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ROLE OF GINKGO BILOBA IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

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REVIEW **OPEN ACCESS**

ABSTRACT

Introduction – Attention-deficit Hyperactivity Disorder (ADHD) is a chronic, neurological condition that happens in many children and is defined by a high level of hyperactivity, inattention, and impulsivity that is persistent and debilitating. Currently, the first-line treatment for ADHD is the use of stimulant medicines such as Methylphenidate and Amphetamine, although they have a variety of undesirable side effects, including growth retardation, addiction, and substance misuse. Ginkgo biloba is a traditional herbal medicine that has been used to treat early-stage AD, vascular dementia, and other forms of dementia in the early stages. This paper aims to evaluate the role of Ginkgo biloba as a promising alternative treatment to Attention-deficit hyperactivity disorder.
Methods – The article is made by reviewing and evaluating several literatures that discusses ADHD, ginkgo biloba, and also the role and effectiveness of ginkgo biloba in managing symptoms found in patients with ADHD. The literature used is limited to articles published between 2010 – 2022.
Results – Studies that were reviewed has shown that ginkgo biloba significantly improves the symptoms of patients with ADHD. The improvement is related to ADHD symptoms which is shown by the significant reduction in Parents and Teacher ADHD Rating score.
Discuss – Although ginkgo biloba has shown significant advantage when compared to placebo treatment, it is still inferior compared to stimulant drugs such as methylphenidate. These improvements can be correlated to EGb761's neuroprotective ability and some studies suggests that EGb761 improves neurotransmission particularly in glutamatergic, cholinergic, and dopaminergic systems.
Conclusion – Ginkgo biloba has shown a role in managing symptoms of ADHD in children by improving the symptoms and parent and teacher ADHD rating scale. It is suggested to further evaluate the clinical efficacy, long-term safety, and dose finding of ginkgo biloba in ADHD and possibly, a combination therapy with stimulant medication in future research.

Keywords: *Attention-Deficit Hyperactivity Disorder, ADHD, management, Ginkgo biloba*

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INTRODUCTION

ADHD is a chronic, neurological disease defined by a pattern of one or more instances of persistent inattention, hyperactivity, and impulsivity, which is undesirable or more destructive than similar children of the same age, that leads to dysfunction in many situations, and these behaviors lasted for at least 6 months.[1]

ADHD is a prevalent neurodevelopmental disease in children, with a prevalence incidence of 2 – 7 percent in children of school-age and 5% of the worldwide population.[2] The prevalence of ADHD in Indonesia is unknown at this time. According to Pham et al. research on the incidence rate of ADHD in Vietnam, the incidence of ADHD is 6.7 percent in the 5-7 years age group, around 6.5 percent in the age group of 8-10 years, and around 12 percent in the 11-13 years age group. The incidence of ADHD did not differ significantly between these age groups, however, there was a substantial variation in prevalence between urban and rural locations, with urban children having a 2.2-fold greater incidence of ADHD than in rural children.[3]

Ginkgo biloba is a Japanese, Korean, and Chinese alternative herbal traditional medicine. It has been used as a herbal medicinal for over two millenia and has often been referred to as a "living fossil". For generations, Ginkgo biloba has been used as a traditional Chinese medicine, and research has shown that it has cardiovascular, photoprotective, hepatoprotective, anti-inflammatory, and antioxidant properties.[4] It's often used to treat Alzheimer's disease in its early stages, as well as vascular dementia, peripheral claudication, and vascular tinnitus.[5]

Stimulant drugs like Amphetamine and its formulation and Methylphenidate are considered the first-line therapy for ADHD, although there are concerns about the long-term effects of stimulant medications, as well as substance misuse and dependence.[6] As a result, alternative ADHD drugs are being studied in order to give a more comprehensive approach to ADHD management. As a result, the purpose of this article is to assess Ginkgo biloba's potential as a promising alternative treatment for ADHD.

