PUMPKIN SEEDS (*CUCURBITA PEPO*) AS A POTENT NUTRACEUTICAL FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): AN INTEGRATIVE REVIEW FROM PEDIATRIC NEURO-DEVELOPMENTAL PERSPECTIVE

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Abstract
Background-Attention-Deficit/Hyperactivity Disorder (ADHD) is a common childhood neurodevelopmental disorder defined by persistent inattention, impulsivity, and hyperactivity, which impair academic, social, and emotional functioning. Although pharmacological treatments such as stimulants and atomoxetine are effective, long-term use often leads to adverse effects along with adherence challenges. Concerns about neurodevelopmental safety have also emerged. As a result, interest is growing in complementary nutritional strategies and functional foods to support neurocognitive health safe fats. Methods-Pumpkin seeds (*Cucurbita pepo*) are a nutrient-dense nutraceutical containing zinc, magnesium, iron, omega-3 fatty acids, tryptophan, phytosterols, tocopherols, and polyphenols. These micronutrients and bioactive compounds help modulate neurotransmission, neuroplasticity, oxidative balance, sleep, and immune function. Evidence shows that children with ADHD frequently have deficiencies in zinc, magnesium, iron, and omega-3 fatty acids, which correlate with symptom severity and treatment response. Result-Ayurveda relates ADHD to conditions such as Vata-dominant Manasika Vikara, Dhee-Dhriti-Smriti Vibhramsha, and Rajas-Tamas prakopa, all involving impaired cognition, self-control, and behaviour. Pumpkin seeds are considered to enhance cognition, promote nourishment and strength, and support vitality due to their healthy fats, nutrients, and antioxidants. Discussion-his review integrates biomedical evidence and Ayurvedic perspectives to assess the rationale, mechanisms, safety, dosage, and practical use of pumpkin seeds as an adjunct nutraceutical for pediatric ADHD

KEYWORDS: ADHD, brain-gut axis, Pumpkin seeds, Nutraceuticals, Medhya Rasayana, Pediatric neurodevelopment, Micronutrients

1. INTRODUCTION
Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic neurodevelopmental condition affecting 5–8% of children globally.(1-3)Diagnoses are increasing in low- and middle-income countries due to greater awareness and access. ADHD is defined by inattention, hyperactivity, impulsivity, emotional dysregulation, executive dysfunction, and poor social

integration. Longitudinal studies indicate that symptoms persist into adolescence and adulthood for 50–60% of individuals, increasing the risk of academic underachievement, substance abuse, psychiatric comorbidities, and social and economic difficulties.(4) ADHD neurobiology involves dysregulation of the dopaminergic and noradrenergic pathways, primarily in the prefrontal cortex, basal ganglia, and cerebellum. Impaired synaptic pruning, neuroinflammation, oxidative stress, and altered neuroplasticity are also present (5,6). Genetic susceptibility interacts with environmental influences such as prenatal stress, nutrient deficiencies, toxic exposure, premature birth, and early adversity. (7)
Pharmacological treatment is the primary approach for symptom control, but stimulant drugs can cause appetite suppression, sleep disturbances, irritability, heart problems, and growth delays. Long-term adherence is often poor, especially in younger children. These difficulties have increased interest in nutraceuticals, dietary interventions, and integrative pediatric approaches that support neurodevelopment with fewer adverse effects.(8)
Pumpkin seeds (*Cucurbita pepo*) have long been used as food and medicine in Asia, Europe, and the Middle East. They are now recognised for their neuroprotective, metabolic, and immunomodulatory properties. (121) Their rich micronutrient profile addresses nutritional deficits often observed in children with ADHD.
Ayurveda classifies pediatric neurobehavioral disorders as Manasika Vikara and stresses early Rasayana use to strengthen cognitive function and support the nervous system. (122) Incorporating pumpkin seeds into a combined Ayurvedic and biomedical approach may supply valuable, evidence-based options for integrative pediatric care.

