

REVIEW ARTICLE

Curcumin and neuroinflammation in autism: Mechanistic insights and therapeutic implications

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Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by impairments in social interaction and communication. According to recent research, neuroinflammation may play a role in the pathogenesis of ASD. Curcumin, the active compound in turmeric, has been demonstrated to exhibit neuroprotective, antioxidant, and anti-inflammatory properties. This review summarizes the potential mechanisms by which curcumin may influence the inflammatory pathways implicated in ASD. Curcumin can suppress nuclear factor kappa-light-chain-enhancer of activated B-cell activation, thereby reducing the levels of pro-inflammatory cytokines. In addition, it can protect mitochondrial function, upregulate antioxidant enzymes, scavenge reactive oxygen and nitrogen species, and modulate the gut-brain axis. Animal studies have shown that curcumin can improve sociability, repetitive behaviors, and enhance cognitive function in ASD models. The beneficial effects of curcumin supplementation on autism symptoms have also been documented in several small clinical trials involving children with ASD. Overall, curcumin is a natural compound with the potential to modulate neuroinflammatory pathways implicated in ASD; however, its therapeutic role remains under investigation.

Keywords: Autism spectrum disorder; Neuroinflammation; Curcumin; Anti-inflammatory effects; Animal models; Clinical trials

1. Introduction

Neuroinflammation is a type of inflammation that occurs in the brain or central nervous system (CNS) due to the activation of microglial cells. It can be triggered by infection, injury, or autoimmune disorders.¹⁻⁴ Autism spectrum disorder (ASD) is a neurodevelopmental condition that can be diagnosed at any age.⁵ Individuals with ASD typically face challenges in social interaction and communication. As most symptoms of autism often appear within the first 2 years of life, ASD is classified as a “developmental disability”.⁶ Several studies have found increased levels of inflammatory markers in the cerebrospinal fluid of individuals with ASD. Inflammation has been linked to a higher risk of ASD, although the mechanisms underlying immune system activation in the brain related to autism remain unclear. Important factors include microglial and astrocytic activation, an elevated pro-inflammatory cytokine profile, and aberrant expression of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B).⁷ These are considered biomarkers associated with ASD and create an inflammatory environment in the brain that may lead to the destruction of critical brain tissues. Microglia are generally activated in response to inflammation in the brain and cerebrospinal fluid. This activation contributes to disease progression by causing the loss of healthy brain cells through the engulfment of synapses and neuronal tissues, resulting in reduced neural connectivity, a feature commonly observed in ASD. NF- κ B is a transcription factor that promotes the expression of genes related to inflammation. Aberrantly activated NF- κ B can cause chronic inflammation. In individuals with ASD, NF- κ B is expressed in the orbitofrontal cortex, leading to inflammation within immune cells of brain regions responsible for behavioral symptoms.⁸ Recently, the potential involvement of astrocytes and activated microglia in ASD has attracted considerable research interest. These cells regulate brain cell communication and participate in immune responses, in addition to responding to inflammatory signals.⁹ Astrocytes and microglia control the release, uptake, and recycling of neurotransmitters such as glutamate and gamma-aminobutyric acid (GABA).¹⁰⁻¹² and modulate neuropeptide signaling pathways involved in stress response and social behavior.¹³⁻¹⁵ Many natural bioactive compounds are showing promising results for treating ASD.¹⁶ Curcumin, a naturally occurring substance found in turmeric, has potent anti-inflammatory and antioxidant properties.¹⁷ It has shown potential benefits in treating a range of chronic inflammatory conditions, such as Alzheimer’s disease (AD), Parkinson’s disease (PD), epilepsy, multiple sclerosis (MS), cancer, asthma, diabetes, depression, and metabolic syndrome. Curcumin inhibits

NF- κ B, the transcription factor regulating inflammation. However, inconsistent results and a lack of definitive scientific evidence have been reported, leaving its precise role in ASD treatment unclear.¹⁸

The influence of curcumin on inflammatory processes specifically associated with ASD remains poorly understood. This review aims to fill these gaps by closely examining the effects of curcumin on neuroinflammation in individuals with ASD. Our primary objective is to investigate whether curcumin can reduce neuroinflammatory markers and whether such changes correspond with improvements in ASD symptoms. Ultimately, this review seeks to evaluate curcumin’s therapeutic potential and inform future strategies for managing ASD by elucidating the relationship between curcumin and neuroinflammation. Through this work, we hope to contribute to improving the quality of life for individuals with ASD and offer insights into novel approaches for managing this complex condition.

