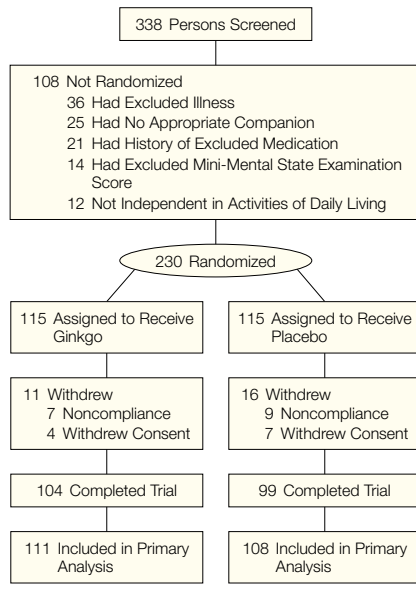
Participants

Following approval by the Williams College institutional review board, participants were recruited from newspaper advertisements that solicited individuals who would participate in a study designed to improve memory. An initial telephone interview was conducted to determine if the participant was likely to meet entry criteria for the study. Those who passed the

screen provided informed consent and a medical history including current medications, neurologic or psychiatric

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Figure 1. Study Flow Diagram

illness, and incidence of head trauma, stroke, mental illness, mental retardation, or life-threatening illness over the last 5 years. Participants were included in the study if they were community dwelling, older than 60 years, and could provide informed consent. They also needed to have a companion who had contact with them on a regular basis (>4 times per week for ≥ 1 hour) and was willing to complete a questionnaire. The baseline Mini-Mental State Examination⁷ score was required to be greater than 26. All participants reported to be independent in instrumental activities of daily living including shopping, transportation, and managing finances. Participants were excluded if they had a history of psychiatric or neurologic disorder or had a life-threatening illness in the last 5 years. They were also excluded if they had taken antidepressant or other psychoactive medications in the past 60 days. A total of 338 community-dwelling participants were screened over a 26-month period from July 1996 to September 1998, and 230 participants (98 men and 132 women) aged 60 to 82 years were randomized in the study.

Study Design

A 6-week double-blind placebo-controlled study was conducted at a single site. FIGURE 1 summarizes the study participation. Participants were randomly assigned to 1 of 2 conditions: ginkgo (Ginkoba, Boehringer Ingelheim Pharmaceuticals)¹ or placebo control (1:1 ratio). Random assignment of participants to each condition was determined by 1 of the investigators (P.R.S.) using a table of random numbers.⁸ Medication was placed in sealed envelopes by a research assistant and provided to the participants by 1 of 3 other investigators (F.A., A.S., J.Z.). Dosages for ginkgo were determined by following the manufacturer's label instructions: 1 tablet (40 mg) 3 times a day, with meals. The placebo group took lactose gelatin capsules of similar appearance and on the same schedule as the ginkgo group. At the beginning of the double-blind period, participants were provided with sealed and dated envelopes, each containing medication for 1 day.

One day prior to taking ginkgo or placebo and again at the end of the 6-week double-blind period (while still taking ginkgo and within 3 days of the end of the study), participants underwent neuropsychological evaluation including tests of learning, memory, attention and concentration, and expressive language. They also completed a questionnaire regarding subjective impressions of their memory. Additionally, at the end of the 6 weeks of treatment, the companion was asked to complete a global questionnaire designed to provide an overall impression of change in memory for the participant. Evaluators (F.A., A.S., J.Z.) were blinded to which randomized treatment the participants received.

Participants were contacted by telephone twice (at the end of weeks 2 and 4) during the 6-week period to evaluate compliance. They were excluded from the study if they missed 6 doses in any 2-week period or did not take 3 consecutive doses. At this time, they were asked to stop taking study medication. As an additional measure of

compliance, participants were asked to return all dated envelopes at the end of the study.

Outcome Measures

Outcome measures consisted of the following standardized tests of learning, memory, attention and concentration, expressive language, and mental status. Tests of learning and memory included the California Verbal Learning Test (CVLT),⁹ in which the participant is asked to learn a 16-item shopping list over 5 trials and then to later recall and subsequently recognize the information; the Logical Memory subscale of the Wechsler Memory Scale-Revised (WMS-R),¹⁰ in which the participant is asked to recall paragraphs both immediately after hearing them and then after a 30-minute delay; and the Visual Reproduction subscale, in which the participant is asked to draw designs both immediately after seeing them and after a 30-minute delay.