2. Botanical Identity and Phytochemical Profile of *Cucurbita pepo*

2.1 Botanical Description

- **Family:** Cucurbitaceae
- **Genus:** *Cucurbita*
- **Species:** *Cucurbita pepo*
- **Common names:** Pumpkin seed, kushmanda, Kaddu beej
- **Part used:** Mature dried seeds (Pumpkin Seed Kernels)

The seeds are flat, oval, greenish kernels encased in a white fibrous hull. They are traditionally consumed roasted, powdered, or cold-pressed for oil extraction. (29-31)

2.2 Nutritional Composition

Pumpkin seeds contain polyunsaturated fatty acids (linoleic and α-linolenic acids), phytosterols (β-sitosterol), tocopherols (γ-tocopherol), carotenoids, phenolic acids, and flavonoids. These compounds contribute to the seeds' antioxidant, anti-inflammatory, and neuroprotective activities [29,32–38]. Mineral profiling reveals high concentrations of magnesium, zinc, iron, phosphorus, and copper. These minerals support neurometabolic and enzymatic functions [34,35]. Amino acid analysis shows substantial levels of tryptophan, arginine, glutamic acid, and leucine, which enhance neurotransmitter biosynthesis and protein turnover [34].
Cold-pressed pumpkin seed oil is oxidatively stable and retains high tocopherol content, providing membrane protection and resistance to lipid peroxidation [29,36]. These qualities support classifying pumpkin seeds as a functional nutraceutical with diverse health benefits.
Pumpkin seeds contain approximately:

- **Protein:** 25–30%
- **Lipids:** 45–50% (rich in polyunsaturated fatty acids)
- **Dietary fibre:** 6–8%
- **Minerals:** Zinc, magnesium, iron, phosphorus, copper
- **Vitamins:** Vitamin E (tocopherols), B-complex
- **Phytochemicals:** Phytosterols, carotenoids, phenolic acids, flavonoids

The detailed description of nutrients present in pumpkin seeds along with their approximate content and scientific value mentioned in Table 1

Table 1. Nutritional Profile of Pumpkin Seeds per 100 g (SOURCE: FDC, USDA, nut and seed products, FDC id 170188, 2019)

Component	Approximate Content	Neurofunctional Relevance
Energy	559 kcal	Caloric support in undernourished children
Protein	30 g	Neurotransmitter synthesis
Total fat	49 g	Neuronal membrane integrity
Omega-3 fatty acid	0.1–0.3 g	Anti-inflammatory, neuroplasticity
Zinc	7–8 mg	Dopamine metabolism
Magnesium	530 mg	NMDA receptor regulation
Iron	8–9 mg	Myelination
Tryptophan	0.57 g	Serotonin synthesis

Vitamin E	2–3 mg	Antioxidant potential

2.3 Ayuvedic pharmacodynamics (*Rasa – panchak*):
The illustrated and detailed pharmacodynamics as per classical Ayurvedic literatures along with their therapeutic interpretation explained in Table 2

TABLE 2: Ayurvedic Pharmacodynamics (Rasa- Panchak) with scientific relevance

Parameter	Description	Therapeutic Interpretation	Citation
Rasa (Taste)	Madhura (Sweet); mridu Kashaya (Astringent – mainly seeds)	Brimhana, Balya, Ojas-vardhana; supports Majja Dhatu nourishment and cognitive stability	[54,55]
Guna (Qualities)	Guru (Heavy), Snigdha (Unctuous)	Dhatu Poshana, Vata stabilisation, neuronal membrane support	[54–57]
Veerya (Potency)	Sheeta (Cold)	Pitta shamana, neurocalming, anti-inflammatory effect	[57,60]
Vipaka (Post-digestive effect)	Madhura Vipaka	Rasayana action, tissue regeneration, immunity enhancement	[54,59,60]
Prabhava (Specific action)	Brimhana, Balya, Krimighna (seed), functional Medhya	Strength promotion, neuroprotection, gut health support	[55,59–62]
Dosha Karma	Vata–Pitta shamana; Kapha may increase if excessive	Autonomic stability, calming effect	[54–56]