1.1. Curcumin and the inflammatory pathway of neurological disorders

The primary factors contributing to neurodegenerative diseases include oxidative stress, aging, injury, inflammation, vascular issues, mitochondrial dysfunction, metabolic irregularities, and genetic predispositions. Due to mitochondrial impairment, affected areas release an abundance of reactive oxygen species (ROS).¹⁹ Autophagy is pivotal in mitigating this oxidative burden by eliminating dysfunctional mitochondria, thereby shielding neurons.^{20,21} Autophagy’s ability to hinder mitochondrial apoptosis and suppress neuroinflammation offers rejuvenating effects crucial for reinstating neuronal balance. To prevent post-injury apoptosis and aid in controlling neuronal degeneration, the phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin signaling cascade can be strategically activated.²² NF- κ B can be activated by substances originating both internally and externally. Once activated, it disrupts the normal functions of neurons and glial cells during various inflammatory conditions. Moreover, interleukin (IL)-6 and other inflammatory molecules are released when NF- κ B is activated, which increases the risk of subsequent brain damage.^{19,23} Curcumin has been shown to cross the blood–brain barrier and activate nuclear factor erythroid 2-related factor 2 (Nrf2) and its associated genes while blocking inflammatory cytokines and NF- κ B, thereby reducing neuroinflammation. Furthermore, curcumin is known to scavenge ROS and free radicals.¹⁹ By increasing neurotrophic factors such as brain-derived neurotrophic factor and modulating dopamine and serotonin levels, curcumin may exert antidepressant effects.²⁴

Curcumin has demonstrated potential in the management of several neurological disorders, such as tardive dyskinesia (TD), PD, AD, MS, amyotrophic lateral sclerosis, migraines, and others. Extensive

discussions have explored both the effectiveness of curcumin in treating these conditions and its impact on the inflammatory pathways associated with them (Figure 1).