Tests of attention and concentration included the Digit Symbol subscale of the Wechsler Adult Intelligence Scale-Revised (WAIS-R),¹¹ in which the participant must rapidly copy symbols that are paired with numbers; the Stroop Test,¹² which requires the participant not to be distracted by extraneous aspects of stimuli; the Digit Span (WMS-R), which requires the participant to repeat increasingly longer strings of numbers immediately after hearing them; and Mental Control (WMS-R), in which the participant must recite strings of numbers and letters.

Tests of expressive language included the Controlled Category Fluency test,¹² which requires the participant to name members of a particular category (animals) over a 1-minute period; and the Boston Naming Test,¹³ which requires the participant to name pictures of items.

Additionally, the Memory Questionnaire¹⁴ as well as a global evaluation completed by a spouse, relative, or friend with whom the patient had regular contact (at least 4 interactions per week) was completed. The Memory Questionnaire consisted of 27 ques-

tions that asked the participant to rate how often certain memory lapses occurred. The participant answered on a 4-point scale with descriptors used as anchors: 1 indicating very often, 2 indicating sometimes, 3 indicating rarely, and 4 indicating not at all. The global evaluation was based on the Caregiver Global Impression of Change rating scale.¹⁵ Informants were asked to indicate the option that best described the change in memory over the preceding 6 weeks. The options included: (1) very much improved, (2) much improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) much worse, or (7) very much worse.

All outcome measures, with the exception of the global evaluation, were administered at both the beginning and end of the study. The global evaluation was administered only at the end of the study. Participants who withdrew from the study, or who were dropped because of noncompliance, were asked to return at the end of the study for evaluation. Adverse events were not specifically monitored in this study. Patients who experienced an adverse event were instructed to discontinue study medication and to contact their primary care physician.

Statistical Methods

Analysis for efficacy was performed on 2 participant samples: the modified intent-to-treat primary analysis and the fully evaluable population. The modified intent-to-treat population included all participants who were randomized to treatment, underwent baseline analysis, received at least 1 dose of study drug, and returned for post-treatment evaluation. The fully evaluable population was defined as participants who completed 6 weeks of double-blind treatment and who complied with the standards for taking medication.

Differences in group means for all neuropsychological tests were assessed using both individual *t* tests and repeated-measures analysis of variance in which treatment condition served as the predictor and the cognitive tests served as the repeated measures. The test by con-

dition-interaction term was then tested for statistical significance. Demographic variables were analyzed using the individual *t* tests. Categorical variables were analyzed using the χ^2 test. Results were considered statistically significant if differences reached the .05 level. Nonparametric analyses were used to assess the changes from baseline to week 6 for the Caregiver Global Impression of Change. We sought to detect differences of .05 SD with a power of 90% ($\alpha = .05$), requiring a sample size of 172 participants.¹⁶ JMP version 5.0 (SAS Institute Inc, Cary, NC) statistical software was used for all analyses.

RESULTS

A total of 230 participants were enrolled in the study over a 26-month period, with 203 participants (88%) completing the study (Figure 1). The percentage of participants who completed the study did not differ significantly by treatment group. Of the 27 participants who did not complete the study, 16 (7 ginkgo and 9 placebo) did not comply with the medication dosage regimen and 11 (4 ginkgo and 7 placebo) withdrew consent. All participants were requested to return at the end of week 6 for evaluation.

Modified Intent-to-Treat Analysis

A total of 219 participants (111 ginkgo and 108 placebo) returned at the end of the 6-week period for reevaluation. This included the 203 participants who completed the protocol as well as 13 of 16 participants (6 ginkgo and 7 placebo) who were noncompliant and 3 of the 11 participants (2 ginkgo and 1 placebo) who withdrew consent. The remaining 11 participants (4 ginkgo and 7 placebo) did not return for evaluation and were excluded from the analysis. There were no significant differences between the ginkgo and placebo groups for any of the outcome measures. Neither demographic characteristics nor Mini-Mental State Examination scores varied as a function of treatment condition at baseline (TABLE 1).

