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Phytopharmacology in Autism: A Review from the Perspective of Iranian Traditional Medicine

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ABSTRACT

In Iranian Traditional Medicine (ITM), autism spectrum disorder is conceptualized as a disturbance in cerebral temperament, leading to behavioral, cognitive, and social challenges. While no definitive cure exists, ITM historically employs medicinal plants as brain tonics and temperament correctors. This narrative review explores these plants and their proposed mechanisms of action from both traditional and modern scientific perspectives. The study synthesizes information from canonical ITM texts and contemporary scientific databases, including PubMed, Scopus, and Google Scholar. The findings identify several prominent plants, such as *Melissa officinalis*, *Crocus sativus*, and *Lavandula angustifolia*, traditionally used to alleviate symptoms associated with autism. According to the integrated analysis, these plants are believed to exert beneficial effects through multiple pathways, including enhancing memory and concentration, inducing calming effects, improving cerebral blood flow, and reducing neuroinflammation and anxiety. From the ITM viewpoint, their primary action is to restore the functional balance of the brain and mental faculties by modulating the body's innate heat and moisture. This review concludes that select medicinal plants from the ITM pharmacopeia present a complementary approach for managing autism symptoms. Their potential lies in a multi-target mechanism that aligns with both traditional principles and modern neurobiological understanding. However, the translation of this traditional knowledge into clinical practice necessitates rigorous, large-scale human trials to conclusively establish their efficacy and safety.

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Introduction

Mental disorders are among the most significant public health challenges, profoundly affecting individuals' quality of life, social functioning, and overall societal well-being (Mohammadi et al., 2022; Gholipoor et al., 2017; Mohammadi et al., 2019). Autism Spectrum Disorder (ASD) is among the most complex neurodevelopmental conditions, characterized by significant deficits in social communication, interpersonal interactions, and the presence of restricted and repetitive behaviors (Lord et al., 2000). Manifesting early in childhood, ASD profoundly impacts the quality of life of affected individuals and their families (Geschwind, 2009). The global prevalence of ASD is rising, with the World Health Organization estimating that approximately one in every 100 children is affected (Muhle et al., 2004; Rice et al., 2012).

Etiologically, autism is a multifactorial disorder influenced by genetic, environmental, neurobiological, and biochemical factors (Folstein and Piven, 1991). Research indicates that alterations in brain structure and function, dysfunctions in neurotransmitter systems, chronic neuroinflammation, and metabolic abnormalities are among the key contributors to its pathophysiology (Currenti, 2010). While the precise mechanisms remain incompletely understood, a complex interplay between genetic predispositions and environmental factors particularly during critical periods of neurodevelopment plays a central role in the emergence of clinical symptoms (Folstein and Piven, 1991; Currenti, 2010).

From the perspective of Iranian traditional medicine (ITM), autism is viewed as a disorder resulting from an imbalance of temperament and deficiencies in the body's natural faculties, especially those related to cerebral and nervous functions (Levy and Hyman, 2015). According to ITM principles, maintaining equilibrium among different temperamental states namely heat, cold, dryness, and moisture is essential for physical and mental health. Any disruption in this balance may predispose an individual to neuropsychiatric disorders (Levy and Hyman, 2008, 2015). Classical Iranian texts describe pediatric neuropsychiatric disorders, including autism, as conditions arising from cerebral coldness or dryness and weakness of nervous faculties, highlighting the necessity of temperamental correction and cerebral fortification (Levy and Hyman, 2015; Rezapour et al., 2016).

In contemporary medicine, the management of ASD primarily involves behavioral, educational, and pharmacological interventions (Fombonne, 2003). Common pharmacotherapies mainly target secondary symptoms, such as anxiety, aggression, and sleep disturbances, but these treatments often have limited efficacy and may induce notable side effects (Turner, 2020). Reported adverse effects of conventional medications include weight gain, sleep disruption, restlessness, appetite changes, metabolic alterations, gastrointestinal issues, and, in some cases, motor symptoms such as tremors (Kumar et al., 2012). These limitations have prompted increasing interest in complementary approaches, particularly the use of medicinal plants with sedative, anti-inflammatory, and neuroprotective properties (McCracken, 2005).