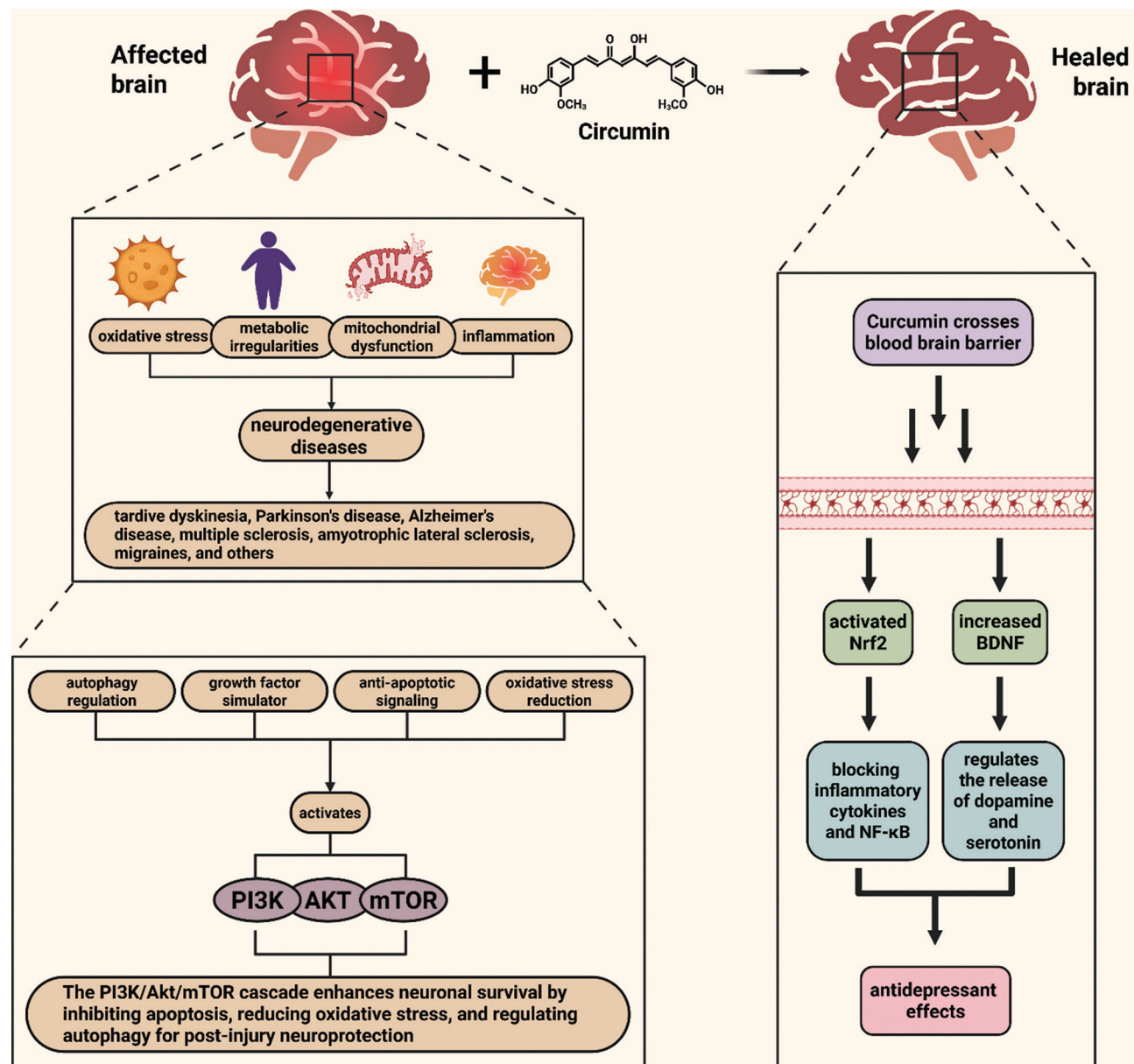


Figure 1. Mechanisms of curcumin in mitigating neurodegenerative diseases and promoting brain health. The figure illustrates how curcumin—a natural compound found in turmeric—works to protect and heal the brain. On the left, an “affected brain” shows key issues like oxidative stress, inflammation, and mitochondrial dysfunction, which contribute to diseases such as Parkinson’s, Alzheimer’s, and multiple sclerosis. Curcumin crosses the blood–brain barrier and combats these problems by activating pathways like PI3K/AKT/mTOR, which help neurons survive by reducing cell death, managing oxidative damage, and regulating autophagy. It also boosts BDNF (a protein vital for brain cell growth) and Nrf2 (which fights oxidative stress), while blocking harmful inflammation and balancing mood-related chemicals such as dopamine and serotonin. These combined effects lead to a “healed brain,” highlighting curcumin’s potential as a neuroprotective and antidepressant agent. The diagram succinctly summarizes how a simple spice compound can target multiple pathways to support brain health.

Abbreviations: AKT: Protein kinase B; BDNF: Brain-derived neurotrophic factor; mTOR: Mammalian target of rapamycin; Nrf2: Nuclear factor erythroid 2-related factor 2; PI3K: Phosphoinositide 3-kinase.

1.2. AD

AD is recognized as a progressive neurodegenerative disorder primarily characterized by cognitive decline and memory loss.²⁵ Although its exact cause remains unclear, both genetic predispositions and environmental exposures have been implicated in its development. Neuroinflammation and oxidative stress have been identified as central contributors to disease progression.²⁵⁻²⁷

Approved pharmacological treatments, including non-competitive N-methyl-D-aspartate receptor antagonists and acetylcholinesterase inhibitors, have shown limited efficacy in halting disease progression and have been associated with adverse effects.^{28,29} As a result, interest has grown in alternative therapeutic agents that may target underlying mechanisms more effectively.²⁵

Curcumin has been investigated in both *in vitro* and animal models of AD.³⁰ It has been shown to inhibit the aggregation and deposition of amyloid β oligomers and reduce tau protein phosphorylation,^{26,31,32} both of which are associated with neuronal damage.^{33,34} In addition, curcumin has been found to activate the Nrf2 signaling pathway,^{35,36} leading to increased expression of antioxidant enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase, and sulfiredoxin.^{37,38} Through these mechanisms, oxidative stress and neuroinflammation have been reduced, and neuroplasticity is promoted.

