

Nutrition and Herbal Interventions in Attention Deficit Hyperactivity Disorder

¹Kshama Mundokar, ¹Shraddha Raut, ²Pranali Chandurkar, ³Sneha Gaurkar

¹M. Pharm (Pharmacology), ^{2,3}Assistant Professor, Department of Pharmacology, Dr. Rajendra Gode Institute of Pharmacy, Amravati, India

kshamamundokar18@gmail.com¹, shraddharaut19122000@gmail.com¹

ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is the most prevalent behavioral disorder in children, marked by difficulties with attention, alertness, and executive functions, which result from alterations in neurotransmitter systems such as noradrenaline and dopamine. During childhood, a balanced diet is crucial for healthy growth and development. A recent review highlights a potential link between dietary habits and ADHD. Poor eating habits are positively associated with ADHD symptoms, while healthier diets show a negative correlation. Studies also explore the use of natural products, particularly medicinal plants, in managing ADHD symptoms. These natural compounds have shown promise in mitigating the effects of the disorder. In addition, it has been noted that people with ADHD may be deficient in polyunsaturated fatty acids (PUFAs), zinc, iron, magnesium, and vitamin D. These deficiencies may contribute to the manifestation of symptoms. While dietary adjustments and supplementation with specific nutrients or medicinal plants appear promising in managing ADHD, more robust scientific evidence is needed to establish their efficacy conclusively. Further research is essential to develop clear guidelines on dietary treatments for ADHD management.

KEYWORDS: Attention Deficit Hyperactivity Disorder, Correlation, Diet, Herbs, Nutrition Management

1. INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a persistent ailment typically from which children suffer, characterized by symptoms such as inappropriate levels of activity, difficulty concentrating, impulsivity, and organizational challenges [1]. It is also known as hyperkinetic disorder (HKD) [2]. ADHD is quite common, affecting between 3–7% of kids in school and accounting for a significant portion of referrals to child mental health services [3][4]. The mental health implications of ADHD are profound, particularly in childhood, affecting education and potentially influencing future employment opportunities [5]. These effects can persist into adolescence and adulthood [5]. The history of ADHD dates back over a century, with initial clinical descriptions of hyperactivity in children appearing in 1902. Stimulant medications were first used to treat hyperactivity in 1937 [6]. Originally termed "minimal brain dysfunction," the condition was thought to be linked to subtle neurological issues, although conclusive evidence of specific brain lesions was lacking [7]. Over time, the focus shifted from brain damage theories to recognizing hyperactivity as the primary behavioral issue [7]. The diagnostic criteria for ADHD have evolved through various editions of the Diagnostic and

Statistical Manual of Mental Disorders (DSM). It was renamed attention deficit disorder (ADD) in DSM-III (1980) after being classified as the hyperkinetic reaction of childhood in DSM-II (1968). Subsequent revisions like DSM-III-R (1987) emphasized both inattention and hyperactivity equally. The current DSM criteria, found in DSM-IV (1994) and later editions [8], classify ADHD into three subtypes based on specific symptom patterns:

- (a) predominantly inattentive type
- (b) predominantly hyperactive/impulsive type
- (c) combined type (this includes inattention and hyperactivity/ impulsivity symptoms)

The inattentive type, characterized by difficulty in focusing on tasks and forgetfulness; the hyperactive type, marked by restlessness, impulsivity, and interruptive behaviour; and the combined type, which exhibits features of both. The disorder impacts various aspects of life, including behaviour, self-regulation, emotional control, and academic performance. These challenges can strain relationships, lower self-esteem, and affect social interactions. Despite the increasing prevalence of ADHD and the rise in medication prescriptions like methylphenidate and dextroamphetamine, concerns about their side effects persist among parents and caregivers. Research, such as the Multimodal Treatment Study of Children with ADHD (MTA), continues to explore long-term outcomes and treatment efficacy [9]. ADHD is complex and multifactorial, influenced by genetic predispositions (with heritability estimated at 0.75-0.91) and environmental factors [10][11]. Cognitive deficits are common among individuals with ADHD, with a significant portion experiencing specific learning disabilities in subjects like mathematics, reading, or spelling [12]. Attention difficulties correlate with delays in cognitive development, poorer language skills, and difficulties adjusting in classroom settings [13].

