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Review Article

Herbal Supplements Used in the Treatment of Attention Deficit and Hyperactivity Disorder

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ABSTRACT: Attention-deficit/hyperactivity disorder (ADHD) is a multifactorial neurodevelopmental disorder with cognitive, motor, sensory, emotional and behavioural problems. Treatment of the disorder varies according to age. Behavioural therapy is mainly recommended for cases aged 4-5 years. If no results are obtained or if symptoms persist, medication may be added. The use of medical treatment, particularly in childhood, is viewed with suspicion by families because of some undesirable side effects and the risk of addiction and abuse. In this article, we would like to discuss some medicinal plants that are used in ADHD patients without or in addition to medical treatment, and their safety and efficacy.

Keywords: *herbal supplements, attention-deficit/hyperactivity disorder, plants, natural products*

1 INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental and neuropsychiatric disorder characterised by primary core symptoms including distractibility, inability to sustain attention, irritability, impulsivity and hyperactivity [1,2].

It is a disorder that affects the quality of children's daily lives, disrupts their development and continues into adulthood, and therefore needs to be properly diagnosed and treated. The aetiology of ADHD is multifactorial. It is defined in relation to various genetic, biological, environmental and psychosocial factors. It affects around 3-7% of the child population. It is three times more common in men than in women. People with ADHD usually show symptoms before the age of 7 and these symptoms last for at least 6 months [3-5].

For a diagnosis of ADHD, problems must occur in at least 2 different areas. ADHD has three clinical manifestations: hyperactivity subtype, attention deficit subtype and combined manifestation. Children with ADHD have difficulty focusing and sustaining attention. Behaviours such as difficulty waiting in line, wanting to give an answer before the question is finished, inability to postpone their requests, interrupting the words of speakers, rushing, and as a result of these behaviours, negatively affecting the child's functionality, suggest impulsivity problems [6,7].

Some studies have shown that dietary

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supplements (such as minerals, vitamins, omega-3 fatty acids) given to children with ADHD can reduce the symptoms of the condition. Zinc, which is used as a cofactor in the production of norepinephrine and dopamine, and iron and copper deficiencies are thought to be related to the aetiology or symptoms of ADHD. It is thought that the consumption of foods with a high glycaemic index may be associated with inattentive and hyperactive behaviour, and that behavioural problems may be caused by additives such as preservatives and food colorings [8,9].

Non-drug methods are recommended as first-line treatment for children with ADHD. In cases where these methods do not work, medication is tried. Medications used in treatment are thought to work by reversing neurotransmitter dysfunction in the prefrontal cortex and reducing ADHD symptoms. Medications used to treat people with ADHD include psychostimulants (dextroamphetamine, methamphetamine, amphetamine salts, methylphenidate, methylphenidate transdermal system, dexmethylphenidate, lisdexamfetamine), selective norepinephrine reuptake inhibitors (atomoxetine), alpha-2 adrenergic agents (guanfacine, clonidine), antidepressants, and dopaminergic agents [10].

Current treatment options mainly include a pharmaceutical component, a behavioural component and a psychosocial component, separately or in combination. Concerns about the adverse effects of pharmacotherapy have stimulated research into alternative treatment strategies, including the use of dietary supplements, and the role of nutrition and dietary supplements in the aetiopathophysiology and treatment of ADHD has become a focus of clinical interest and research. In recent years, the use of herbs as adjuvant therapy to conventional pharmacological treatments in the control of ADHD symptoms has been evaluated. In this article, we aim to discuss some of the herbs used in ADHD patients without or in addition to medical treatment, and their safety and efficacy.

2 Herbal Supplements Used

2.1 *Ginkgo biloba* L.