Behavioral improvements have also been observed following curcumin administration in AD models.³⁹ These findings support curcumin's potential as a multi-target neuroprotective agent and reinforce its relevance in broader neuroinflammatory contexts, including ASD.

1.3. PD

PD is a progressive neurodegenerative disorder characterized by the selective degeneration of dopaminergic neurons in the substantia nigra.^{40,41} This neuronal loss leads to hallmark motor symptoms such as tremors, rigidity, and bradykinesia, along with non-motor features including cognitive decline and mood disturbances.⁴¹ The underlying pathogenesis involves oxidative stress, mitochondrial dysfunction, and chronic neuroinflammation.⁴²

A central component of PD-related inflammation is the activation of the NF- κ B signaling pathway, which promotes the release of pro-inflammatory cytokines and contributes to neuronal damage.⁴³⁻⁴⁵ In addition, the accumulation of misfolded α -synuclein proteins exacerbates neurotoxicity and immune activation, further driving disease progression.^{46,47}

Curcumin has shown promise in PD models by targeting these pathological mechanisms. It inhibits α -synuclein

aggregation, reduces oxidative burden, and suppresses NF- κ B-mediated inflammatory responses.⁴⁸⁻⁵⁰ These effects highlight curcumin's potential as a neuroprotective agent.

Although PD and ASD differ in clinical presentation, they share overlapping molecular features, particularly in the dysregulation of neuroimmune signaling.^{51,52} The anti-inflammatory and antioxidant actions of curcumin observed in PD reinforce its relevance in ASD, where similar pathways contribute to neurodevelopmental disruption.^{53,54}

1.4. Huntington's disease (HD)

HD is a hereditary illness that causes the brain's nerve cells to gradually degenerate over time and is passed down through families. This leads to a range of symptoms, including problems with movement, thinking, and mood.^{55,56} It is inherited such that if one parent carries the gene mutation, there is a 50% chance of passing it on to their children.^{57,58} A mutation results from the expansion of cytosine-adenine-guanine repeats in the *Huntingtin* gene, which causes the polyglutamine section of the *Huntingtin* protein to lengthen.^{59,60} Increasing evidence suggests that curcumin and its formulations may offer therapeutic benefits for treating HD.⁶¹⁻⁶⁶ Curcumin effectively improves symptoms of HD in a *Drosophila* model by reducing cellular dysfunction with minimal adverse effects.⁶²

1.5. TD

TD is a condition affecting the movement of the mouth and face, typically caused by prolonged use of certain medications that affect the nervous system.⁶⁷ TD involves involuntary movements, often in the face but also in the limbs and trunk. Grimacing, tongue protrusion, lip smacking, rapid eye blinking, and jerky movements of the arm, leg, and trunk are among the symptoms. Finger movements might resemble playing an invisible instrument. Currently, there is no universally agreed on treatment for TD.⁶⁸ Extended haloperidol usage has been associated with increased lipid peroxidation and decreased levels of catalase, SOD, and reduced glutathione in different parts of the brain. However, pretreatment with curcumin reversed these effects. According to neurochemical research, administering haloperidol lowered serotonin, norepinephrine, and dopamine levels in cortical and subcortical areas, including the striatum. Curcumin pretreatment at dosages of 25 and 50 mg/kg prevented this decrease (Bishnoi *et al.*⁶⁷) Based on the available data, it seems plausible that curcumin might be an effective therapy for TD. It would be intriguing to investigate in clinical trials whether combining a reduction in neuroleptic dosage with the addition of curcumin to patients' medication regimens could enhance TD symptom management.⁶⁸

