ORIGINAL ARTICLE

Efficacy of Gingko Biloba Extracted EGb 761® in Treating Primary Tinnitus: A Randomize, Placebo-Controlled, Triple-Blind Clinical Trial

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Background: Primary tinnitus is a common condition that can significantly impair a patient's quality of life. Currently, there is no standardized treatment that can completely cure tinnitus and no studies in Thailand have examined the efficacy of EGb 761® in reducing tinnitus symptoms.

Objective: To study of the efficacy of EGb 761® in treating primary tinnitus compared to placebo and side effects of EGb 761®.

Materials and Methods: The present study was a randomized, placebo-controlled, triple-blind clinical trial of 71 patients aged 20 years and older with primary tinnitus lasting for three months or longer who presented to the Department of Otolaryngology at Burapha University Hospital between July 2022 and May 2024. Divided into two groups, 36 patients received treatment with EGb 761® and 35 received placebo. Data were collected using an 11 point-box scale to assess the loudness and annoyance of tinnitus and tinnitus handicap inventory (THI) to evaluate the severity of its impact. Measurements were taken prior to treatment and in weeks 2, 6, and 12 following treatment initiation.

Results: Patients in both the EGb 761® and the placebo groups showed significant reductions in tinnitus loudness and annoyance scores, as measured by the 11-point box scale and THI, over the 12-week treatment period, with improvements observed as early as week 2. Compared between groups, the EGb 761® group showed significantly lower THI scores in weeks 2, 6, and 12. No serious adverse effects were reported in either group.

Conclusion: Both EGb 761® and placebo were found to reduce the loudness, annoyance, and perceived severity of the impact in patients with primary tinnitus. Significant reductions in scores were observed starting from week 2.

Keywords: Tinnitus; EGb 761®

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Tinnitus is the perception of noise in the ear in the absence of an external sound source. It can be categorized as either primary or secondary. Primary tinnitus is idiopathic and may be associated with sensorineural hearing loss. Secondary tinnitus has a specific, identifiable cause other than hearing loss. Common symptoms of primary tinnitus include ringing, buzzing, or hissing sounds in the ears. Primary tinnitus is often incurable, and there is currently no standard treatment that can completely eliminate the condition[1,2]. In cases where tinnitus significantly impairs quality of life, medication may be prescribed to alleviate its annoyance. These may include vasodilators, anti-anxiety medications, or sound therapy to mask the tinnitus. For patients whose tinnitus does not interfere with daily life, education about the nature of the condition and available management strategies may be sufficient, without the need for pharmacological treatment.

EGb 761® is a standardized dry extract derived from the leaves of Ginkgo biloba. It contains 24% flavonoids, 6% terpenoids, and no more than five parts per million (ppm) of ginkgolic acid. EGb 761® has been used in the treatment of various conditions, including cerebrovascular disease, Alzheimer's disease, dementia, intermittent claudication (ICD), dizziness, and tinnitus[3]. The mechanism of action of EGb 761® is multifactorial. It includes increasing blood flow to the brain and inner ear by enhancing the elasticity of red blood cells and blood vessels, as well as reducing blood viscosity[4]. These actions improve microcirculation and offer neuroprotective effects, potentially reducing the perception of tinnitus.

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However, the results of the previous studies remain inconsistent, and there is a lack of clinical research in Thailand regarding its efficacy in reducing tinnitus symptoms.

Objective

The present study aimed to study the efficacy of EGb 761® in the treatment of primary tinnitus compared with placebo and the side effects of using EGb 761®.

Materials and Methods

The present study was a triple-blind randomized controlled trial that enrolled 71 patients aged 20 years and older with primary tinnitus presenting to the Otolaryngology Department at Burapha University Hospital between July 2022 and May 2024.

Inclusion criteria were symptoms of primary tinnitus in one or both ears of unknown cause lasting for three months or longer, tinnitus loudness and annoyance rated using the 11-Point Box Scale with a score greater than three prior to treatment initiation, and no prior use of EGb 761® or medications in the same class within eight weeks before study enrollment.

Exclusion criteria included a history of hypersensitivity to EGb 761® or adverse reactions to EGb 761® or components of Ginkgo biloba leaves, and pregnancy or breastfeeding.

The present study was approved by the Human Research Ethics Committee of Burapha University (certificate number 077/2565).

The sample size was calculated using the formula for comparing the means of two independent populations, as described by Rosner (2000)[5]. Using a significance level (α) of 0.05 and power of test 0.8. The standard deviation of the 11-point box scale in the EGb 761® group was derived from a study by Procházková et al.[6], which reported a mean score of 5.3 and a standard deviation of 1.3.