METHOD

This article used the literature review method by evaluating several literatures that discusses ADHD and the effect of Ginkgo biloba in ADHD patients. The literature that is reviewed in this article is limited to those published between 2010 and 2022.

RESULT

Efficacy of Ginkgo biloba Related to ADHD Symptoms

Shakibaei et al.. found a substantial reduction in parent and teacher evaluation ratings for inattention and hyperactivity over the course of the study (P < 0.001). However, the primary effect of the medication for inattention (P = 0.734) and hyperactivity-impulsivity (P = 0.799) were not significant.[7] When comparing the primary result of the study between the Ginkgo and placebo groups, there is a substantial reduction in both parent assessment rating and teacher assessment ratings of inattention with Ginkgo biloba (P < 0.001). However, there were no discernible differences in hyperactivity and impulsivity ratings in both parents and teachers (P = 0.203).[7] Based on the ADHD-RS-IV parent assessment, the Ginkgo biloba group had a significantly higher clinical treatment response rate than the placebo group (93.5 percent vs 58.6 percent, P = 0.002). However, based on the ADHD-RS-IV teacher evaluation, there was no meaningful difference in treatment response rate between both groups (83.9 percent vs 79.3 percent, P = 0.451)[7]. Both groups' general functions improved significantly after therapy (P 0.001), and there were no meaningful differences between them in the case of CGAS change after medication (P = 0.901).[7]

Salehi et al.. did a study in Iran in 2010 that used double-blind, RCT to assess the effects of treatment between Ginkgo biloba and Methylphenidate groups. The changes in the parent ADHD rating scale for both groups were significant when compared to the baseline (P = 0.005), with the changes in the ginkgo group being -6.52 ± 11.43 (mean ± S.D.) and the changes in the methylphenidate group being -15.92±11.44 (mean±S.D.). 8. Only the methylphenidate group had a significant effect on the Teacher ADHD Rating Score, and there was a noticable difference between both groups with changes at the endpoint compared to baseline for the ginkgo group (-0.84 ± 6.79 (mean ± S.D.)) and methylphenidate group (-14.04 ± 8,67 (mean ± S.D.))[8]. The adverse effects were also investigated, and 10 were discovered during the experiment, all of which were mild to moderate and tolerated. Except for a few side effects such as a decrease in appetite, sleeplessness, and headache, which were noticed more frequently in the methylphenidate group, there was no substantial difference in side effects between the Ginkgo and methylphenidate groups.[8]

Patients reported significant improvement in functioning, as evidenced by the overall score on the 60 item Wender-Utah Questionnaire (P < 0.013) in which the average score prior to the medication was 1.16 and the mean score after ginkgo administration was 0.84, according to a 2010 study in which subjects were given only ginkgo biloba extract Egb761 which was consumed for 4 weeks with 200mg of daily dose and received no other medication.[9]

DISCUSS

ADHD is a widespread and disabling neurodevelopmental disease that affects 3-5 percent of children.[10,11] The existence of a chronic and detrimental level of overactivity, inattention, and impulsivity that lasts for at least 6 months is used to diagnose it.[10,11] Stimulant medicines such as amphetamine and its formulation and methyphenidate are currently the primary Drug of Choice for ADHD, but there are concerns about the pills' negative effects, as well as prejudice around their use, prompting parents to seek out other options.[3,10]

The cause of ADHD is still a source of debate and ongoing research. The original idea of lower function in the brain was based on multiple findings that indicated either the decline of functionality or volume of gray and white matter inside the brain, which leads to cognitive processing, speed processing, motor planning, attention, and other behavioral difficulties seen in ADHD.[12] The prefrontal cortex, caudate, and cerebellum have been identified as the key areas that demonstrate impairments in ADHD, according to recent research. Attention, emotions, behavior, thought, and actions are all regulated by these areas, which are connected by a network of many neurons.[12] For the past decade, ADHD's neurobiological theory has focused on two prominent but not exclusive models. One stresses top-down, regulated processing problems in those with executive functioning, while the other, Sensory/Reward Theory or Bottom-up theory.[13]