1.6. MS

MS is a long-term condition involving inflammation and autoimmune activity within the CNS.⁶⁹ The fundamental mechanism involves an autoimmune assault that triggers the formation of inflammatory lesions. These lesions lead to the breakdown of myelin, damage to axons and neurons, disruption of the blood–brain barrier, and consequent neurological harm. Plaques in the white and gray matter of the brain and spinal cord accumulate as a result of this process.^{70,71} The defining characteristic of MS has long been recognized as the abundance of small lesions in the brain's white matter, categorizing it as a prototypical white matter disorder. Nonetheless, recent findings have revealed damage to gray matter as well, leading to neuronal loss and, consequently, persistent neurological deficits.⁷² Many molecular targets, including growth factors, transcription factors, inflammatory cytokines, and enzymes, have been demonstrated to interact with curcumin. This interaction contributes to its ability to exert numerous therapeutic effects against several neurological disorders, including MS.⁷³

1.7. Epilepsy

Epilepsy is a long-term neurological condition characterized by recurrent, unpredictable seizures. These seizures are classified into two main categories: generalized and partial. Partial seizures are localized, whereas generalized seizures involve the entire brain. At times, generalized seizures emerge from partial or focal seizures that spread across the brain. Despite the availability of approximately 26 antiepileptic medications that effectively manage epilepsy in about two-thirds of patients, around one-third continue to experience seizures and are deemed treatment-resistant.⁷⁴ The current medications used to treat epilepsy are associated with side effects and potential long-term complications, some of which may include hepatotoxicity.⁷⁵ Recent preclinical research suggests that curcumin may offer therapeutic potential for epilepsy and related disorders, demonstrating a favorable safety profile with no adverse effects reported.⁷⁶

1.8. Migraine

Migraine, a disorder impacting the neurological and vascular systems, is a chronic and widespread condition affecting roughly 1 billion individuals globally. Those afflicted, along with their families, coworkers, employers, and society at large, experience significant negative effects, including disability.⁷⁷ Migraine attacks lead to diminished quality of life, fertility, and workforce participation.^{78,79} Migraines are also correlated with various conditions such as anxiety, depression, cerebrovascular accidents, cardiac disorders, epilepsy, and obesity.^{80,81} The CNS is likely the origin of migraines, which alter the brain's neurovascular

and metabolic processes. These alterations are associated with dysfunction of blood vessels both within and outside the skull.⁸² Although the specific cause of migraines remains unknown, multiple factors, including genetics and environmental influences, have been linked to their onset.⁸³ Despite the availability of several medications tailored for migraine treatment, prolonged use can result in dependence, tolerance, and addiction.^{84,85} The use of drugs not specifically intended for migraine relief to manage pain is concerning and represents a major risk factor for the development of chronic migraines.⁸⁴⁻⁸⁶ Several studies have shown that curcumin may reduce migraine symptoms in both preclinical and clinical contexts. For instance, Ouyang *et al.*⁸⁷ showed that curcumin, at concentrations between 10 and 50 μM , increases the expression of glutathione, SOD, and B-cell lymphoma 2, while concurrently lowering levels of lactate dehydrogenase, ROS, malondialdehyde, p21, p53, caspase-3, and Bcl-2-associated X protein. This improves the survival of endothelial cells exposed to hydrogen peroxide.⁸⁷ This research indicates that curcumin could be beneficial in managing migraines by reducing oxidative stress and cellular damage induced by hydrogen peroxide.⁸⁷

2. Inflammatory cascade in ASD

ASD is a diverse neurodevelopmental illness characterized by challenges in daily living, communication, and social interaction. The exact triggers of ASD remain unknown.⁸⁸ Recent scientific studies have revealed the involvement of the inflammatory cascade in ASD pathogenesis. Research on the inflammatory cascade in ASD has been conducted from multiple perspectives.