3. ADHD Pathophysiology and Nutritional Dysregulation
3.1 Neurotransmitter Imbalance
Dopamine deficiency in mesocortical circuits impairs attention regulation, working memory, and impulse control. Zinc acts as a cofactor for enzymes involved in dopamine synthesis. It also modulates dopamine transporter expression.(9)

3.2 Excitatory Neurotoxicity
Low magnesium raises glutamate activity, leading to hyperactivity and poor emotional control [10].

3.3 Oxidative Stress
Elevated malondialdehyde and reduced glutathione levels are seen in ADHD groups. This implies elevated oxidative neuronal injury.(11)

3.4 Gut–Brain Axis
New data connect altered gut microbiota in ADHD to neuroimmune signalling and micronutrient absorption [12].

4. Ayurvedic Conceptualisation of ADHD
In Ayurveda, behavioural and cognitive disorders are categorised under Manovikara and Unmada-Apasmara spectrum. (54-57) ADHD symptoms correlate with:
- **Vata Prakopa:** Hyperactivity, restlessness, impulsivity
- **Raja's dominance:** Agitation, irritability
- **Tamas dominance:** Inattention, dullness
- **Dhee-Dhriti-Smriti Vibhramsha:** Impaired intellect, memory, executive function(61-64)

Neurodevelopmental vulnerability reflects Ojas kshaya, Majja dhatu dushti, and impaired Agni. (54-56) These factors lead to inadequate brain nourishment. (63-65) Medhya Rasayana therapy seeks to improve cognition, stabilise nervous function, improve neurotransmission, and strengthen neuroplasticity (59,62,101)
The multiple spectrum of symptoms in ADHD has been scientifically correlated with the lakshana (sign-symptoms) mentioned in classical ancient Ayurvedic literatures.the detailed description has been mentioned in Table 3.

Table 3. ADHD Symptom Correlation with Ayurvedic Concepts

ADHD Domain	Biomedical Feature	Ayurvedic Correlations
Inattention	Poor executive function	Dhee Vibhramsha
Hyperactivity	Motor overactivity	Vata Prakopa
Impulsivity	Poor inhibition	Rajas Vriddhi
Emotional dysregulation	Mood instability	Manodosha imbalance
Sleep disturbance	Circadian dysregulation	Vata-Pitta imbalance

5. Pumpkin Seeds as Medhya Rasayana

Pumpkin seeds exhibit:

- **Snigdha Guna:** Supports neuronal membrane integrity and synaptic lubrication through lipid enrichment [29,34,37]
- **Madhura Rasa:** Contributes to Brimhana and Balya effects, promoting tissue nourishment and anabolic support [54,55].
- **Sheeta Virya:** Provides autonomic stabilisation, beneficial in hyperexcitability states [57,60].
- **Rasayana Karma:** Facilitates cellular rejuvenation, antioxidant defence, and neuroprotection [31–38,66–68].
- **Ojas-vardhana:** Enhances immune–neuroendocrine stability and resilience against stress-mediated neurotoxicity [60,101].

The lipid content of pumpkin seeds supports Majja Dhatu, and their micronutrients help maintain Agni and neuronal metabolism.

6. Molecular and Neurobiological Mechanisms of Pumpkin Seeds in ADHD

Pumpkin seeds exert multimodal neurobiological actions through synergistic micronutrients and phytochemicals that directly target the pathophysiology of ADHD. (123)

6.1 Zinc-Mediated Dopaminergic Modulation

Zinc is concentrated in synaptic vesicles of glutamatergic neurons and modulates dopamine transporter (DAT) activity. Zinc deficiency reduces dopamine in the prefrontal cortex, impairing working memory and inhibitory control. Clinical studies show lower serum zinc levels in children with ADHD compared to controls, with an inverse correlation between zinc status and hyperactivity scores. (16,17) Pumpkin seeds provide bioavailable zinc in organic complexes, supporting dopamine synthesis, vesicular storage, and receptor responsiveness. Zinc also modulates melatonin synthesis by regulating pineal gland function, thus indirectly improving sleep control in children with ADHD.(18)

Ayurvedic correlation: Zinc supports Majja Dhatu poshana, stabilises Vata, and improves Smriti and Dhee—core objectives of Medhya Rasayana.