In the present study, the minimum expected difference in mean scores between the EGb 761® group and the placebo group was set at 1 unit (Δ=1).

Based on this assumption, the required sample size was calculated to be 27 participants per group. Accounting for an anticipated dropout rate of 30%, the final planned sample size was adjusted to 39 participants per group, resulting in a total of 78 participants.

Seventy-eight patients were enrolled in the present study and randomly assigned into two groups using simple randomization. The study was triple-blinded, the researchers, participants, and research assistants were all blinded to the group allocation. One group of 39 participants received treatment with one tablet of EGb 761® once daily after breakfast. The other group of 39 participants received a placebo tablet identical in shape, color, and size to the EGb 761® tablet.

Data were collected using an 11-point box scale to assess the loudness and annoyance of tinnitus, along with the tinnitus handicap inventory (THI)[7] to evaluate the severity of the impact tinnitus had on patients. Assessments were conducted at baseline, or before treatment, and after the second, sixth, and twelfth weeks of treatment.

Statistical analysis

Baseline clinical characteristics between two groups were performed using chi-square test or Fisher's exact test for categorical data and unpaired t-test for continuous data.

Within-group and between-group comparisons of tinnitus loudness and annoyance scores on the 11-point box scale were analyzed using repeated measures ANOVA with Bonferroni corrected t-test.

Results

Of the 78 patients screened for eligibility, 71 were enrolled in the study, 36 in the EGb 761® group and 35 in the placebo group. One patient in the EGb 761® group and three in the placebo group were lost to follow-up. Additionally, two patients in the EGb 761® group discontinued treatment due to drowsiness and sore throat, while one patient in the placebo group discontinued treatment due to dizziness (Table 1).

Within the treatment groups, significant reductions in tinnitus loudness and annoyance were observed over the 12-week treatment period, as measured by the 11-point box scale and the THI (Figure 1-3). Notably, significant improvements were observed from week 2 in both the EGb 761® group ($p<0.01$) and the placebo group ($p=0.01$).

When comparing data between groups, no significant differences were observed at baseline (week 0) in 11-point box scale scores for tinnitus loudness and annoyance, or in THI scores between the EGb 761® and the placebo groups. Following treatment, no significant differences were observed in loudness and annoyance scores between the groups at weeks 2, 6, or 12. However, the THI scores were significantly lower in the EGb 761® group than in the placebo group at all follow-up time points, which were weeks 2, 6, and 12.

Table 1. Baseline clinical characteristics of each group and comparative analysis

Characteristics	EGb 761® (n=36)	Placebo (n=35)	p-value
Sex; n (%)			0.72
Male	18 (50.0)	16 (45.7)	
Female	18 (50.0)	19 (54.3)	
Age (years); mean±SD	55.06±15.39	56.77±13.82	0.55
Duration of tinnitus (months); mean±SD	13.81±22.13	10.86±10.99	0.77
Hearing level; n (%)			0.61
Normal hearing	20 (55.6)	18 (51.4)	
Mild hearing loss	11 (30.6)	9 (25.7)	
Moderate hearing loss or higher	5 (13.9)	8 (22.8)	
Underlying disease; n (%)	16 (44.4)	13 (37.1)	0.53
DM	2	5	
HT	8	9	
DLP	9	7	
Other	6	4	
Drug allergy; n (%)	4 (11.1)	2 (5.7)	0.42
Penicillin	2	2	
Itraconazole	1	0	
Celecoxib	1	0	

SD=standard deviation; DM=diabetes mellitus; HT=hypertension; DLP=dyslipidemia

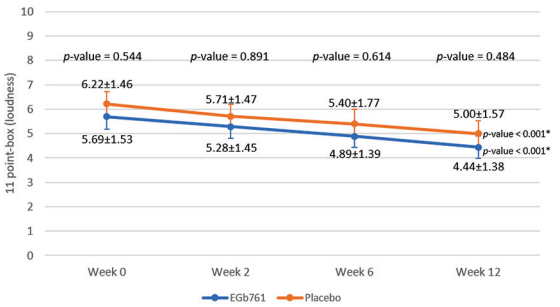

Figure 1. The 11-point-box scale (loudness) scores at week 0, 2, 6, 12 of EGb761® group and placebo group.