There were no significant differences between the ginkgo and placebo groups

Table 1. Demographic Characteristics at Baseline of Participants Who Returned for Week 6 Evaluation (Modified Intent-to-Treat Analysis)

Characteristic	Mean (SD)		P Value
	Ginkgo (n = 111)	Placebo (n = 108)	
Age, y	68.7 (4.7)	69.9 (5.4)	.73
Men, No. (%)	46 (41)	45 (42)	.81
Education, y	14.4 (4.5)	14.0 (3.9)	.85
Mini-Mental State Examination score	28.7 (1.4)	28.8 (1.5)	.53

on any of the objective neuropsychological tests. In general, participants performed better during their second evaluation than during their first, but there were no significant test-by-treatment condition interactions as tested by a repeated-measures analysis of variance ($F_{14,172}=0.099$, overall $P=.31$). Superior performance in all groups at the second testing session was likely due to a practice effect.

When tested by individual *t* tests, measures of attention and concentration, including the Digit Symbol subscale of the WAIS-R, the Stroop Test, and the Mental Control and Digit Span (forward and backward) subscales of the WMS-R, showed no significant differences between the ginkgo and placebo groups (TABLE 2 and FIGURE 2). Similarly, tests of verbal and nonverbal learning and memory, including the Logical Memory (I and II) and Visual Reproduction (I and II) subscales of the WMS-R, and the CVLT (initial acquisition, short and long delay, and recognition), also showed no significant differences between the ginkgo and placebo groups. There were no differences in tests of naming (Boston Naming Test) or verbal fluency (Controlled Category Fluency) between the ginkgo and placebo groups. Finally, self-report on the Memory Questionnaire was scored on a scale of 27 to 108 with higher scores indicating more difficulties. There was no difference in the mean reported scores for participants in the ginkgo and placebo groups ($P=.26$).

At the end of the second testing session, participants were asked if they

thought they had been taking ginkgo or placebo. Self-report in the ginkgo group indicated that 79 participants (71%) thought they were taking ginkgo, and self-report in the placebo group indicated that 81 participants (75%) thought they were taking ginkgo ($P = .49$). Informant response to the global rating indicated no difference between the ginkgo and placebo groups ($P = .76$). TABLE 3 shows the distribution of responses.

Figure 2 shows the 95% confidence intervals (CIs) for differences (treatment group minus control) for performance on each test in the modified intent-to-treat analysis. Each interval contains a zero, indicating that none of the differences are statistically significant. Moreover, 7 of the point esti-

mates are positive (favoring ginkgo) and 7 are negative (favoring placebo).

Evaluable Participant Analysis

A total of 203 participants completed the protocol (fully evaluable population). There were no significant differences between the ginkgo and placebo groups for any outcome measure (Table 2).

COMMENT

The results of this 6-week study indicate that ginkgo, marketed over-the-counter as a memory enhancer, did not enhance performance on standard neuropsychological tests of learning, memory, naming and verbal fluency, or attention and concentration. Moreover, there were no differences between ginkgo participants and pla-

cebo controls on subjective self-report of memory function or on global rating by spouses, friends, and relatives. These data suggest that when taken following the manufacturer's instructions, this compound provides no measurable benefit in cognitive function to elderly adults with intact cognitive function.

In total, 14 different measures of cognition were evaluated in the present study. Seven of the measures were better in the placebo group, and 7 of the measures were better in the ginkgo group. None of the differences between the means of the 2 groups were statistically significant. The 95% CIs were calculated for each mean difference. Even if one assumes that the true difference between treatments is the up-