6.2 Magnesium and Neuronal Responsiveness Control

Magnesium blocks the NMDA receptor channel. This prevents excessive calcium influx and excitotoxicity. Magnesium deficiency increases neuronal firing rates, leading to hyperactivity, irritability, and poor affective regulation. Several pediatric trials show behavioural improvement after magnesium supplementation, especially when combined with vitamin B (19,20). Pumpkin seeds contain one of the highest natural magnesium densities among edible foods, offering sustained replenishment. (21)

Ayurvedic correlation: Magnesium's calming effect is consistent with Vata shamana, improving Chitta Sthirata and sleep quality.

6.3 Omega-3 Fatty Acids and Neuroplasticity

Pumpkin seeds contain alpha-linolenic acid (ALA), which can be partially converted to EPA and DHA. Omega-3 fatty acids regulate neuronal membrane fluidity, synaptic transmission, neuroinflammation, and gene expression related to neurodevelopment. Meta-analyses show modest but consistent improvement in attention and executive function following omega-3 supplementation in ADHD [22,23].

Ayurvedic correlation: Unsaturated lipids support Sneha Guna, nourish Majja Dhatu, and enhance Ojas.

6.4 Tryptophan and Serotonergic Balance

Tryptophan is an essential aromatic amino acid serving as the primary precursor for serotonin and melatonin synthesis, neurotransmitters that regulate mood stability, impulse control, circadian rhythm, and sleep architecture [42]. Altered serotonergic signalling has been implicated in emotional dysregulation, aggression, and sleep disturbances commonly observed in children with ADHD [44–46].

Pumpkin seeds are among the richest plant-based dietary sources of tryptophan, providing about 0.5–0.6 g per 100 g of seeds, which may enhance central serotonin availability through increased plasma tryptophan ratios [34,42]. Dietary tryptophan intake has been shown to improve sleep onset latency and sleep quality, indirectly supporting attention regulation and behavioural stability among pediatric populations [96,97].

Adequate tryptophan availability supports melatonin synthesis in the pineal gland, improving circadian entrainment and reducing evening hyperarousal often seen in ADHD [46].

Ayurvedic correlation:

Tryptophan-mediated serotonergic stabilisation supports Manas Prasadanam, promotes Sattva Guna, and enhances Nidra quality, in accordance with Medhya Rasayana objectives.

6.5 Antioxidant and Anti-inflammatory Activity

Pumpkin seed polyphenols, tocopherols, and carotenoids reduce lipid peroxidation, suppress NF-κB signalling, and enhance antioxidant enzyme activity. ADHD patients show elevated oxidative biomarkers, suggesting therapeutic relevance [24–26].

Ayurvedic correlation: Detoxification and Rasayana rejuvenation, improving Ojas.

Nuutrients present in pumpkin seeds along with their molecular actions relevant to ADHD with probable Ayurvedic correlation has been mentioned in detail in Table 4.

Table 4. Mechanistic Mapping of Pumpkin Seed Nutrients with ADHD Pathways

Nutrient	Molecular Action	ADHD Benefit	Ayurvedic Correlation
Zinc	DAT regulation	Attention improvement	Majja poshana
Magnesium	NMDA blockade	Hyperactivity reduction	Vata shamana
Omega-3	Synaptic plasticity	Executive function	Sneha guna
Tryptophan	Serotonin synthesis	Sleep & mood	Manas prasada
Polyphenols	Antioxidant	Neuroprotection	Rasayana

7. Experimental and Clinical Evidence

7.1 Preclinical Studies

Animal studies show that pumpkin seed extract improves memory, reduces anxiety-like behaviour, and protects against oxidative neuronal injury. Neuroprotective effects have been observed in models of neurotoxicity, ischemia, and metabolic stress [27–29].