Moreover, there is compelling evidence suggesting that diets rich in specific nutritional groups like fruits, fish, vegetables, and complex carbohydrates can decrease the occurrence and prevalence of various common clinical conditions such as neurodegenerative disorders, cardiovascular diseases, diabetes, cancer, and others [14][15]. Additionally, herbal plants such as *Ginkgo biloba*, *Bacopa monnieri*, *Valeriana officinalis*, *Prunus pinaster* extract, and others contain active compounds that may help prevent certain brain disorders and associated conditions. Preventive or protective agents, including nutraceuticals derived from natural products or herbal formulations, are increasingly used and their market is growing. These agents are believed to have therapeutic efficacy in preventing ADHD and related issues. According to the American Academy of Child and Adolescent Psychiatry (AACAP), specific behaviors must be present in a child before they can be diagnosed with ADHD.

1.1 Symptoms

In children, it's typical to encounter challenges with focusing and behaviour. However, children with ADHD do not naturally outgrow these difficulties. Instead, their symptoms persist, often intensifying and leading to

difficulties at school, home, or in social settings [16][17]. Figure 1 illustrates the symptoms associated with ADHD in both children and adults.

Symptoms of ADHD		
Symptom Category	Teens	Adults
INATTENTION	<ul style="list-style-type: none"> Easily distracted Makes careless mistakes Loses items often Struggles with organization and task completion 	<ul style="list-style-type: none"> Chronic procrastination Easily distracted Poor organization Loses items often Trouble following conversations
HYPERACTIVITY	<ul style="list-style-type: none"> Constantly fidgeting Difficulty sitting still Feels restless Talks excessively 	<ul style="list-style-type: none"> Feels restless Difficulty sitting still Constantly needs to stay busy Multitasks inefficiently
IMPULSIVITY	<ul style="list-style-type: none"> Frequently interrupts Poor self-control, takes risks Acts impulsively Difficulty waiting their turn 	<ul style="list-style-type: none"> Makes quick, impulsive decisions Spends impulsively or takes risks Frequently interrupts Struggles to control temper

Figure 1: Symptoms of ADHD

1.2 Causes and Risk Factors

The exact cause of ADHD remains unclear, and ongoing research continues to explore various factors, as outlined in Figure 2. In addition, Table 1 illustrates the various risk factors which are responsible for development of ADHD. While genetics are likely a significant factor, recent studies have also linked ADHD to environmental exposures such as lead or pesticides, as well as maternal alcohol consumption and smoking during pregnancy. Notably, "poor parenting" does not cause ADHD; but parenting practices might affect a child's capacity for self-regulation. Inconsistent discipline, for example, may make it harder for children to control impulses or maintain focus later in life [18]-[22]



Figure 2. Causes of ADHD

Table 1. Causes and Risk Factors associated with ADHD

Sr No.	Factors	References	
1)	Environmental Factors		
	Maternally related prenatal risk	Foetal exposure to alcohol Foetal exposure to maternal smoking Maternal stress in pregnancy Maternal health in pregnancy Maternal use of illicit drugs	[18][19]
	Pregnancy and birth complications	Bleeding in pregnancy Protracted delivery Low birth weight Intrauterine growth restrictions	[19]
2)	Genetic factors		
	Dopamine Receptor Genes ((DRD4, DRD5) Dopamine transporter gene (DAT1) Gene encoding Catechol O methyl transferase (COMT) Chromosomal anomalies (Fragile X Syndrome)		[20]
3)	Psychological factors		
	Low socioeconomic status Peer victimization Negative Parenting Family discord Intra/interpersonal violence exposure Foster placement		[21][22]
4)	Social media and Television		
	Screen-based media consumption Television watching Internet addiction Internet gaming		[23][24]
5)	Toxins and Diet		
	Toxins	Heavy metals (lead, mercury) Chemicals (Organophosphates) Organic pollutants (pesticides, polychlorinated biphenyls)	[25]-[27]

	Diet	Sugar Artificial food colouring Low levels of zinc, iron, magnesium Low Omega-3-fatty acid levels	[28][29]
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2. PATHOPHYSIOLOGY OF THE DISEASES

