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Ginkgo Biloba extract: review and assessment of health benefits and potential side effects

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ABSTRACT:

Introduction

Ginkgo biloba (L.) is used in pharmacotherapy as an extract rich in bioactive compounds, which is obtained from its leaves. The improvement of age-associated cognitive decline and quality of life in mild dementia is a well-established use of Ginkgo Biloba extract (GBE) medicines. In Europe, it is also used as complementary therapy for Alzheimer's disease and cardiovascular disorders. Its use also shows promising research outcomes for potential future indications, including in the treatment of tinnitus, age-related macular degeneration, and the prevention of high-altitude cerebral edema.

Aim of the Study

The aim of the study is to present recent findings on Ginkgo biloba extract medicines used in modern pharmacotherapy and its potential side effects, which should be considered during the treatment tailoring process.

Materials and methods

A thorough literature search was conducted in electronic databases, including PubMed, Google Scholar and ScienceDirect for relevant articles. The search terms included "Ginkgo Biloba", "Ginkgo Biloba extract", "GBE", " EGb 761". All retrieved studies were screened for relevance based on their titles, abstracts, and full texts.

Conclusion

Ginkgo biloba extract is commonly used in the management of neurodegenerative diseases in Europe. Moreover, the latest reports indicate that it also has promising effects in the treatment of several conditions of different origins. Pharmaceuticals containing GBE may interact with a variety of medications, in formulations with inadequate quality control or exceeding the recommended therapeutic dose. However, when appropriately integrated into a well-managed pharmacotherapy regimen, they have the potential to positively influence patient health outcomes, thereby enhancing overall therapeutic effects.

Search

Gingko biloba, Ginkgo biloba extract, GBE, EGb 761

INTRODUCTION

In recent years, there has been a noticeable shift in medicine toward combining traditional pharmacotherapy with phytotherapy. Patients are increasingly turning to herbal medicines, often incorporating them into their medication regimens independently. It is good practice for healthcare professionals to be well-informed about the actions of phytopharmaceuticals to safely guide patients through their pharmacotherapy, helping to achieve the health goals set by both parties. With appropriate knowledge of the health benefits of phytopharmaceuticals, as well as their potential adverse effects and interactions, healthcare professionals themselves can recommend these therapeutics to patients as part of their pharmacotherapy.

Elderly individuals commonly incorporate GBE, as it is available over-the-counter, into their therapy to improve cognitive abilities, alleviate memory impairment, and enhance mental function. It is also used to improve the quality of life for patients with mild dementia [1]. Increasingly, healthcare professionals recommend medications containing Ginkgo Biloba extract in the early stages of therapy for these conditions.

Moreover, medications supporting cognitive abilities, including those containing Ginkgo biloba extract, may gain popularity in the coming years due to the growing number of patients diagnosed with neurodegenerative diseases.

AIM OF THESTUDY

Over-the-counter medications containing Ginkgo biloba extract are gaining popularity among both patients and healthcare professionals. The aim of this paper is to evaluate and review the health benefits of Ginkgo biloba extract-based medications, analyze their current clinical applications, and assess their potential adverse effects.

THE STATE OF KNOWLEDGE:

Ginkgo biloba is a source of bioactive molecules with multifaceted effects. It is used in the treatment of various conditions, several of which have well-documented effects in scientific literature.

Ginkgo biloba, considered one of the oldest surviving tree species on Earth, is believed to have originated in eastern China [2], [3] . To obtain Ginkgo biloba extract (GBE), which contains active compounds, both the fan-shaped leaves and seeds are utilized [4], [5] . In Europe, the greatest popularity of GBE has been seen in medications and supplements containing extracts from its leaves, whereas in China, extracts from the seeds of this plant are commonly used [6].

The Ginkgo biloba leaf extract, primarily characterized by flavonol glycosides and triterpenes, is known for its antioxidant and anti-inflammatory properties, as well as its role in enhancement of cognitive function and positive impact on vascular health. Most medicinal extracts contain a specific concentration of flavonoids and terpenoids, which have various health-promoting effects [4], [7]. GBE is available in over-the-counter medications in doses of 80 mg, 160 mg, and 240 mg [1], [4].

Due to its chemical structure and properties, GBE finds application in the pharmacotherapy of age-related diseases. It is important to emphasize that neurodegenerative diseases represent a significant proportion of age-related conditions in the patient population of developed countries [8] . One of the most prevalent neurodegenerative disease is Alzheimer's disease, which is the most common cause of dementia and ranks among the leading causes of death in the United States, according to ongoing statistics [8], [9].