The development of executive control systems is reflected in the major measurable cognitive changes that occur throughout childhood. The top-down cognitive process in the higher order that allows for the structuring of behavior through optimal process selection and goal maintenance across time is referred to as executive function. The core problem of ADHD is executive control, which has been a source of debate. One of the most well-developed ideas suggests that response inhibition impairments, which affect the four particular executive functions, are to blame for the disorder's symptoms, such as aberrant behavioral inhibition.[13]

While top-down theories have received the majority of attention in the neurophysiologic theories of ADHD, bottom-up, or Sensory/Reward Theories, have recently seen an upsurge in literature. Positive and negative affectivity as a result of motivated or reward responding are frequently associated with emotional symptoms such as trouble controlling anger, mood, and affect regulation in people with ADHD. While ascending dopamine circuits are important for anticipating rewards, the limbic system, which includes the amygdala, Pre-Frontal Cortex, Anterior Cingulate Cortex, insula and nucleus accumbens or ventral striatum, is also important for processing emotions and motivation.[13] Emotional processes are linked to motivation, which is related to approach when experiencing an event or scenario. Individuals with ADHD are hypersensitive to delayed benefits and tend to give instant rewards disproportionate weight, producing in behavior that is characterized by excessive approach. Aside from their excessive approach, they also

exhibit a failure in avoidance, which enables them to continue to engage in similar actions even when the outcome is negative.[13,14] Dopamine modulates the reward pathway, which comprises the NAc of the ventral striatum, as well as the ACC and orbitofrontal cortical areas, in a similar way to the top-down paradigm. The mesolimbic dopamine pathway, in contrast to the executive function, is the dopamine pathway involved in reward processing.[13,15]

Ginkgo biloba is a traditional Chinese herb that has been utilized in traditional Chinese medicine for generations. The role of ginkgo biloba as a free radical scavenger, a membrane stabilizer, a neuroprotective agent, an antioxidant, and an inhibitor of platelet activating factor through the terpene ginkgolide B5 is thought to be the mechanism of action. Ginkgo biloba contains flavonoids, proanthocyanidines, ginkgolic acid, terpene trilactones, polyflavones, biflavones, and ginkgotoxins. The terpene trilactones (TTL) and flavonoids, which make up 22-27 percent of the standardized Ginkgo biloba extract (GBE), are two significant fractions with distinct pharmacological characteristics. The flavonols quercetin, isorhamnetin, and kaempferol, which are united into at least a single sugar moiety, make up the majority of flavonoids.[14]

Ginkgo biloba standardized extract EGb761 has been found to defend mitochondria from age-related damage and increase mitochondrial activity and metabolism of energy. Although the precise chemical basis of EGb761 is unknown, it has been shown to have neuroprotective effects, including the capacity to diminish amyloid-β (Aβ) aggregation and toxicity. In addition, EGb761 is a polyvalent radical scavenger that increases mitochondrial activity, improves microperfusion, and lowers blood viscosity. Several animal research have also revealed improvements in neurotransmission, particularly in the glutamatergic, cholinergic, and dopaminergic systems.[14,15]

CONCLUSION

In conclusion, usage of ginkgo biloba extract in ADHD patients has shown a significant role in reducing the symptoms experienced by ADHD patients according to the parent and teacher ADHD rating scale. Ginkgo biloba has also shown significant difference compared to placebo treatment, but is still inferior compared to stimulant drugs such as methylphenidate. Since these findings indicate that ginkgo biloba does have a role and certain effectiveness in the management of ADHD symptoms, it is suggested to further evaluate the long-term safety, clinical efficacy, and dose finding of ginkgo biloba in ADHD, and also to evaluate possible combination therapy with stimulant medications in clinical trial research.

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