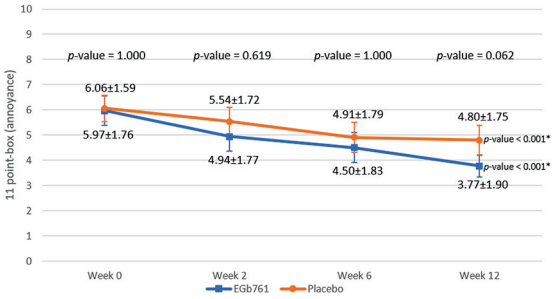

Figure 2. The 11-point-box scale (annoyance) scores at week 0, 2, 6, 12 of EGb761® group and placebo group.

In terms of adverse effects, the most commonly reported side effects were gastrointestinal symptoms, headache, and dizziness. These side effects were mild and not considered serious.

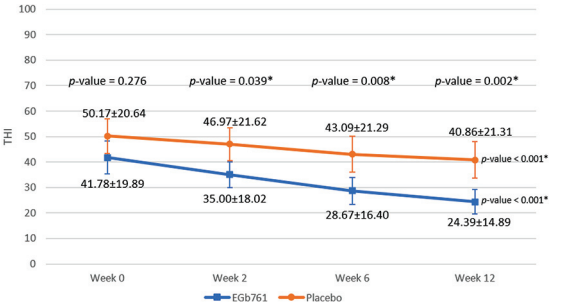

Figure 3. Tinnitus handicap inventory index (THI) at week 0, 2, 6, 12 of EGb 761® group and placebo group.

Discussion

Primary tinnitus is a prevalent auditory symptom that significantly affects quality of life by interfering with hearing, sleep, and emotional well-being. The current study aimed to evaluate the efficacy of EGb 761® compared to placebo in reducing tinnitus loudness and annoyance over a 12-week treatment period. Both treatment groups demonstrated statistically significant improvements in tinnitus symptoms, as measured by the 11-point box scale and the THI. Notably, symptom reductions were observed as early as two weeks into the treatment.

The improvement observed in the placebo group may be explained by the psychological impact of

patient education. Patients in both groups were provided with information regarding the nature and possible causes of tinnitus, which could have contributed to reduced anxiety and better coping mechanisms. This phenomenon, commonly referred to as the placebo effect, has been consistently reported in tinnitus trials and highlights the importance of non-pharmacological interventions such as counseling and reassurance.

Despite this, the EGb 761® group demonstrated greater symptom improvement compared to placebo. Specifically, THI scores in weeks 2, 6, and 12, were significantly lower in the EGb 761® group. These findings indicate that EGb 761® has a more pronounced effect in alleviating the subjective burden of tinnitus.

The results of the present study are consistent with those of Radunz et al.[8] conducted a study comparing EGb 761® and hearing aids in patients with tinnitus and found a significant improvement in patients' self-perception of tinnitus loudness and severity after 90 days of treatment with EGb 761®, hearing aids, or a combination of both. Procházková et al.[6], reported that EGb 761® and pentoxifylline both significantly reduced tinnitus symptoms over a 12-week period. Similarly, Morgenstern & Biermann[9] found that EGb 761® was significantly more effective than placebo in treating tinnitus. In contrast, Polanski et al.[10], and Drew & Davies[11] reported no significant benefit of EGb 761® compared to placebo, highlighting the variability in study designs, dosages, and patient populations across studies.

A potential explanation for the observed benefit in this study may lie in the specific formulation and dosage of EGb 761®, which has been standardized and used in the previous clinical trials. EGb 761® is known to have antioxidant, neuroprotective, and microcirculatory-enhancing properties, which may contribute to symptom reduction in tinnitus patients.

The findings support the use of EGb 761® as a treatment option for patients with primary tinnitus, especially in those whose symptoms persist after initial counseling. An initial approach involving patient education and reassurance is recommended. If symptoms did not improve within two weeks and continued to interfere with daily functioning, EGb 761® may be considered as a cost-effective pharmacological option to enhance patient outcomes.

Limitation

The present study had a short follow-up period of 12 weeks. Long-term efficacy and safety data are still needed. In addition, subjective measures such as THI and self-reported loudness and annoyance may be influenced by individual psychological factors, which should be accounted for in future research using objective assessments.

Conclusion

EGb 761® and placebo were found to reduce the loudness, annoyance, and perceived severity of the impact in patients with primary tinnitus. Significant reductions in scores were observed starting from week 2. No serious adverse events were observed in patients in either group.

What is already known about this topic?

EGb 761® has been used as a therapeutic option for tinnitus, but current clinical evidence supporting its efficacy remains limited.

What does this study add?

Treatment with both EGb 761® and placebo led to improvements in tinnitus symptoms.

Funding disclosure

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Conflicts of interest

The authors declare no conflicts of interest.

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