Improvement of age-associated cognitive decline and memory impairment

Age is a contributing factor to the development of neurodegenerative diseases. However, factors such as lifestyle modifications, diet, genetics, and overall health can influence the onset of such conditions. Nevertheless, researchers studying age-related disorders, after analyzing global statistics, estimate that up to 40% of the population over the age of 60 experiences varying degrees of cognitive decline, the prevalence of which continues to rise and progress into more severe disorders [10], [11]. Due to the chemical structure of Ginkgo extract, the most commonly used and well-researched GBE in the treatment of age-associated cognitive decline and memory impairment is the standardized extract EGb761. According to chemical analyses conducted by researchers, it contains approximately 24% flavonoids and 6% terpenes [3] [4]. **S**tudies have been conducted showing that EGb761 can be successfully used in the treatment of dementia associated with neuropsychiatric symptoms [3]. This is significant, as studies have shown that the overall prevalence of neuropsychiatric symptoms was over 40% in individuals with mild cognitive impairment and over 70% in dementia patients [12]. The data indicate that a daily dose of 240 mg of EGb 761 may provide positive effects in these conditions, as studies have shown it enhances the cognitive abilities of patients compared to those who received a placebo [3], [13].

The potential for treating psychiatric disorders with Ginkgo biloba extract

Treatment of psychiatric disorders with Ginkgo biloba extract also appears to be beneficial in patients with mild cognitive impairment. Studies indicate that the use of EGb 761 in this specific group of patients, who are diagnosed with neuropsychiatric symptoms such as depression, can have a positive effect on their mental health [14], [15]. The action of the GBE may be attributed to its antioxidant properties and its ability to improve cerebral circulation.

Potential impact on preventing the development of Alzheimer's disease

Studies have also observed the neuroprotective effect of GBE, which involves reducing the aggregation of amyloid beta, thereby decreasing its toxicity [16]. Recent studies suggest that EGb 761 may influence free cholesterol levels in the bloodstream, which in turn seems to reduce the synthesis of amyloid β [2], [17]. Furthermore, researchers propose GBE may also regulate glucose metabolism by influencing its uptake, protect against mitochondrial damage, and prevent the accumulation of reactive oxygen species, thereby contributing to the inhibition of amyloid formation [2], [18], [19]. Researchers suggest that GBE may serve as an

adjunct to conventional cholinesterase inhibitor therapy in Alzheimer's disease, because it potentially operates through different pharmacological mechanisms [20].

The prevention and treatment of cardiovascular diseases

Researchers suggest that the protective effects of Ginkgo biloba extract on cardiovascular diseases may result from several mechanisms. Due to its antioxidant properties, which stem from the presence of flavonoids and terpenoids, Ginkgo biloba extract reduces the levels of reactive oxygen and nitrogen species, protecting cells from damage [21]. Studies on animal models demonstrate the cardioprotective effects of EGb 761 on the heart muscle cells [22], [23], as well as its protective role against atherosclerosis [24]. Additionally, researchers point to the benefits of the protective action of the GBE on the endothelium, improvement of blood flow through the relaxation of smooth muscle cells in the blood vessel walls, and prevention of the inactivation of secreted nitric oxide [25]. However, studies on larger patient groups are needed to confirm the therapeutic effect of Ginkgo biloba usage in cardiovascular diseases [26].

Relief of discomfort caused by Tinnitus

Tinnitus is the perception of a bothersome sound in the ear or head without an external source. Its etiology differs among patients [27], [28]. Scientists have shown that cochlear damage-induced primary tinnitus may improve, as Ginkgo biloba positively affects vascular perfusion and neuronal metabolism [27]. It has also been demonstrated in studies that patients with cognitive insufficiency report tinnitus differently compared to cognitively healthy individuals. Therefore, the improvement in cognitive function associated with Ginkgo biloba may potentially influence tinnitus reduction in these patients [27], [29].

Prevention of Acute Mountain Sickness and High-altitude Cerebral Edema

Acute mountain sickness (AMS) and high-altitude cerebral edema (HACE) are conditions affecting individuals ascending to high altitudes. These conditions can occur when individuals exceed their current level of acclimatization due to rapid ascent. They may cause symptoms such as headaches, dizziness, nausea, and, in some cases, even hallucinations [30]. There are studies indicating the effectiveness of Ginkgo biloba extract in the prophylaxis of acute mountain sickness; however, its effect has not been found to be statistically significant [31].

