

Autism: Synthetic- and plant-derived control and treatment

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Abstract

Autism is a very complex neurological disorder characterized by abnormal social behavior, poor communication skills, communication difficulties and, in some cases, compulsive or repetitive behavior. There is usually no specific drug therapy for it, and the chemical drugs used lead to certain complications. This article addresses the use of medicinal plants in the pharmaceutical industry to treat autism. In this review article, the keywords such as medicinal plants, herbal drugs, herbal medicine, traditional medicine, and autism were used to retrieve eligible articles indexed in the Scopus, PubMed, ISI, Google Scholar, SID, and Magiran databases. Medicinal plants such as *Cirsium vulgare*, *Vitis vinifera*, *Brassica rapa*, *Daucus carota*, *Malus domestica*, *Punica granatum*, *Juglans regia*, *Lens culinaris*, *Terminalia chebula*, *Glycine max*, *Spinacia oleracea*, *Prunus dulcis*, *Cucurbita pepo*, *Helianthus annuus*, *Brassica oleracea*, *Ginkgo biloba*, *Portulaca oleracea*, and *Curcuma longa* are the effective anti-autism plants. Based on the results of this study, the most important medicinal plants affecting autism are a promising source for the preparation of new anti-autism drugs.

Key words: Autism, medicinal plants, therapy

INTRODUCTION

Autism is a very complicated neurodegenerative disorder that naturally manifests itself from birth, and for this reason, people will notice it in the first 2 years of life when personality growth begins. Autism is usually characterized by abnormal social behavior, poor communication skills, communication difficulties and/or, in some cases, compulsive or repetitive behavior.^[1] One of the symptoms of autism is that unusual sensitivities may be seen in the five senses of sight, hearing, touch, smell, and taste. The central core of impairments due to autism is impaired communication. Some other symptoms of autism include repeated thoughts, activities, and behaviors. The impairment begins in the first 3 years of life.^[2-6] Studies have shown that the incidence of this disease is 10/10,000 individuals. The proportion of boys to girls in autism spectrum disorders (ASD) is approximately one-third to one-fourth.^[7] These disorders are usually diagnosed before the age of 3 years, but by careful examining the child's behavior, the age of diagnosis can be reduced to <2 years.^[8] Autism treatments include behavioral therapy and communication improvement, speech therapy, improvement of problem-solving skills, communicating

through pictures sharing, diet therapy, and pharmacotherapy. Medicinal treatments include antidepressants, antipsychotics, mega-vitamins, thyroid hormone, serotonin reuptake inhibitors, clonidine, naltrexone, and lithium.^[9-12] Until now, no definitive treatment for autism has been reported, but there are many ways to help these people and improve their skills and conditions.^[13-16] Historically, plants have been highly important in the development of various communities because these natural drugs have various active pharmaceutical ingredients.^[17-20] In this regard, the use of some medicinal plants is traditionally commonplace and is still popular; therefore, extensive researches are being carried out to seek out medicinal products and substances.^[21,22] Today, the importance of medicinal plants and their vital role in advancing national, regional, and global goals to achieve health, pharmaceutical self-sufficiency, entrepreneurship, and economic development is clear to all people, and these plants are investigated extensively.^[23,24] Medicinal plants, as genetic reserves and treasures of the planet, as important agricultural products with therapeutic properties, can be

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considered the largest national asset for any country.^[25,26] Medicinal plants have a special value in biological sciences, medicine, and veterinary with respect to prevention and treatment of disease.^[27-29] In recent years, the use and investigation of medicinal plants have been increasing due to their beneficial effects, cheapness, comparatively fewer side effects, and also environmental compatibility.^[30-33] In this regard, medicinal plants have revealed promising results in the treatment and prevention of various neuropsychological problems.^[34-36] In natural remedies for autism, natural drugs, herbal supplements, and holistic therapies serve as alternatives to conventional medications. In addition to antipsychotic drugs, supplementary pharmacotherapies are also used in the treatment of autism. This article addresses the use of medicinal plants in the pharmaceutical industry to treat autism.

MATERIALS AND METHODS

In this review article, the keywords such as *medicinal plants*, *herbal drugs*, *herbal medicine*, *traditional medicine*, and *autism* were used to retrieve eligible articles indexed in the Scopus, PubMed, ISI, Google Scholar, SID, and Magiran databases.

RESULTS

Based on the materials mentioned in herbal medicine and traditional medicine, the medicinal plants such as acanthus, grapes, turnips, lobster, apple, pomegranate, walnut, lentil, black helium, soybean, spinach, almonds, pumpkin, sunflower, broccoli, jingo, persimmon, and turmeric were found to be among the most important plants effective on autism [Table 1].