Medicinal plants, owing to their diverse bioactive compounds and abilities to modulate neural function, reduce inflammation, and regulate temperament, hold a prominent place in ITM (Sevindik et al., 2023). Many of these plants, traditionally described as cerebral tonics and nervine relaxants (Ghavam, 2025), have demonstrated promising effects in contemporary studies, improving neurological symptoms and enhancing cognitive function (Urdaneta et al., 2018).

Among the most notable of these plants are *Melissa officinalis, Crocus sativus, Echium amoenum, Lavandula angustifolia* (lavender)*, Valeriana officinalis, Matricaria chamomilla, Zingiber officinale, Ziziphus jujuba, violet oil, Prunus dulcis, Cynara carduncul*us, and *Cannabis sativa* (Christie, 2016; Mars and Fiedler, 2024). These plants may alleviate behavioral and cognitive disturbances associated with autism through mechanisms such as enhancing cerebral blood flow, reducing inflammation and anxiety, modulating central nervous system activity, and correcting temperamental imbalances (Bahmani et al., 2016).

Conventional pharmacological treatments for ASD include agents such as risperidone and aripiprazole, primarily used to reduce irritability, aggression, and repetitive behaviors. Other medications include methylphenidate for attention-deficit/hyperactivity disorder (ADHD) symptoms, as well as anxiolytics and antidepressants, such as fluoxetine.

This review examines medicinal plants described in Iranian Traditional Medicine and integrates contemporary evidence to identify those with potential to improve behavioral, cognitive, and social disturbances in autism, highlighting their underlying mechanisms and therapeutic relevance.

Methodology

This narrative review was conducted to identify and evaluate medicinal plants reported to improve symptoms of ASD based on Iranian traditional medicine teachings and contemporary scientific evidence. The research process was systematically designed and executed in sequential stages.

Sources of Data

Initially, authoritative ITM texts, including works of prominent scholars and reference books, were comprehensively examined. Subsequently, extensive searches were performed in scientific databases, including PubMed, Scopus, Google Scholar, SID, and Magiran, to gather relevant contemporary studies and evidence.

Search Strategy

Keywords included "autism," "autism spectrum disorder," "medicinal plants," "Iranian traditional medicine," "herbal therapy," and "mechanism of action," along with their English equivalents. Boolean operators (AND, OR) were used to enhance the precision and comprehensiveness of the search.

Inclusion Criteria

Studies examining the effects of medicinal plants on autism symptoms or related behavioral and cognitive outcomes were included. ITM sources describing plants used for neuropsychiatric disorders analogous to autism were also considered.

Exclusion Criteria

Studies lacking full text, review articles without empirical evidence, low-quality research, or non-peer-reviewed publications were excluded. Articles addressing unrelated psychiatric disorders or non-herbal interventions were also omitted.

Data Analysis

Extracted information was systematically categorized and presented in tables and analytical charts to facilitate a detailed examination of the roles and mechanisms of medicinal plants in managing ASD.

Results

Based on a comprehensive review of traditional and contemporary sources, several medicinal plants including *Melissa officinalis L., Crocus sativus* L., *Borago officinalis* L., *Lavandula angustifolia* Mill., *Valeriana officinalis* L., *Matricaria chamomilla* L., *Zingiber officinale* Roscoe, *Ziziphus jujuba* Mill., *Viola odorata* L., *Prunus amygdalus* Batsch, *Cynara scolymus* L., and *Cannabis sativa* L. emerged as the most significant plants traditionally used in Iranian medicine for modulating behavioral and cognitive disturbances associated with autism. These plants exert notable effects on symptom improvement through mechanisms such as enhancing cerebral function, inducing relaxation, improving blood circulation, and reducing inflammation and anxiety.

From the perspective of Iranian traditional medicine, these plants contribute to mental and neurological health by correcting temperament imbalances, regulating the body's heat and moisture, and modulating cerebral and psychological faculties. Collectively, they support cognitive enhancement and alleviate neurobehavioral symptoms in individuals with ASD. Detailed botanical characteristics and traditional therapeutic effects of each plant are summarized in table 1.

Based on the analysis of the plant families used, it was observed that the most frequently represented families were Lamiaceae and Asteraceae, each appearing twice among the studied samples. Other plant families, including Iridaceae, Boraginaceae, Valerianaceae, Zingiberaceae, Rhamnaceae, Violaceae, Rosaceae, and Cannabaceae, were each represented only once. These findings indicate that Lamiaceae and Asteraceae hold greater significance and utilization in the examined samples, whereas the other families were used to a lesser extent and in a more limited manner.