Ginkgo biloba is the oldest tree species, having lived on earth for around 200 million years. The therapeutic use of *Ginkgo biloba* leaves and seeds was first mentioned in Chinese sources 5000 years ago. The health benefits of *Ginkgo biloba* are thought to be due to the polyphenols, flavonoids and ginkgolides it contains. While ginkgolides inhibit platelet activating factor in the metabolism, the antioxidants in its structure protect cells from protein and lipid oxidation by quenching free radicals such as hydroxyl, superoxide and peroxyl radicals in the environment. Clinical studies show that standardised Ginkgo extract can be used to treat poor circulation, heart

disease, eye disease, tinnitus, chronic brain disease, short-term memory loss, brain trauma, depression, dementia and age-related conditions. The primary clinical use of ginkgo is in the treatment of peripheral vascular disease such as brain failure. Ginkgo leaf extract is effective in improving memory and treating multiple sclerosis. It may also help prevent and treat Alzheimer's disease and other types of dementia [11,12].

Various doses of *Ginkgo biloba* were shown to be effective in reducing ADHD symptoms by Uebel-Von Sandersleben et al. (2014), Shakibaei et al. (2015) and Salehi et al. (2010). While mild to moderate side effects were observed in the study by Salehi and Shakibaei, no side effects were observed in the study by Uebel-Von Sandersleben et al. (2014) [13-15]. Again, Chutko et al. (2019) reported that 240 mg of *Ginkgo biloba* daily was effective in reducing symptoms in adult patients with ADHD after 8 weeks of treatment [16].

2.2 *Valeriana officinalis* L.

Valerian (*Valeriana officinalis* L.), a member of the Valeriaceae family, is a flowering plant native to Europe and Asia, used mainly for the treatment of insomnia and anxiety disorders. Valerian species have been reported to have many therapeutic properties such as hypnotic, sedative, anxiolytic, anticonvulsant and antidepressant. In traditional medicine, various herbal formulations of this plant have been recommended for the treatment of hypertension, angina, palpitations, asthma, hepatic colic and menstrual cramps [17]. Razlog et al. (2011) reported that this herb was effective in reducing symptoms in patients with ADHD [18].

2.3 *Bacopa monnieri* L.

It is a perennial herb found in the wetlands of India, Nepal, Sri Lanka, China, Florida, Hawaii and the southern states of the USA. It is of great importance in traditional medicine due to its active compounds such as alkaloids (brahmin and herpestine), saponins (d-mannitol and hersaponin, acid A and monnierin), flavonoids, betulinic acid, stigmastrol, beta-sitosterol and bacopa saponins. In addition to its antidepressant, anti-inflammatory and antimicrobial effects, it is also the most popular neurotonic and memory enhancer. It has also been reported to aid physical processes associated with relaxation and heightened mental awareness, and extracts of this plant have been shown to improve cognitive function in animals. Ethanolic extracts of this plant have been found to increase antioxidant enzyme activity in various brain regions of rats [19,20]. Dave et al. (2014) reported that this plant was effective in improving learning and psychiatric problems and reducing symptoms of ADHD. In this study, a daily dose of 225 mg was given for 6 months [21]. In another study conducted by

Kean et al. (2022), the use of different doses did not result in regression of ADHD symptoms at the end of 14 weeks, while cognitive flexibility, sleep quality and mood improved [22].

2.4 *Matricaria chamomilla* L.

It is native to Eastern Europe and Asia. However, in recent centuries it has spread to central Europe. It was brought to America and Australia with cereals. The largest producers are Germany, Hungary, Russia, Belgium, France, Spain, Greece and Turkey. It is used for coughs and bronchitis, whooping cough, skin inflammations, itching, acne, shingles, skin cracks and tears, muscle contractions of nervous origin, sleep disorders in children, nervous abdominal pain in children, anxiety, as a calming, relaxing, stress-relieving, anti-inflammatory and antispasmodic, antibacterial, antifungal, antiviral, wound healing accelerator, pain reliever and skin care aid [23,24]. In the study of Niederhofer (2009), it was reported that this plant was mildly effective in regressing ADHD symptoms [25].

2.5 *Ginseng* L.