Table 2. Neuropsychological Test Results for Ginkgo vs Placebo*

Test	Possible Range of Scores (Normative Scores [SD])†	Modified Intent-to-Treat Analysis						Evaluable Participant Analysis	
		Mean Score at Baseline (SD)		Mean Score at Week 6 (SD)		Mean Difference Scores (95% CI of Difference)	P Value	Mean Difference Scores (95% CI of Difference)	P Value
		Ginkgo	Placebo	Ginkgo	Placebo				
Digit Symbol (WAIS-R)	0-90‡	46.7 (12.2)	47.8 (10.1)	47.1 (12.4)	47.6 (10.8)	0.65 (-1.45 to 2.76)	.54	0.60 (-1.59 to 2.80)	.59
Mental Control (WMS-R)	0-6 (5 [1])§	5.6 (0.7)	5.5 (0.6)	5.5 (0.6)	5.6 (0.6)	-0.16 (-0.40 to 0.07)	.16	-0.15 (-0.39 to 0.09)	.22
Digit Span (WMS-R)	0-24 (13 [3])§	16.3 (3.6)	15.7 (3.8)	17.2 (3.5)	17.1 (3.1)	-0.44 (-1.29 to 0.41)	.31	-0.43 (-1.31 to 0.45)	.33
Stroop Test (color/word)	0-112‡	58.7 (3.6)	61.1 (11.1)	63.8 (13.6)	63.1 (10.0)	1.51 (-1.12 to 4.14)	.24	0.88 (-1.41 to 3.17)	.33
Logical Memory I (WMS-R)	0-50 (21 [6])§	20.5 (5.1)	23.6 (4.7)	20.6 (5.2)	24.3 (5.5)	-0.53 (-1.71 to 0.65)	.38	-0.42 (-1.66 to 0.81)	.49
Logical Memory II (WMS-R)	0-50 (16 [7])§	16.2 (6.3)	20.3 (7.2)	17.1 (7.9)	22.3 (8.6)	-1.02 (-2.25 to 0.20)	.10	-0.99 (-2.26 to 0.28)	.12
Visual Reproduction I (WMS-R)	0-41 (28 [6])§	31.7 (5.8)	32.4 (5.3)	33.9 (4.6)	35.5 (3.8)	-0.96 (-2.27 to 0.35)	.15	-1.05 (-2.39 to 0.30)	.12
Visual Reproduction II (WMS-R)	0-41 (19 [10])§	21.5 (9.4)	27.5 (8.2)	31.0 (7.9)	31.8 (6.3)	0.19 (-1.52 to 1.90)	.83	0.26 (-1.52 to 2.05)	.77
CVLT (Trials 1-5)	0-80 (45 [9.3])	43.4 (11.5)	43.0 (11.7)	44.2 (11.7)	44.3 (11.8)	-0.58 (-1.90 to 0.74)	.39	-0.36 (-1.73 to 1.01)	.61
CVLT (Short Delay Recall)	0-16 (9 [2.5])	8.9 (2.8)	9.1 (2.9)	10.2 (3.3)	10.2 (3.1)	0.18 (-0.39 to 0.75)	.54	0.28 (-0.31 to 0.86)	.35
CVLT (Long Delay Recall)	0-16 (10 [2.8])	8.6 (3.0)	8.7 (3.1)	9.8 (3.9)	9.8 (3.6)	0.07 (-0.60 to 0.74)	.84	0.15 (-0.56 to 0.86)	.67
CVLT (Recognition Memory)	0-16 (14 [1.7])	13.4 (1.8)	13.4 (1.8)	14.2 (1.6)	14.2 (1.9)	0.03 (-0.40 to 0.47)	.88	-0.07 (-0.52 to 0.38)	.76
Controlled Category Fluency	0-? (17 [4.7])	18.5 (3.9)	19.3 (3.9)	19.4 (4.2)	20.4 (3.8)	-0.16 (-1.10 to 0.79)	.74	-0.14 (-1.13 to 0.86)	.79
Boston Naming Test	0-30‡	25.8 (2.4)	25.3 (2.7)	26.3 (2.5)	26.3 (2.3)	0.46 (-0.07 to 0.99)	.09	0.51 (-0.04 to 1.06)	.06
Memory Questionnaire	27-108‡	81.3 (12.4)	76.8 (12.0)	79.8 (14.7)	76.3 (12.5)	1.00 (-0.75 to 2.76)	.26	1.36 (-0.44 to 3.15)	.13

*CI indicates confidence interval; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised; and CVLT, California Verbal Learning Test. Mean difference scores were difference of ginkgo (week 6 minus baseline) and placebo (week 6 minus baseline).