Regarding the plant parts used, leaves and flowers were the most commonly utilized. Other parts, such as roots, fruits, seeds, and stems, were used relatively less frequently. This suggests that in the studied traditional or medicinal practices, leaves and flowers attract the most attention, likely due to their richness in bioactive compounds and ease of access.

Table 2 presents the major bioactive compounds of key medicinal plants traditionally used for autism. The listed compounds include antioxidants, anti-inflammatory agents, and neuromodulators, which may contribute to improving cognitive function, reducing anxiety, and modulating behavioral symptoms associated with ASD. The chemical formulas provide precise molecular information for each compound, and the plant images (to be inserted) visually depict each species.

Table 1: Medicinal plants with potential benefits for autism

English Name	Scientific Name	Family	Plant Part Used	Traditional Use	Mechanism of Action
Lemon Balm	*Melissa officinalis* L.	Lamiaceae	Leaf	Sedative, brain tonic	Reduces anxiety and irritability, regulates central nervous system, anti-inflammatory, neuroprotective (Piri and Sepehri, 2025)
Saffron	*Crocus sativus* L.	Iridaceae	Stigma	Memory enhancer, sedative, antidepressant	Increases serotonin and dopamine levels, anti-inflammatory and antioxidant effects, improves cognitive function, reduces repetitive behaviors (Seyedinia et al., 2023)
Borage	*Borago officinalis* L.	Boraginaceae	Leaf and flower	Memory enhancer, sedative, anti-stress	Increases dopamine and GABA levels, reduces anxiety and irritability, neuroprotective (Mallick and Banerjee, 2024)
Lavender	*Lavandula angustifolia* Mill.	Lamiaceae	Flower	Sedative, antispasmodic, sleep aid	Inhibits sympathetic nervous system activity, increases GABA, reduces anxiety and irritability, improves sleep quality (Larit and León, 2023)
Valerian	*Valeriana officinalis* L.	Valerianaceae	Root	Sedative, sleep aid, anxiolytic	Increases GABA neurotransmission in the brain, reduces irritability, sedative and anxiolytic effects (Orhan, 2021)
Chamomile	*Matricaria chamomilla* L.	Asteraceae	Flower	Sedative, anti-inflammatory, antispasmodic	Increases GABA, anti-inflammatory and neurocalming effects, reduces repetitive behaviors (Urdaneta et al., 2018)
Ginger	*Zingiber officinale* Roscoe	Zingiberaceae	Rhizome	Anti-inflammatory, improves circulation	Reduces neuroinflammation, enhances cerebral blood flow, neuroprotective, modulates stress responses (Kardani et al., 2019)
Jujube	*Ziziphus jujuba* Mill.	Rhamnaceae	Fruit	Sedative, memory enhancer	Increases GABA and serotonin, reduces anxiety and irritability, improves sleep quality and cognitive function (Li et al., 2025)
Violet Oil	*Viola odorata* L.	Violaceae	Flower and leaf (for oil extraction)	Sedative, anti-inflammatory, sleep aid	Neurocalming, anti-inflammatory and antioxidant effects, reduces stress-related behaviors (Sevindik et al., 2023)
Sweet Almond	*Prunus amygdalus* Batsch	Rosaceae	Seed	Brain tonic, cerebral moisturizer	Rich in omega-3 fatty acids and antioxidants, neuroprotective, enhances memory and cognitive function (Shamsi et al., 2019)
Artichoke	*Cynara scolymus* L.	Asteraceae	Leaf	Improves circulation, memory enhancer	Enhances cerebral blood flow, antioxidant effects, neuroprotective, improves cognitive function (Saki, 2018)
Hemp	*Cannabis sativa* L.	Cannabaceae	Leaf and flower, seed	Sedative, anxiolytic, memory enhancer	Modulates endocannabinoid system, reduces anxiety, improves social interactions and behavioral symptoms of autism, anti-inflammatory effects (Jawed et al., 2024)

Table 2. Major bioactive compounds of selected medicinal plants relevant to autism spectrum disorder

Scientific name	Active Compound	Chemical Formula	Plant Image
Melissa officinalis L.	Rosmarinic acid	$C_{18}H_{16}O_8$	
Crocus sativus L.	Crocin	$C_{44}H_{64}O_{24}$	
Borago officinalis L.	Gamma-linolenic acid	$C_{18}H_{32}O_2$	
Lavandula angustifolia Mill.	Linalool	$C_{10}H_{18}O$	

Table 2: *Continued*.