7.2 Clinical Evidence for Constituent Nutrients

Although direct pumpkin seed trials in ADHD are limited, constituent nutrient trials provide strong indirect evidence:

- **Zinc trials:** Reduction in hyperactivity and impulsivity scores [30–32].
- **Magnesium trials:** Improved attention span and emotional control [33].
- **Omega-3 trials:** Augmented cognitive performance and lessened inattention [34–36].
- **Iron trials:** Improved mental processing in iron-deficient ADHD children [37].

7.3 Dietary Pattern Studies

Mediterranean and whole-food dietary patterns with seeds and nuts correlate with lower ADHD symptom severity [38].

8. Integrative Clinical Application Framework

Pumpkin seeds may be used as:

- Adjunctive therapy alongside pharmacotherapy
- Early preventive intervention in high-risk children
- Nutritional rehabilitation in undernourished ADHD children

9. Dosage, Formulation, and Pediatric Safety

9.1 Recommended Dosage (29,33,34,51)

- **Whole seeds:** 10–20 g/day
- **Powder:** 2–5 g/day
- **Oil:** 2–5 mL/day

DISCUSSION

This review integrates emerging nutritional neuroscience evidence with classical Ayurvedic principles to evaluate pumpkin seeds (*Cucurbita pepo*) as a potential adjunctive nutraceutical for pediatric Attention-Deficit/Hyperactivity Disorder (ADHD). ADHD is progressively acknowledged as a multifactorial neurodevelopmental disorder involving dysregulated dopaminergic and noradrenergic neurotransmission, impaired cortical maturation, oxidative stress, neuroimmune activation, gut–brain axis perturbation, and nutritional deficiencies [1–7,21–28]. While pharmacological therapy remains effective for symptom control, concerns regarding adverse effects, long-term neurodevelopmental safety, and observance continue to drive interest in complementary nutritional strategies [8,51,52].

Pumpkin seeds uniquely combine zinc, magnesium, iron, omega-3 fatty acids, tryptophan, tocopherols, phytosterols, and polyphenols in a natural food matrix [29–38]. This nutrient synergy directly targets multiple biological vulnerabilities implicated in ADHD pathophysiology.

Micronutrient Deficiency Correction and Cognitive Optimisation

Multiple clinical studies have demonstrated reduced serum zinc, magnesium, and iron levels in children with ADHD, with inverse correlations between micronutrient status and symptom severity [11–17]. Zinc plays a key role in dopamine synthesis, synaptic modulation, and melatonin metabolism [39,40]. Randomised controlled trials have demonstrated that zinc supplementation reduces hyperactivity and impulsivity, particularly in zinc-deficient populations [11,12].

Magnesium deficiency increases neural excitability by diminishing NMDA receptor blockade, leading to behavioural dysregulation and sleep disturbance [15,41]. Magnesium supplementation has been shown to improve attention and emotional control in pediatric ADHD cohorts [16]. Iron deficiency impairs myelination and monoamine neurotransmission, producing cognitive slowing and attentional deficits [13,92].

Pumpkin seeds provide all three minerals in bioavailable forms, conceivably offering sustained physiological repletion without the adverse effects associated with high-dose pharmacological supplementation [34,69–71]. From an Ayurvedic perspective, micronutrient deficiency reflects Agnimandya and Dhatukshaya, particularly of Majja Dhatu, resulting in Vata Prakopa and cognitive instability [54–57,61–65].