2.1. Aspects of cytokines in ASD

Both pro- and anti-inflammatory cytokines play critical roles in autism, as shown by research findings. Experiments have demonstrated that ILs are important components of the inflammatory response chain associated with ASD. Children diagnosed with ASD exhibit abnormally high levels of certain cytokines in specific regions of the cerebellum, including pro-inflammatory IL-18 and its receptor IL-18R, as well as the anti-inflammatory IL-37.⁸⁹ Interrupting the production of these cytokines could have long-term effects on the brain due to their significance in neurodevelopment and neuronal function. Disturbing the expression of cytokines that play critical roles in neurological growth and neuronal activity may therefore contribute to long-term neurological complications.⁹⁰

2.2. Maternal immune inflammation and ASD

Offspring of mothers who experienced immune system activation during pregnancy suffer an increased likelihood

of developing ASD. Whenever maternal immune activation occurs, it can induce the production of inflammation-related mediators, including IL-6 and interferon gamma. Both of these substances can cross the placental barrier and interfere with neurodevelopment. Individuals later diagnosed with ASD have shown elevated levels of both of these cytokines during gestation, suggesting a possible link to the development of ASD-like phenotypes.⁹¹

The pro-inflammatory profile that comes from maternal obesity has also been linked to a greater likelihood of autism in newborns, according to several clinical studies. Maternal programming of the unborn child's immune response through a high-fat diet during pregnancy establishes a profile of inflammatory mediators that may persist into adulthood, contributing to phenotypic changes associated with ASD.⁹² Numerous clinical studies have thus associated maternal obesity and a pro-inflammatory profile with an increased risk of autism in infants. Maternal programming resulting from excessive dietary fat intake during pregnancy promotes an inflammation-based chemical profile, mainly driven by an epigenetic immunological mechanism that contributes to micro- and macrostructural impairments in brain function.⁹³

2.3. Innate immune dysfunction and neuroinflammation

Innate immunological dysfunction has been consistently observed in individuals with ASD and is typically associated with worsening behavioral symptoms. This includes abnormal innate cellular activity, signs of neuroinflammation, and microglial activation, as reported in both animal studies. The presence of restrictive and repetitive patterns of behavior, a hallmark of ASD, can range from mild to severe and is frequently accompanied by difficulties in social interaction and communication.⁹⁴

2.4. Complement system and ASD

Some research has linked ASD to the complement system, a component of the innate immune response. Post-mortem brain samples from individuals with ASD have shown decreased expression of the complement component C3. Similarly, suppression of C3 in the prefrontal cortex of mice has been shown to induce repetitive behaviors and impair social interactions. Collaborative Networking and ASD An inherent immune system component, the complement system, has been connected to ASD. Post-mortem brain samples from people experiencing ASD demonstrated the decreased expression of complement component C3. Likewise, an investigation in mice concluded that C3 knockdown in the prefrontal cortex promoted interaction obstacles and repetitive behavior.⁹¹

Dysregulation of the complement system, its role in neuroinflammation, and its potential contribution to the onset of ASD collectively highlight the complex relationship between immune responses and cognitive development in individuals with ASD. Understanding the connection between the complement mechanisms and inflammatory cascades in ASD is therefore essential for developing targeted treatments that may reduce the impact of immunological dysregulation on the sensory and behavioral manifestations of the disorder.⁹⁵

3. The role of curcumin in modulating inflammatory pathways in ASD

The Asian spice turmeric (*Curcuma longa* L.) contains curcumin, a bioactive compound with anti-inflammatory, neuroprotective, immunomodulatory, and antioxidant properties.¹⁸ Along with its many health benefits, this compound is particularly relevant for reducing inflammation in ASD⁹⁰ (Figure 2). Animal studies on autism have shown that curcumin improves mitochondrial function, reduces oxidative stress, and alleviates behavioral abnormalities.⁹¹ For example, curcumin potentiates $\alpha 7$ nicotinic acetylcholine receptors and improves autism-like social deficits and oxidative status in mice.⁹² These findings suggest that curcumin can counteract several pathophysiological mechanisms implicated in ASD.