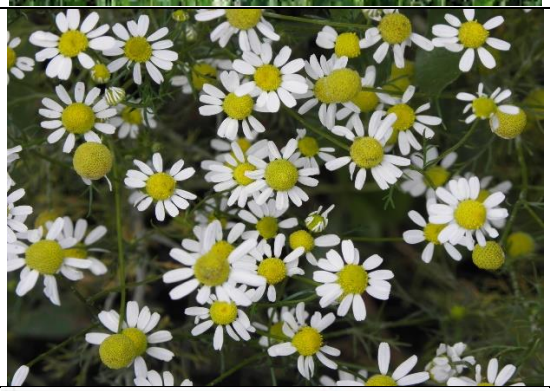
Valeriana officinalis L.	Valerenic acid	$C_{15}H_{22}O_2$	
Matricaria chamomilla L.	Apigenin	$C_{15}H_{10}O_5$	
Zingiber officinale Roscoe	Gingerol	$C_{17}H_{26}O_4$	
Ziziphus jujuba Mill.	Jujuboside	$C_{30}H_{48}O_3$	

Table 2: *Continued*.

Viola odorata L.	Violine	C34H40N4O	
Prunus amygdalus Batsch	Oleic acid	$C_{18}H_{30}O_2$	
Cynara scolymus L.	Cynarin	$C_{25}H_{22}O_{10}$	
Cannabis sativa L.	Cannabidiol	$C_{21}H_{30}O_2$	

Discussion

Autism Spectrum Disorder (ASD) is among the most complex and multifactorial neurodevelopmental conditions, characterized by deficits in social interaction, impairments in verbal and non-verbal communication, and the presence of repetitive behaviors. Recent studies have identified multiple biological contributors to ASD, including oxidative stress, neuroinflammation, mitochondrial dysfunction, and neurotransmitter imbalances. Among these, oxidative stress is considered a key factor in the pathogenesis of autism, as excessive production of reactive oxygen species can lead to neuronal damage and disruption of brain signaling pathways (Piri and

Sepehri, 2025).

Given these underlying mechanisms, the use of natural antioxidant compounds and plant extracts with anti-inflammatory and neuroprotective properties represents a potentially safe and low-risk approach for mitigating ASD symptoms. In recent years, phytotherapy has emerged as a prominent branch of complementary medicine, particularly in the management of neurological and psychiatric disorders, as many medicinal plants can improve behavioral and cognitive outcomes by modulating inflammatory pathways, increasing serotonin and dopamine levels, and enhancing neuronal function.

Evidence from experimental models suggests that Melissa officinalis extract reduces anxiety, alleviates pain, and improves cognitive flexibility in animal models of autism, with these effects exhibiting dose-dependency (Piri and Sepehri, 2025). Similarly, crocin, the active constituent of saffron, exhibits antioxidant and anti-inflammatory properties, providing neuroprotective effects and modulating inflammatory pathways to reduce oxidative damage in the brains of individuals with ASD (Majhi and Singh, 2025).

Additionally, both animal and human studies indicate that Lavandula angustifolia and Echium amoenum can improve sleep quality, reduce irritability, and modulate behavioral disturbances in autistic individuals due to their anxiolytic and calming effects (Christie, 2016). Findings from studies on Valeriana officinalis suggest that this plant can reverse behavioral alterations induced by maternal immune activation, thereby preventing neurodevelopmental impairments (Won et al., 2016).

Human studies have also reported promising outcomes. For instance, de Andrade et al. (2023) demonstrated that chamomile extract enhanced concentration and cognitive performance in students with ASD during educational tasks. Moreover, Zingiber officinale, through its anti-inflammatory and antioxidant properties, has been reported to alleviate autism symptoms in children (Alharbi, 2024). In traditional Greek medicine, Viola odorata has been recommended for modulating behavioral symptoms of autism (Tavassoli et al., 2021). Furthermore, Cynara scolymus, due to its phenolic constituents and modulatory effects on neurochemical pathways, shows considerable potential for development as a novel herbal therapy for ASD (Saki, 2018).