Neurotransmitter Regulation and Behavioural Stability

Dopaminergic dysfunction within the prefrontal cortex remains central to ADHD neurobiology [4,5]. Zinc modulates dopamine transporter activity and receptor responsiveness, consequently enhancing synaptic efficiency [39,40]. Magnesium stabilises glutamatergic neurotransmission and prevents excitotoxicity [41]. Tryptophan serves as a precursor for serotonin and melatonin, influencing impulse control, affective regulation, and sleep architecture [42,44–46].

Omega-3 fatty acids regulate neuronal membrane fluidity, synaptic plasticity, and neuroinflammatory signalling [43,94]. Meta-analyses demonstrate modest but consistent improvements in attention and executive function following omega-3 supplementation in children with ADHD [18,111,112]. The integrated delivery of these neuroactive substrates through pumpkin seeds may generate cumulative neuroregulatory benefits.

Ayurvedically, neurotransmitter equilibrium corresponds to Sattva dominance and Manas Prasadanam, enhancing Dhee, Dhriti, and Smriti—core objectives of Medhya Rasayana therapy [59–62].

Oxidative Stress, Neuroinflammation, and Neuroprotection

Children with ADHD demonstrate elevated oxidative biomarkers and altered inflammatory cytokine profiles, showing a contributory role of neuroimmune dysregulation [21–25,113,114]. Oxidative stress may impair synaptic plasticity, neurotransmitter turnover, and neuronal maturation [66–68].

Pumpkin seed polyphenols, tocopherols, and phytosterols exhibit potent antioxidant and anti-inflammatory activity, reducing lipid peroxidation and suppressing inflammatory signalling pathways [31–38,87,107]. Experimental studies verify neuroprotective effects of pumpkin seed oil against oxidative neuronal injury [31,32,38].

In Ayurveda, oxidative imbalance parallels Ama accumulation and Ojas depletion, leading to neuro-immune vulnerability. Rasayana agents restore redox balance and tissue resilience [60,101,102].

Sleep Control and Cognitive Performance

Sleep disturbances are highly prevalent in ADHD and significantly exacerbate attentional deficits and behavioural instability [44–46]. Tryptophan and magnesium facilitate melatonin synthesis and circadian entrainment [42,96,97]. Improved sleep quality indirectly strengthens cognitive performance, emotional management, and executive functioning [96,97].

Pumpkin seed–derived tryptophan and magnesium may therefore confer secondary therapeutic benefits by normalising sleep, in accordance with Ayurveda's recognition of Nidra as a fundamental pillar of health [63,64].

Gut–Brain Axis and Nutritional Ecology

Emerging evidence shows gut microbiota dysbiosis in ADHD, influencing immune modulation, neurotransmitter generation, and nutrient absorption process [26–28]. Dietary fibre and polyphenols present in pumpkin seeds may promote beneficial microbial diversity, indirectly modulating neurobehavioral outcomes [26,27]. Ayurveda emphasises digestive integrity (Agni) as central to mental health and systemic balance [54–56].

Nutrients present in pumpkin seeds and their role in neurodevelopmentare illustrated in Figure 1 and described in details below.\