The pathophysiology of ADHD involves complex mechanisms that are not yet fully understood. There is evidence that children with ADHD have altered brain structure and function, along with alterations in neurotransmitter levels, particularly dopamine [30]. Executive and cognitive function are severely impaired in people with ADHD [31]. These impairments are traditionally associated with the prefrontal cortex, although recent research implicates broader neural networks, notably the dopaminergic mesolimbic system involved in motivated behaviors, anticipation of outcomes and learning reinforcement [32][33]. It is becoming more well acknowledged that the neurochemical abnormalities associated with ADHD may be sustained by oxidative stress and inflammation-causing neuronal states resulting from etiological variables and disruption in catecholaminergic neurotransmission [34][35]. Studies have shown elevated markers of oxidative and nitrosative stress, coupled with reduced antioxidant levels, in individuals with ADHD [36]. Additionally, dysregulation of mitochondrial function in dopaminergic neurons has been reported, contributing to unregulated manufacturing of reactive oxygen species (ROS) and reactive oxygen nitrogen species (RONS) during ATP production [37][38]. Excessive ROS/RONS can damage neuronal membranes composed of polyunsaturated fatty acids (PUFAs), disrupt apoptotic mechanisms, activate microglia and trigger the release of inflammatory cytokines [39][40]. High concentrations of interleukins that cause inflammation such as IL-6 and IL-13 that cause inflammation have been noted in young ADHD patients, potentially correlating with symptoms of hyperactivity-impulsivity and inattention [41].

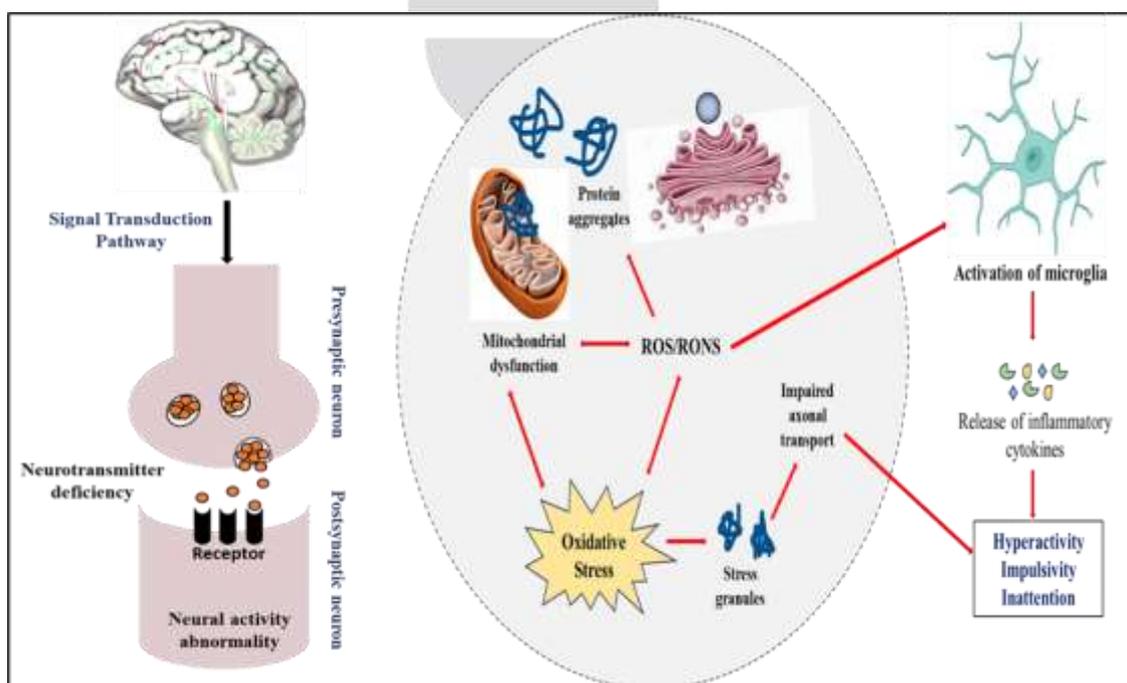


Figure 3. Pathophysiology of ADHD

3. NUTRITION AND ITS ROLE IN ADHD

Nutrition plays a fundamental role in brain development and function, and emerging evidence suggests that diet and nutrient status may influence the onset, severity, and management of ADHD [42]. Several lines of research have highlighted the impact of nutrient deficiencies, dietary patterns, and supplementation on ADHD symptoms[43]. Nutrients are involved in critical brain processes, including neurotransmitter synthesis, brain cell membrane integrity, synaptic plasticity, and inflammatory responses—all of which are crucial for cognitive functions like attention, behavior regulation, and impulse control[44].

The role of nutrition in ADHD is complex, and the relationship between diet and symptoms is not fully understood. However, several key nutritional factors have been identified as influencing ADHD severity, including omega-3 fatty acids, vitamins, minerals, amino acids, and the gut microbiota[45]. This section elaborates on the role of specific nutrients and how deficiencies or imbalances can exacerbate ADHD symptoms, along with the potential benefits of dietary interventions.