Researchers have also analyzed the impact of HACE resulting from AMS. Various studies have explored the potential role of GBE in preventing high-altitude cerebral edema. However, to date, positive effects in alleviating this condition have only been demonstrated in rats. Researchers indicate that this may be associated with the antioxidant properties of GBE and

its ability to suppress caspase-dependent neuronal damage. Further research is needed to determine the effect of the extract in treating this condition in humans [32].

Support in the prevention of age-related macular degeneration

Age-related macular degeneration primarily affects individuals over the age of 55 and can directly lead to vision impairment. It is termed an 'age-related' condition due to its association with the aging process [33]. Studies suggest that Ginkgo biloba may have a positive effect on vision in patients with age-related macular degeneration. However, the author of a review summarizing two randomized clinical trials, highlights that the data are unreliable, as improvements in visual quality were observed in both the treatment and placebo groups. The review emphasizes that, due to its ability to improve blood flow and its antioxidant properties that protect against membrane damage, including in retinal cells, standardized EGb 761 should remain the subject of research for its potential to prevent the progression of age-related macular degeneration (AMD) [34].

Ginkgo biloba extract has a wide range of potential applications beyond the conditions mentioned above. Researchers have noted its potential benefits in conditions such as intermittent claudication [35], angina pectoris [36], [37], glaucoma [38] and reducing glucose and fat levels [39] . However, these findings are based on individual studies that require further confirmation through additional research.

Ginkgo Biloba: Safety and Potential Adverse Effects

Ginkgo Biloba Extract is considered safe and does not show confirmed drug interactions [26]. However, caution should be exercised when prescribing GBE to individuals who are taking anticoagulant medications, as it exhibits antiplatelet activity [3], [40], [41] . Researchers indicate that, due to its properties as a monoamine oxidase (MAO) inhibitor, GBE may produce a synergistic effect when combined with other MAO inhibitors. This is particularly important, as these medications are commonly used to treat conditions such as depression, Parkinson’s disease, and anxiety disorders, which may co-occur in elderly patients using Ginkgo biloba extract [41] . Extracts of Ginkgo biloba may both inhibit and induce cytochrome P450 drug-metabolizing enzymes, which could contribute to unpredictable drug interactions. However, this effect is most commonly observed at doses exceeding the recommended daily limit of 240 mg [26] , or when consumed in poorly standardized formulations that may contain varying amounts of undesired components [6], [41] .

Furthermore, studies indicate that certain unwanted compounds in ginkgo leaves may trigger allergic reactions and result in side effects [41].

Therefore, the use of Ginkgo biloba formulations with inadequate quality control or exceeding the recommended therapeutic dose is strongly discouraged [6], [41].

CONCLUSION

According to the current summary of product characteristics by the European Medicines Agency, over-the-counter medications containing standardized Ginkgo biloba extract are used to support cognitive abilities and mild memory loss [1] . The results of numerous studies provide strong evidence for other potential actions of Ginkgo biloba, which may expand its clinical applications in the future. The unique chemical composition of Ginkgo biloba extract appears to have multifaceted effect [4], [6], [12]. The antioxidant activity, vasodilatory effects on peripheral blood vessels, improvement of peripheral and cerebral circulation, memory support, alleviation of psychiatric symptoms, as well as the potential role in treating brain edema, age-related macular degeneration, and many other conditions, make Ginkgo biloba extract particularly interesting for further study. Therefore, researchers have identified many other diseases in which Ginkgo extract may be used in therapy. It is worth noting that most of these are age-related conditions, which, in our aging society, account for a significant proportion of diseases observed in patients we encounter daily. Moreover, this percentage is expected to continue rising in the coming years [8], [9] . Therefore, further clinical studies should be conducted on various patient groups. This recommendation is further supported by the satisfactory safety profile of Ginkgo biloba extract medications when used at approved doses in pharmacotherapy [40], [41].

DISCLOSURE

Authors' contribution

Conceptualization: JMM and BR;

Methodology: KS and JMM;

Software: AD and MJ;

Check: NK, JMM and MJ;

Formal analysis: NK;

Investigation: BR and KS;
Resources: JMM and KS;
Data curation: NK;
Writing - rough preparation: NK and AD;
Writing - review and editing: KS, AD and MJ;
Visualization: MJ and BR;
Supervision: AD;
Project administration: BR;
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