†Normative data are taken from Spreen and Strauss¹² and to the extent available based on age- and education-matched samples. Controlled Category Fluency has no end score due to participants providing as many names of animals as possible.

‡Appropriate age- and education-matched samples are not available for these tests.

§Normative data for the WMS are for an older sample than those used in the present study (range, 71-81 years; midpoint, 76).

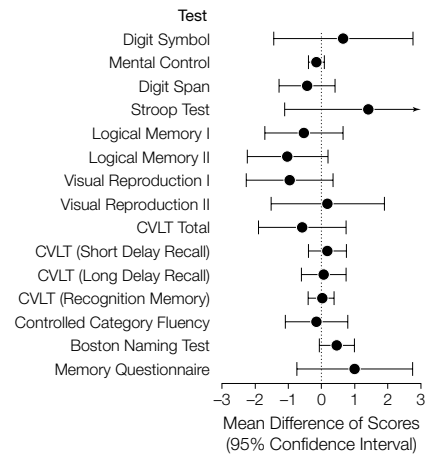
per limit of the 95% CI, it would still be difficult to argue that meaningful benefit was derived from taking ginkgo. For example, the Logical Memory portion of the WMS-R measures the participants' ability to recall 2 paragraphs that they initially heard 30 minutes earlier. There are 25 possible discrete items in each paragraph that the participant could recall. The upper limit of the 95% CI for the mean difference between ginkgo and placebo was 0.20 items (ie, participants in the ginkgo group remembered less than 1 item more than participants in the placebo group). Similarly, on the CVLT, participants learn a 16-item shopping list over 5 trials. A perfect score is 80. The upper limit of the 95% CI for the mean difference between ginkgo and placebo was 1.01 items. It would be difficult to argue that either of these differences are of any clinical significance, even if they are real. The results of the Caregiver Global Impression of Change rating scale further support the failure of ginkgo to provide clinically significant improvement in memory. In general, caregivers did not rate changes in memory over the 6-week trial any differently in participants randomized to ginkgo vs placebo participants. Sixty-six percent of those randomized to placebo and 70% to ginkgo were judged by caregivers as showing no change over 6 weeks. Thirty-three percent of placebo and 28% of ginkgo participants were judged as minimally improved, and 3 participants were judged to be much improved; 2 were in the ginkgo group and 1 was in the placebo group (Table 3).

Ginkgo has been evaluated in several double-blind studies that have reported beneficial effects, but these effects were not broad or consistent. Wesnes et al³ conducted a 3-month double-blind, randomized, placebo-controlled study in 54 patients. Patients were evaluated at weeks 4, 8, and 12. Patients receiving Tanakan (ginkgo extract) performed better on only 2 of 8 tests of memory ($P=.03$) and attention and concentration ($P=.05$) and in each case at only 1 evaluation point. There was not a consistent effect for any outcome measure. Additionally, nei-

ther physicians nor patients could distinguish between placebo and compound on an overall scale. Rai et al² compared 12 ginkgo-treated with 15 placebo-treated participants who were classified as having mild to moderate memory impairment in a double-blind study and reported significant differences in favor of the ginkgo group only on the Kendrick Digit Copying task, but not on tests of learning or memory. Rigney et al¹⁷ evaluated 31 participants and 4 doses of ginkgo in a crossover design. They only reported improvement with 1 dose of ginkgo (120 mg), in only the oldest group of participants (50-59 years), and only in 1 of the multiple tests of memory administered. Other studies that have reported positive effects in favor of ginkgo have also either studied small numbers of participants in uncontrolled studies,^{18,19} have found benefit in one of many cognitive tasks administered,²⁰ or have found changes in objective tests relative to controls but not in physician ratings in clinical populations.^{4,5} Despite the manufacturer's claims of improved memory in healthy adults, we were unable to identify any well-controlled studies that document this claim.