3.1 Omega-3 Fatty Acids: Omega-3 polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are crucial for brain health and development[46]. These fatty acids are integral components of neuronal membranes and are involved in maintaining the structure and function of the brain. They are also involved in the modulation of neurotransmitter systems, particularly those related to dopamine and serotonin, which are key players in regulating attention and mood[47].

Omega-3 fatty acids have anti-inflammatory properties and can help reduce brain inflammation, which has been implicated in ADHD[48]. Increased levels of pro-inflammatory cytokines have been found in the brains of children with ADHD, which could contribute to neuronal dysfunction. Omega-3 fatty acid, especially DHA, influence neurotransmitter receptor function, particularly dopamine receptors, which are critical for attention and impulse control[49]. Omega-3 supplementation can improve dopamine transmission in areas of the brain involved in executive functions, including the prefrontal cortex and basal ganglia. Omega-3 fatty acids contribute to the fluidity and flexibility of neuronal membranes, which can enhance synaptic plasticity and neurotransmission, essential for learning, memory, and behavior regulation[50].

Numerous studies have reported lower levels of omega-3 fatty acids in children with ADHD, particularly in red blood cells and plasma[51]. Clinical trials of omega-3 supplementation have shown improvements in both inattention and hyperactivity symptoms. A meta-analysis of randomized controlled trials (RCTs) concluded that omega-3 supplementation, particularly high doses of EPA, could significantly reduce ADHD symptoms, especially in children with lower baseline levels of omega-3s[52].

3.2 Micronutrients (Vitamins and Minerals)

Several vitamins and minerals have been shown to have a direct impact on ADHD symptoms. Deficiencies in these nutrients can contribute to cognitive dysfunction, hyperactivity, and poor attention. Some of the most studied micronutrients include zinc, iron, magnesium, and vitamin D[53].

3.2.1 Zinc: Zinc is essential for the synthesis of neurotransmitters such as dopamine, which is critical for attention, motivation, and behavior regulation. Zinc also plays a role in the structural integrity of neurons and is involved in modulating the expression of certain genes related to brain function[54].

Zinc modulates the activity of dopamine and norepinephrine, neurotransmitters that are often dysregulated in ADHD. Zinc deficiency has been linked to lower levels of dopamine in the brain, which can contribute to symptoms of inattention and impulsivity[55]. Zinc has antioxidant properties and helps to protect neurons from oxidative stress, which can impair cognitive function. Zinc also supports synaptic plasticity, which is crucial for learning and memory[56].

Several studies have reported that children with ADHD tend to have lower serum zinc levels compared to healthy controls. Zinc supplementation has been shown to improve ADHD symptoms in children with low zinc levels, with some studies demonstrating improvements in hyperactivity, impulsivity, and attention. However, more research is needed to determine the optimal dosage and long-term effects of zinc supplementation in ADHD treatment[57].

3.2.2 Iron: Iron is a key mineral involved in the production of dopamine and other neurotransmitters, which are critical for regulating mood and behavior. Iron deficiency, particularly when it affects brain iron levels, has been linked to cognitive impairments, including attention deficits and behavioral problems[58].

Iron is a cofactor in the synthesis of dopamine and other neurotransmitters. Iron deficiency can lead to reduced dopamine receptor sensitivity, which is a key feature of ADHD. Iron plays a critical role in cognitive processes like learning and attention. Iron deficiency can lead to difficulties with working memory, information processing, and attentional control[59].

Iron deficiency is commonly observed in children with ADHD, particularly in the form of low ferritin levels, which reflect iron stores in the body[60]. Studies have shown that children with ADHD who have low iron levels may experience improvements in attention and behavior following iron supplementation[61]. However, more studies are needed to determine the efficacy of iron supplementation, particularly in children with normal iron levels but abnormal dopamine functioning[58].

3.2.3 Magnesium: Magnesium is a vital mineral involved in hundreds of biochemical reactions in the body, including those that regulate nerve function and neurotransmitter release. Magnesium is essential for maintaining proper brain function, and deficiencies can lead to hyperactivity, anxiety, and poor focus—symptoms commonly associated with ADHD[62].

Magnesium regulates the activity of excitatory neurotransmitters like glutamate and inhibits excessive release of dopamine, which is thought to contribute to hyperactivity and impulsivity in ADHD [55]. Magnesium has a calming effect on the nervous system and has been shown to reduce anxiety and hyperactivity. It also plays a role in regulating the hypothalamic-pituitary-adrenal (HPA) axis, which controls the body's stress response [63].