Chemical drugs used for autistic individuals are listed in Table 2.^[52]

DISCUSSION

Autism is a complex neurobehavioral condition that includes impaired social interactions, verbal development, and communication skills associated with repeated and difficult behaviors. Due to the wide range of symptoms that this disorder causes, it is called ASD. The disease involves impairment in a wide range of symptoms and skills at different levels. This disorder affects children, with an estimated eight of 10,000 children diagnosed with the disorder. Autism is one of the pervasive developmental disorders in which the development of social skills, language, communication, and behavioral resources is delayed and impaired. In addition to antipsychotic drugs, supplementary therapies are also used in the treatment of autism.^[52-59] In this study, the medicinal

plants such as acanthus, grapes, turnips, lobster, apple, pomegranate, walnut, lentil, black helium, soybean, spinach, almonds, pumpkin, sunflower, broccoli, jingo, persimmon, and turmeric were found to be among the most important plants effective on autism. The mechanism actions of these plants are not fully clear. However, oxidative stress has been shown to play an important role in the pathogenesis of various neurological disorders including Parkinson's disease, Alzheimer's disease, and autism and some other neurological diseases,^[60-65] in which extent oxidative stress is involved in autism is not clear. However, recently extensive researches have been done and confirmed it. Low activity of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase in autism confirms this involvement.^[66] Therefore, these medicinal plants in which all have antioxidant activity might, at least in part, induce their effects through antioxidant activity. There are a lot of other plants and plant-derived materials which have antioxidant properties.^[67-74] If we accept the involvement of antioxidant, hence, these plants should also have positive effects in autism. This should be researched in pre-clinical and clinical trials.

The change of redox homeostasis causes stress to cells by increased reactive oxygen sepsis (ROS) generation.^[75] A chain reaction exists between the polyunsaturated fatty acids and ROS-producing lipid peroxides that reflect lipid peroxidation. Lipid peroxidation is highly toxic to cells. There are also a lot of medicinal plants which inhibit lipid peroxidation.^[76-78] These plants might also be effective in autism. In this regards, peroxidation of lipids has been shown to increase in plasma.^[66]

Inflammation and immune dysregulation have been shown to be implicated in various psychiatric disorders. Neuroinflammation is known to be implicated not only in autism but also in various other psychiatric disorders such as Parkinson's and Alzheimer's diseases.^[79,80] Therefore, medicinal plants effective on immune system and inflammation may also be effective in autism.^[81-83]

It should be noted that medicinal plants usually have various effects on different diseases.^[84-87] Oxidative stress has been implicated in a wide variety of disorders, including cardiovascular disease,^[33] diabetes,^[34] and hypertension.^[35] Furthermore, oxidative stress has been implicated in several psychiatric disorders,^[13] including schizophrenia,^[36,37] depression,^[38] bipolar disorder,^[39,40] and Alzheimer's disease.^[41] Oxidative stress has also been reported in some individuals with ASD.^[6,42] Finally, dysfunction in mitochondria, distinct cellular organelles that oxidize glucose and fatty acids to generate adenosine triphosphate, and the energy carrier in most mammalian cells^[43] have been implicated in several psychiatric disorders including schizophrenia,^[44-47] bipolar disorder,^[44-46] depression,^[45,46] dementia,^[45,46] and ASD.^[4,48,49] In addition to energy production, mitochondria are intimately involved in programmed cell death (apoptosis), calcium homeostasis, synaptic plasticity, and neurotransmitter

Table 1: Medicinal herbs affecting autism according to traditional and herbal medicine