Recently, ginkgo was reported to be beneficial in a sample of patients with dementia.⁴ Mildly to severely demented patients characterized as having either Alzheimer disease or multi-infarct dementia were given either ginkgo (120 mg/d) or placebo for 52 weeks in a randomized double-blind study. The intent-to-treat analysis on 202 patients indicated a 0.1-point decline on the Alzheimer Disease Assessment Scale-Cognitive portion (ADAS-Cog) in the ginkgo group compared with a 1.48-point decline in the placebo group. No subjective differences were reported by either family members or physicians. While provocative, these differences on the ADAS-Cog are significantly smaller than those reported for approved cholinesterase inhibitors in treating patients with Alzheimer disease.¹⁵ Moreover, the failure to find any differences in either physician or family rating raises the is-

Figure 2. Differences (Treatment Group Minus Control) for Performance on Each Test



CVLT indicates California Verbal Learning Test. Data are based on the modified intent-to-treat analysis with 111 participants in the ginkgo group and 108 participants in the placebo group.

Table 3. Companion Response on the Caregiver Global Impression of Change Rating Scale*

Response	No. of Responses (%)	
	Ginkgo (n = 110)	Placebo (n = 106)
1 - Very much improved	0 (0)	0 (0)
2 - Much improved	2 (2)	1 (1)
3 - Minimally improved	31 (28)	35 (33)
4 - No change	77 (70)	70 (66)
5 - Minimally worse	0 (0)	0 (0)
6 - Much worse	0 (0)	0 (0)
7 - Very much worse	0 (0)	0 (0)

*Two companions of participants in placebo group and 1 companion of participant in ginkgo group were not available at week 6 to complete the evaluation.

sue of whether the small difference on the ADAS-Cog is clinically significant.

Despite the paucity of well-controlled studies, ginkgo continues to be marketed and widely used.^{21,22} Sales in the United States reached \$240 million in 1997²³ and more than 5 million prescriptions are written each year in Germany primarily for dementia, cerebral decline, and peripheral arterial insufficiency.¹⁸

Our study has limitations. It is certainly possible that higher doses or longer periods of exposure than used in this study are necessary to detect changes; however, we administered the

compound following the manufacturer's instructions. The manufacturer's label indicates that ginkgo should be administered at a dose of 120 mg/d and that doses of greater than 120 mg show no additional benefit.⁶ This is also the dose suggested by the German Commission E.²⁴ The daily dose in the present study was 120 mg/d. The label also states that a noticeable benefit should be apparent after 4 weeks of usage. The present study evaluated cognition after a 6-week interval. Moreover, there was no indication of a statistical trend toward significance for any of the compounds on any of the measures. Nevertheless, it is possible that longer exposures could produce beneficial effects.

We did not monitor adverse effects in the present study. Although ginkgo is generally characterized as a benign compound,²¹ it is not without adverse effects. Reported adverse effects include bleeding, mild gastrointestinal upset, and headache.²⁵ None of the participants in the present study discontinued treatment due to adverse effects and none spontaneously reported any adverse effects. This finding is generally consistent with studies that did systematically monitor adverse effects.⁴

The issue of quality control has also been raised as a potential source of variance in studies using over-the-counter compounds.²⁶ One limitation of the present study is that we did not analyze the content of the ginkgo used in this study. However, the manufacturer claims that ginkgo "is processed under strict guidelines . . . ensured through extensive quality control."⁶

We recognize the possibility that ceiling effects may have contributed to the nonsignificant findings in the present study. However, we selected tests that are normalized for the age group that we studied and, as such, have an appropriate range of scores. For example, in the Logical Memory WMS-R scale (Logical Memory I), the potential range of scores is 0 to 50. The ginkgo participants in the present study scored a mean of 20.49 (SD, 5.08) and the placebo participants scored a mean of 23.61 (SD, 4.65). Each of these is well below the maximum score of 50. In addition, none of the participants obtained a maximum score on this scale or any of the other scales used in this study.

We also recognize that the method of blinding in this study could have resulted in unblinding for some par-

ticipants. However, the finding that participants taking ginkgo as well as those taking placebo reported in equal proportions taking the active compound ginkgo (71% vs 75%) mitigates this concern.

In summary, this study does not support the manufacturer's claims of the benefits of ginkgo on learning and memory. Treatment over a 6-week period following the manufacturer's dosing suggestions did not produce objective benefit on any of 14 standard neuropsychological tests, nor were any benefits detected in self-report by the participants or observation by a family member or friend.

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Study supervision: Solomon.

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