One of the main anti-inflammatory actions of curcumin is the inhibition of NF- κ B, a transcription factor that regulates pro-inflammatory cytokines such as tumor necrosis factor α , IL-6, and IL-1 α .⁹³ Several curcumin analogs, including EF24 and EF31, have been developed to enhance this effect, with EF31 showing stronger inhibition of NF- κ B signaling than curcumin itself.⁹⁵ Beyond NF- κ B, curcumin reduces oxidative stress by scavenging ROS and reactive nitrogen species and by activating antioxidant enzymes such as SOD, catalase, and glutathione peroxidase.⁹⁶ These mechanisms help restore redox balance and reduce chronic inflammation, which are commonly observed in ASD.⁹¹

Mitochondrial dysfunction has been strongly linked to ASD. Curcumin enhances mitochondrial biogenesis and activity by upregulating peroxisome proliferator-activated receptor γ coactivator 1 α , preserving mitochondrial membrane potential, and reducing ROS production.^{97,98} Through these effects, curcumin supports synaptic plasticity and neuroprotection, both of which are impaired in ASD. By maintaining mitochondrial integrity, curcumin may help alleviate neuronal dysfunction and behavioral deficits associated with the disorder.⁹¹

Curcumin may also influence the gut-brain axis, a bidirectional communication system that is