Ginseng has been an important herb in traditional Chinese medicine for thousands of years. The roots and rhizomes of Korean *ginseng* (*Panax ginseng* C.A. Meyer) and American *ginseng* (*Panax quinquefolius* L.) are the main sources of ginseng. *Ginseng* products are generally used to maintain homeostasis and protect the body from physical, chemical and biological influences. The tonic and adaptogenic effects of *ginseng* are thought to reduce the negative effects of the ageing process, support the body by strengthening bodily functions against disease, and increase physical performance and overall fitness in healthy individuals. The predicted clinical and physiological activities of *ginseng* are summarised as increasing endurance against stress, regulating cardiovascular activities, facilitating and improving the learning process, enhancing memory, regulating neuroendocrine system activities, regulating carbohydrate, fat and protein metabolism [26,27]. Lyon et al. (2001) reported that an extract of Panax quinquefolius L led to a reduction in the symptoms of ADHD [28]. In the study by Ko et al. (2014), a significant reduction in attention and hyperactivity scores was observed at the end of 8 weeks in patients given 40 ml of Korean red *ginseng* twice Daily [29]. Lee et al. (2011) reported in their observational study that Korean red *ginseng* extract 1000 mg twice daily for 8 weeks improved attention deficit symptoms [30].

2.6 *Pine Bark Extract* [Pycnogenol (French Maritime Pine Bark Extract)]

It is a plant extract with a flavonoid/polyphenol structure obtained from *Pinus pinaster (Pinus maritima)*, which grows on the south-west coast of France. It is known that pine bark was used in ancient times for

inflammatory diseases, wound healing, haemorrhage prevention, cough syrup and treatment of toothache. Its powerful antioxidant and anti-inflammatory properties have been demonstrated in in vitro, in vivo and clinical studies. Pycnogenol is used orally throughout the world as a dietary supplement to support the treatment of many physiological disorders such as dysmenorrhoea, muscle and spasm pain, attention deficit, hyperactivity, allergies and respiratory disorders, to protect against cardiovascular disease, to control blood sugar levels in diabetics and to improve complications [31,32]. It was observed that catecholamine levels reached normal levels and hyperactivity decreased in children treated with Pycnogenol for attention deficit and hyperactivity. A statistically significant decrease in dopamine levels was observed in 57 children (47 boys, 10 girls, aged 6-14 years) with attention deficit and hyperactivity after administration of 1 mg/kg Pycnogenol for 1 month [33]. Iravani and Zolfagharin (2014) reported that Pycnogenol reduced hyperactivity and improved antioxidant status in children [34]. Trebaticka et al. (2006) reported that 1 mg/kg/day of pycnogenol improved ADHD symptoms after 1 month of treatment [35]. Chovanova et al. (2006) reported that 8-oxo-7,8-dihydroguanine (8-oxoG) levels were increased in children with attention deficit hyperactivity disorder compared to controls. The significant reduction in 8-oxoG levels in children taking pycnogenol supplements suggests that pycnogenol may be an indicator that pycnogenol protects DNA from damage [36].

2.7 *Melissa officinalis* L.

It is a Mediterranean plant from the Labitae family and has a lemon scent. Lemon balm is a perennial herbaceous plant that grows to a height of 60-100 cm. It is a plant that has long been known and used for its pleasant odour. In vitro, in vivo and clinical studies on *M. officinalis*, which has been used for medicinal purposes for many years, have shown that its essential oil and extracts of different polarities have various biological activities. It has been reported to have antiviral, antibacterial, antifungal, antioxidant, antiulcer, antispasmodic, hypolipidaemic, sedative, cytotoxic and protective effects against Alzheimer's disease [37,38]. A study by Katz et al. (2010) reported positive results, particularly in patients with attention deficit. No major side effects related to the plant were reported in this study [39].

2.8 *Crocus sativus* L.