Notably, CBD-enriched Cannabis sativa extract has demonstrated therapeutic effects in human studies, improving multiple symptoms including seizures, sleep disturbances, attentional deficits, and social communication impairments. Importantly, this intervention enhanced the quality of life for both patients and caregivers without inducing dependence or severe side effects (Fleury-Teixeira et al., 2019). The mechanism of action of CBD likely involves modulation of the endocannabinoid system and reduction of neuroinflammation, both of which are key pathways implicated in autism pathology.

Collectively, these studies indicate that most medicinal plants effective in ASD act through shared mechanisms, including reduction of oxidative stress, inhibition of pro-inflammatory cytokines (particularly TNF-α and IL-6), elevation of GABA and serotonin levels, and improvement of mitochondrial function. These pathways not only enhance cognitive performance but also contribute to mood regulation and reduction of stereotypical behaviors in patients. Medicinal plants used in the management of autism primarily act on several key neurochemical and neurological pathways. Many of these plants increase levels of GABA, dopamine, and serotonin, thereby reducing anxiety, irritability, and repetitive behaviors. Their anti-inflammatory and neuroprotective properties help mitigate neural damage and enhance cognitive function. By improving cerebral blood flow and exerting antioxidant effects, these plants also support memory and attention, while their calming and stress-reducing actions facilitate emotional regulation and control over impulsive behaviors. Certain species further modulate the endocannabinoid system, enhancing social interactions and alleviating behavioral symptoms associated with autism. Nutrient-rich compounds, such as omega-3 fatty acids, additionally strengthen memory and cognitive performance. Overall, these mechanisms underscore the potential of traditional medicinal plants as complementary interventions for alleviating behavioral and cognitive challenges in individuals with ASD.

This review is subject to several methodological limitations. Most evidence regarding the efficacy of medicinal plants in autism is derived from preclinical studies, animal models, or small-scale clinical trials, which may limit the generalizability of findings to human populations. Additionally, variations in plant composition, extraction methods, and dosing regimens across studies introduce heterogeneity, potentially affecting the reproducibility of results. While traditional Iranian

medicine provides valuable insights into the therapeutic potential of these plants, integrating classical concepts with contemporary scientific evidence remains interpretive and may be subject to bias. Furthermore, some relevant studies may have been overlooked due to language barriers or incomplete indexing in scientific databases.

Conclusion

The findings of this review suggest that phytotherapy can serve as an effective complementary approach alongside conventional ASD treatments. Medicinal plants such as Melissa officinalis, Crocus sativus, chamomile, lavender, ginger, and Cannabis sativa contain bioactive compounds that exert anti-inflammatory, antioxidant, and neuromodulatory effects, thereby improving behavioral and cognitive symptoms. However, due to variability in plant composition, differences in dosing, and limitations in human studies, randomized, multicenter clinical trials are necessary to confirm efficacy and determine safety profiles for each compound.

Integrating the knowledge of traditional medicine with modern scientific evidence may open new avenues for the development of evidence-based, natural therapies for individuals with ASD. Future research should focus on identifying active constituents, investigating their pharmacokinetics in the brain, and evaluating potential interactions with psychiatric medications, enabling safe and effective application of these natural interventions to enhance quality of life in autistic patients.

Declarations

Conflict of Interest

The author declares no conflict of interest related to the publication of this article.

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Consent for Publication

The author confirms that the final version of the manuscript has been reviewed and approved for publication.

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Authors' Contributions

AK was responsible for conceptualization, review, data collection, analysis, writing, and manuscript preparation.

Ethical Approval

As this study is a review article, it does not involve human or animal subjects and therefore does not require ethical approval or informed consent.

AI Use Disclosure

The authors confirm that QuillBot AI and Grammarly were used strictly for language editing, grammar correction, and paraphrasing assistance during the preparation of this manuscript. Specifically, these tools were applied to improve clarity, sentence structure, and overall readability in the Abstract, Introduction, Methods, Results, Discussion, and Conclusion sections. No AI tools were used for data generation, experimental design, statistical analysis, molecular docking simulations, or interpretation of results. All AI-assisted content was thoroughly reviewed, edited, and validated by the authors to ensure scientific accuracy, originality, and full compliance with academic and ethical standards.

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