Scientific name	Herbal family	Persian name	Effect ^[37-51]
<i>Cirsium vulgare</i>	Asteraceae	Kangar	Another drug used in the phytotherapy of autism is arcanthus. Edible arcanthus, like grapes, has countless benefits in treating autism.
<i>Vitis vinifera</i>	Vitaceae	Angour	In patients with autism, ammonia increases in the blood. The natural fruit of grapes greatly reduces blood ammonia levels. To treat autism in traditional medicine, give the sick person grapes in the morning, noon, and night, or take three glasses of natural grape juice a day.
<i>Brassica rapa subsp. rapa</i>	Brassicaceae	Shalgham	Another way to help treat autism is to use <i>Brassica rapa</i> juice with honey in the evening.
<i>Daucus carota</i>	Apiaceae	Zardak	In the middle of the day, <i>Daucus carota</i> fruit can be used to supplement phytotherapy for autism.
<i>Malus domestica</i>	Rosaceae	Sib	Eating apple and apple juice with honey helps autism symptoms be treated.
<i>Punica granatum</i>	Lythraceae	Anar	Eating pomegranate has been reported to treat autism symptoms.
<i>Juglans regia</i>	Juglandaceae	Gerdou	One of the ways to treat urinary incontinence in children is the consumption of a glass of boiled hard, brown skin (the outer shell, not the kernel itself) of walnut per day. If the person is unable to hold urine, he/she should use three cups every 24 h
<i>Lens culinaris</i>	Fabaceae	Adas	To treat autism symptoms, one lentil is put under the tongue of the patient.
<i>Terminalia chebula</i>	Combretaceae	Helileh siah	The first drug of choice for autism in adults and children with slowness is processed <i>Terminalia chebula</i> combined with honey.
<i>Glycine max</i>	Fabaceae	Soya	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is also helpful for autistic patients. It is recommended that people with autism use magnesium-rich sources such as soybean.
<i>Spinacia oleracea</i>	Amaranthaceae	Esfenaj	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is helpful for autistic patients. It is recommended that autistic people use magnesium-rich sources such as spinach.
<i>Prunus dulcis</i>	Rosaceae	Badam	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is helpful for autistic patients. It is recommended that autistic people use magnesium-rich sources such as almonds.
<i>Cucurbita pepo</i>	Cucurbitaceae	Kadou	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is helpful for autistic patients. It is recommended that autistic people use magnesium-rich sources such as pumpkin seeds.
<i>Helianthus annuus</i>	Asteraceae	Aftabgardan	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is helpful for autistic patients. It is recommended that autistic people use magnesium-rich sources such as sunny flowers.
<i>Brassica oleracea</i>	Brassicaceae	Kalame broukli	Studies have shown that taking Vitamins B6 and B12, magnesium, and selenium is helpful for autistic patients. It is recommended that autistic people use magnesium-rich sources such as broccoli sprouts.
<i>Ginkgo biloba</i>	Ginkgoaceae	Ginko	A study also found that a chemical compound called sulforaphane, obtained from broccoli sprouts, may help improve the symptoms of autism in some people.

(Contd...)

Table 1: (Continued)

Scientific name	Herbal family	Persian name	Effect ^[37-51]
<i>Portulaca oleracea</i>	Portulacaceae	Khorfeh	There are some assumptions that the deficiency of omega-3 fatty acid may be the reason for exacerbation of autism, which is why it is recommended to include this substance in the diet of children with autism, and even all children. Foods containing omega-3 fatty acids include freshly brewed or grilled (not canned or fried) shrimp or fish, nuts especially walnut, and oily seeds, especially fresh <i>Portulaca oleracea</i> .
<i>Curcuma longa</i>	Zingiberaceae	Zardchoubeh	Turmeric has been reported to be effective in animal models but needs to be studied with autistic patients.

Table 2: Remedies for autism

Drug	Effect
N-acetylcysteine: Mucolytic, antioxidant	Effective in autism as well as other neurological disorders
Oxytocin: Neuropeptide	Improve social recognition and stare
Propranolol is a beta-adrenergic receptor antagonist	Improving interaction and anxiety
Rivastigmine: Acetylcholinesterase inhibitor	Strengthening autistic behaviors and strengthening the word
Bumetanide: Diuretic Loop Henle	Effective in patients with autistic and animal models
Luteolin: Flavonoids with antioxidant and anti-inflammatory properties	Positive effects on individuals and reduced TNF and IL-6
Memantine NMDA glutamate receptor antagonist	Effective on autism symptoms
Donepezil: An acetylcholine esterase inhibitor	Improve REM behavior and sleep in several autistic patients
Arbaclofen: GABA Receptor agonist	Improving social behavior, reducing pruritus
Buspiron is a relative serotonin receptor agonist	Improvement of repetitive and cluster behaviors in 6–2-year-old children with autistic children

GABA: Gamma-aminobutyric acid, TNF: Tumor necrosis factor, IL-6: Interleukin-6

release.^[50,51] Therefore, mitochondrial dysfunction can cause profound dysfunction of the central nervous system as well as other organ systems, particularly high-energy organs such as the gastrointestinal tract.^[4] The goal of this manuscript is to examine the evidence of these systemic physiological abnormalities in ASD. We have approached this in several ways. First, we analyzed trends in the number of publications in four specific areas of research over the past four decades and compared these trends with four other areas of research in ASD involving non-physiological abnormalities. Second, we have identified what percentage of studies in each of these research areas supports these physiological mechanisms in ASD. Third, we rate the strength of these studies within each research area.

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