Studies have found that children with ADHD often have lower levels of magnesium, and supplementation has been shown to reduce symptoms of hyperactivity, inattention, and impulsivity [64].

3.2.4 Vitamin D: Vitamin D is essential for brain function, influencing neurotransmitter synthesis and immune system regulation. Vitamin D receptors are present in areas of the brain involved in mood regulation, attention, and cognitive function[65]. Low vitamin D levels have been associated with a variety of neurodevelopmental and psychiatric conditions, including ADHD [66].

Vitamin D is involved in the synthesis of serotonin, a neurotransmitter that influences mood, sleep and cognitive functions like attention [67]. Vitamin D has anti-inflammatory properties and may help regulate the inflammatory processes that are thought to contribute to ADHD symptoms. Neuroinflammation has been implicated in the pathophysiology of ADHD, and vitamin D supplementation may help reduce this inflammation [68].

Research indicates that children with ADHD often have lower levels of vitamin D [69], and several studies have suggested that vitamin D supplementation may help improve symptoms of inattention and hyperactivity, particularly in children with low baseline levels of the vitamin [70]. While the results are promising, more clinical trials are needed to confirm the benefits of vitamin D supplementation in ADHD management.

3.3 Dietary Patterns and ADHD

In addition to specific nutrient supplementation, overall dietary patterns can influence ADHD symptoms. Diets rich in whole foods, including fruits, vegetables, lean proteins and healthy fats, support brain function and can help mitigate symptoms[71]. Conversely, diets high in processed foods, refined sugars, artificial food colourings and preservatives may exacerbate ADHD symptoms[72].

Dietary patterns high in refined sugars and simple carbohydrates can lead to blood sugar spikes and crashes, which may worsen symptoms of hyperactivity and inattention[73]. Research has shown that diets with a high glycaemic load can negatively affect behaviour, especially in children with ADHD. Reducing sugar intake and consuming complex carbohydrates that promote stable blood sugar levels can help mitigate these effects[74]. There is some evidence that food additives, including artificial colourings and preservatives, may exacerbate hyperactivity in children with ADHD. The well-known Feingold Diet, which eliminates artificial colours and preservatives, has shown positive effects on behaviour in some children with ADHD, though the evidence is mixed[75]. A diet rich in anti-inflammatory foods such as fruits, vegetables, whole grains and fatty fish—may help reduce neuroinflammation, which has been implicated in the pathophysiology of ADHD[76]. The Mediterranean diet, for example, which is high in omega-3 fatty acids and antioxidants, has been associated with improved cognitive function and behavior in children with ADHD[77].

3.4 Probiotics

Intestinal microbiota and probiotics have been shown to influence brain activity, behaviour, and mental health[78][79]. As a result, there is expanding interest in investigating the influence of gut microbiota and the gut-brain axis on the development of ADHD[80]. Animal studies suggest that gut microbiota could potentially

be a target for managing ADHD[81]. According to research, the gut microbiota of people with ADHD differs from that of people without the disorder, with certain bacterial taxa being more common and others being less abundant[82]. Nevertheless, currently available research does not completely understand the microbiome-mediated mechanisms underlying ADHD or identify particular microbiome biomarkers for the illness. Nevertheless, studies that only look at the taxonomic makeup of the microbiota may not be sufficient and should be enhanced by looking at the molecular functions of microbes or genetic variations among subspecies[83].

4. HERBAL HERITAGE IN MANAGEMENT OF ADHD

Medicinal plants with cholinergic effects and memory-enhancing properties have garnered attention in both preclinical and human studies[84]. Ayurvedic medicine has contributed several lead compounds that are currently undergoing clinical trials[85]. These plants and their extracts have shown promise in managing various conditions including multiple sclerosis (MS), schizophrenia, stroke, ADHD and others [86]-[89].