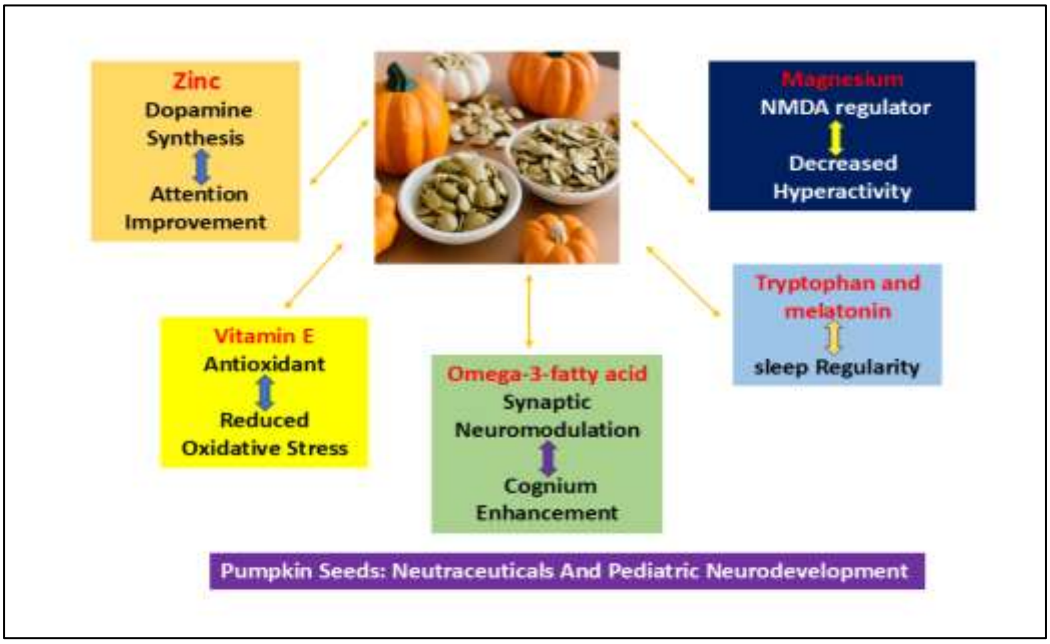

FIGURE 1: Nutritive enrich ingredients of pumpkin seeds and its role in pediatric neurodevelopment

Clinical Translation and Integrative Applicability

Pumpkin seeds demonstrate several advantages for pediatric integrative use:

- Excellent safety profile and tolerability [51–53]
- Nutritional synergy and bioavailability [34,69–71]
- Cultural acceptability and financial feasibility
- Minimal drug–nutrient interactions
- Maintains long-term neurodevelopmental resilience [72–76]

They may be notably valuable in:

- Mild to moderate ADHD
- Nutritional deficiency states
- Early preventive neurodevelopment programs
- Integrative pediatric care [85,86,101]

Integrative Synthesis: Pumpkin seeds are a pharmaco-biologically potent, culturally accessible nutraceutical capable of addressing multiple neurodevelopmental vulnerabilities in ADHD through micronutrient replenishment, neurotransmitter stabilisation, antioxidant effect, sleep regulation, and gut–brain modulation. (124) Their mechanistic convergence with Ayurvedic Medhya Rasayana principles supports rational inclusion into evidence-based pediatric care frameworks.

CONCLUSION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a complex neurodevelopmental condition involving neurotransmitter dysregulation, oxidative stress, neuroimmune imbalance, gut–brain axis alterations, and frequent micronutrient deficiencies. Pumpkin seeds (*Cucurbita pepo*) are a nutrient-dense functional food that provides zinc, magnesium, iron, omega-3 fatty acids, tryptophan, and antioxidant phytochemicals, which collectively target multiple pathogenic pathways relevant to ADHD. Evidence supporting the roles of these nutrients in improving attention, behavioural regulation, neuroplasticity, and sleep physiology strengthens their translational relevance in pediatric care. From an Ayurvedic perspective, pumpkin seeds exhibit properties consistent with Medhya Rasayana, supporting Majja Dhatu Poshana, Vata Shamana, and Ojas Vardhana, thereby aligning traditional neurocognitive rejuvenation concepts with modern neuroscience.

Limitations and Evidence Gaps

Despite strong pharmaco-literary research, direct randomised clinical trials evaluating pumpkin seeds in ADHD populations remain absent. Variability in seed preparation, nutrient bioavailability, and dietary background may influence treatment results [69–71]. Standardised dosing protocols and biomarker-driven trials are necessary to establish efficacy.

Future Research Directions

Priority areas include:

1. Pediatric randomised controlled trials evaluating symptom scales and biomarkers
2. Comparative nutraceutical efficacy studies
3. Bioavailability optimisation studies
4. Integration with Medhya Rasayana protocols
5. Longitudinal neurodevelopmental outcome tracking

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