It is a precious plant of the Iridaceae family, known as saffron and used as a spice throughout the world and in Anatolia. The stigmas of C. sativus, the powdered spice made from the dried stigmas, and the plant itself are known as saffron. The dried stigmas of saffron flowers have medicinal properties such as antidepressant, antioxidant, anticarcinogenic,

aphrodisiac, antispasmodic, anti-inflammatory and cholesterol and blood sugar regulating [40,41]. Baziar et al. (2019) compared the efficacy of safron and methylphenidate (MPH) in improving ADHD symptoms. Patients were randomised by weight to treatment with MPH or safron capsules. Symptoms were assessed at baseline, week 3 and week 6 using the Attention Deficit/Hyperactivity Disorder Rating Scale for Teachers and Parents IV (ADHD-RS-IV). The authors found no significant difference in ADHD-RS-IV scores between the two groups at baseline or at the end of the study [42]. Blasco-Fontecilla et al. (2022) reported that in patients given safron and methylphenidate, safron was effective for hyperactivity symptoms and methylphenidate was effective for attention deficit symptoms [43]. Again, Khaksarian et al. (2021) reported lower test scores in patients with ADHD who received safron with methylphenidate [44].

2.9 *Scutellaria baicalensis* L.

The plant, native to China, Korea, Mongolia and parts of Russia and Siberia, is a flowering plant in the Lamiaceae family traditionally used in Chinese medicine. The extract from its roots consists of compounds such as baicalein, baicalin and beta-sitosterol. More than 100 flavonoids have been isolated from the roots, the part used in treatment. Baicalein, baicalein, baicalein, wogonoside, wogonin, scutellarein are the main flavonoids found in the plant and have been extensively studied for many bioactivities. Bioactivity studies have shown that extracts or pure substances isolated from the plant have anti-inflammatory, antibacterial, antiviral, antioxidant, anti-diabetic, anticancer, anti-Alzheimer, neuroprotective and hepatoprotective effects [45,46]. Zhou et al. (2017) reported that baicalin and MPH were able to normalise exercise capacity and impulsivity in animal experiments [47].

2.10 *Passiflora ıncarnata* L.

Passion flower (passiflora incarnata or passion flower) is an herbal supplement historically used to treat anxiety, insomnia, and hysteria. This plant, which was grown specifically in Europe in the last century, is used extensively in complementary medicine. The plant is available in forms used as tea, liquid extract and tincture [48]. In the study conducted by Akhondzadeh et al. (2005) on 34 children with ADHD, no difference was reported between the group receiving passion flower twice a day and the group receiving methylphenidate. In the same study, the potential for side effects was observed to be less in the group receiving passion flower [49].

2.11 *Hypericum perforatum* L.

It is one of the 500 species of the Hypericum family. Although the Mediterranean region is a very rich region for Hypericum species, Asia and America also show significant biodiversity for many endemic Hypericum species. It is especially

widely used in the treatment of patients with mild to moderate depression. This plant, which contains many active ingredients, is also reported to have antibacterial, antinociceptive, neuroprotective, healing dermal activity in some skin disorders, especially wounds and burns, and activity in reducing menopausal symptoms [50,51]. Niederhofer (2010) reported that it is beneficial in improving symptoms in children with ADHD [52]. On the other hand, Weber et al. reported in their study that *H. Perforatum* did not have an effect on reducing ADHD symptoms [53]. Therefore, more studies are needed on the use of this herb in ADHD symptoms.

3 CONCLUSION

In summary, all studies included in this article focused on plants with proven potential against inflammatory processes, positioning them as promising candidates for the treatment of ADHD, especially in patients who may not respond well to conventional medications. The use of plants for medicinal purposes has a long history in human history. However, it is important to note that although natural remedies are generally considered safe, they have not yet achieved status as a standard source of treatment for ADHD. Additionally, there is no established standard animal or in vitro experimental model for using plant-derived compounds to improve ADHD symptoms. Further studies are needed with the plants presented here.

4 AUTHOR CONTRIBUTIONS

Hypotesis: Ö.Ç.; Design: Ö.Ç.; Literature review: Ö.Ç.; Data Collection: Ö.Ç.; Analysis and/or interpretation: Ö.Ç.; Manuscript writing: Ö.Ç.

5 CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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