As the incidence of neurological disorders increases, medicinal plants are gaining popularity due to their perceived lower side effects compared to synthetic treatments and their potential to meet medical needs effectively. Numerous studies have highlighted the efficacy of various medicinal plants in treating ADHD. Examples include *Passiflora incarnata* (passionflower), *Primus vulgaris* (ginseng), *Pinus pinaster* (French maritime pine bark extract), *Ginkgo biloba*, *Valeriana officinalis* (valerian), *Hypericum perforatum* (St. John's wort), *Crocus sativus* (saffron), *Bacopa monnieri*(brahmi), *Matricaria chamomilla* (chamomile), *Prunus dulcis* (almond), *Rehmannia radix* (Chinese foxglove root), *Ziziphus jujuba* (Chinese date), *Panax ginseng* (Asian ginseng), *Acorus calamus* (sweet flag), and many others. Table 2. Herbs and their formulation in management of ADHD provides detailed information on these plants' abilities to improve ADHD symptoms, along with the active ingredients responsible for their effects.

Table 2. Herbs and their formulation in management of ADHD

Sr. No.	Herbs	Active Constituent	Dosage Form	Effect	Ref.
1.	<i>Passiflora incarnata</i> 	Apigenin, Luteolin, Quercetin, Kaempferol	Tablets	Increase sleep quality and cognitive function	[90]
2.	<i>Primus vulgaris</i> 	Antioxidants Polyphenols	Capsule (Efamol)	Improves accuracy of psychomotor function	[91]

3.	<p><i>Pinus pinaster</i></p> 	Pycnogenol	Capsule	Improve attention, impulsivity and decrease plasma lipid peroxidation level	[92]
4.	<p><i>Ginkgo biloba</i></p> 	Ginkgolide B	Capsule, Enteric coated tablet	Improves memory	[93] [94]
5.	<p><i>Valeriana officinalis</i></p> 	Hydroxy Valeranic acid, Volvalerenone A	Mother tincture	Improves the cortical processing of attention and alertness	[95]
6.	<p><i>Hypericum perforatum</i></p> 	Hypericin, Hyperforin	Capsule	Boosts the memory	[96]
7.	<p><i>Crocus sativus</i></p> 	Picrocrosin, Safranal, Crocetin	Capsule	Controls hyperactivity and impulsivity	[97]
8.	<p><i>Bacopa monnieri</i></p> 	Bacopaside I	Capsule	Reduces restlessness	[98]
9.	<p><i>Matricaria chamomilla</i></p> 	Levomenol	Tablet	Improves attention and controls hyperactivity as well as impulsivity	[99]
10.	<p><i>Prunus dulcis</i></p> 	Amygdalin, Prunasin	Syrup	Increases essential unsaturated fatty acid level	[100]

11.	<i>Rehmannia radix</i> 	Catalpol	Tonic	Elevates Brain-Derived Neurotropic Factor and attenuates neural apoptosis	[101]
12.	<i>Ziziphus jujuba</i> 	Mahdia, Mahres, Sfax	Syrup or Capsule	Reduce stress and protects from neuronal damage	[102]
13.	<i>Panax ginseng</i> 	Ginsenoside	Capsule (Softgel)	Reduce stress and improve concentration	[103] [104]
14.	<i>Acorus calamus</i> 	β -asarone	Capsule	Neuroprotective and antideementia agent	[104]

5. CONCLUSION

In this study, we thoroughly explored the potential therapeutic benefits of medicinal plants and the use of dietary supplements in managing ADHD. Despite the vast amount of information available on this complex condition, symptom management remains the primary focus. There is compelling evidence supporting the effectiveness of dietary supplements such as omega-3 fatty acids, vitamins, and other micronutrients in alleviating ADHD symptoms. Additionally, melatonin has shown promise in treating sleep-onset insomnia in individuals with ADHD. This review includes guidelines for the appropriate use of dietary supplements in ADHD treatment. Globally, significant research efforts are dedicated to identifying effective therapies for ADHD. Herbal therapy is emerging as a potential treatment option due to its potential to reduce symptoms and potentially slow the progression of the disorder. Numerous herbs and plants, including *Prunus dulcis* (almond), *Rehmannia radix* (Chinese foxglove root), *Ziziphus jujuba* (Chinese date), *Panax ginseng* (Asian ginseng), *Hypericum perforatum* (St. John's wort), *Bacopa monnieri* (brahmi), *Pinus vulgaris* (pine), *Pinus pinaster* (Pine bark extract), *Valeriana officinalis* (valerian), *Ginkgo biloba*, *Crocus sativas* and *Passiflora incarnata* (passionflower), have been chemically analyzed, with some currently undergoing clinical trials. While there are many nutritional and herbal supplements commonly used for ADHD, ongoing research is essential because the precise and universally effective treatment for ADHD remains uncertain. This study contributes to understanding the management of ADHD through nutrition and herbal approaches, yet further research is crucial for identifying optimal therapies.

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