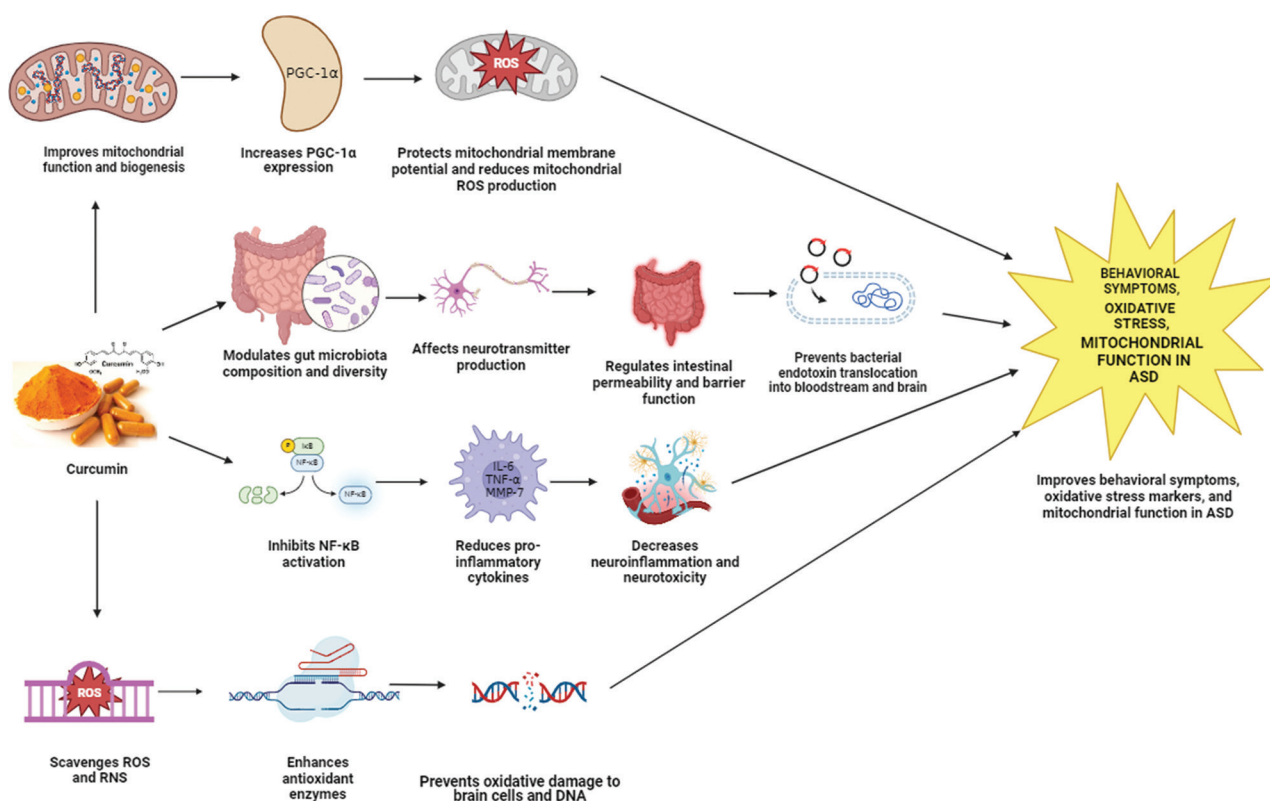


Figure 2. Schematic illustration of curcumin's role in modulating inflammatory pathways in autism spectrum disorder (ASD). Curcumin reduces oxidative stress by scavenging ROS/RNS, enhances antioxidant enzymes (SOD, CAT, GPx), inhibits NF-κB activation, protects mitochondrial function, and improves gut–brain axis communication. These combined actions help alleviate neuroinflammation and ASD-related behavioral abnormalities.

Abbreviations: CAT: Catalase; GPx: Glutathione peroxidase; IL-6: Interleukin-6; MMP-7: Matrix metalloproteinase 7; NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cell; PGC-1α: Peroxisome proliferator-activated receptor γ coactivator 1α; ROS: Reactive oxygen species; RNS: Reactive nitrogen species; SOD: Superoxide dismutase; TNF-α: Tumor necrosis factor α.

Table 1. Clinical studies of curcumin use in ASD patients

Study	Participants	Intervention	Outcome measures	Results
Al-Askar <i>et al.</i> ¹⁰⁶	24 Wistar male rats with ASD caused by propionic acid (PPA)	Curcumin (50 and 100 mg/kg) or vehicle for 28 days	Behavioral tests, oxidative stress markers, mitochondrial function, cytokines, and matrix metalloproteinase-9 (MMP-9) levels in brain tissue	Curcumin improved social interaction, locomotor activity, and exploratory behaviors in PPA-treated rats. It also reduced oxidative stress, mitochondrial dysfunction, TNF-α, and MMP-9 levels in the brain
Yang <i>et al.</i> ⁹⁷	60 children with ASD aged 3–12 years	Curcumin (100 mg/kg/day) or placebo for 6 months	Childhood Autism Rating Scale (CARS), Aberrant Behavior Checklist (ABC), and Social Responsiveness Scale (SRS)	In a small-scale clinical trial, curcumin supplementation was associated with reductions in CARS, ABC, and SRS scores; however, further studies are needed to confirm these effects
Zhong <i>et al.</i> ⁹⁹	Male BTBR model mice aged 6 days	BRBT+curcumin (20 mg/kg) for 3 days (P6–P8)	Sociability, repetitive behaviors, cognitive performance, and hippocampal neurogenesis	Neonatal curcumin treatment improved autism-related symptoms in BTBR mice, enhancing sociability, reducing repetitive behaviors, ameliorating cognitive impairments, and decreasing the suppression of hippocampal neurogenesis
Al-Askar <i>et al.</i> ¹⁰⁶	40 male rats (10 in each group)	Prenatal VPA exposure followed by postnatal curcumin (50 mg/kg/day) or saline for 7 days	Body and brain weights, maturation parameters, biochemical markers of oxidative stress, inflammation, and mitochondrial function	The curcumin-treated group showed improvements in body and brain weights, maturation parameters, and biochemical markers compared to the VPA group

Abbreviations: TNF-α: Tumor necrosis factor α; VPA: Valproic acid; ASD: Autism spectrum disorder.

frequently disrupted in ASD. It can alter gut microbiota composition, improve intestinal barrier function, and reduce the translocation of bacterial endotoxins into the bloodstream.⁹⁹ These actions may indirectly modulate neurotransmitter systems such as GABA, dopamine, and serotonin, thereby influencing behavior. Given that gastrointestinal inflammation and dysbiosis are commonly reported in ASD, curcumin's effects on gut health may contribute to its overall neuroprotective potential.¹⁰⁰

Several preclinical studies and limited clinical trials support these mechanisms. For instance, curcumin has been reported to improve social interaction and oxidative stress markers in rodent ASD models; however, these findings are preliminary and require replication.¹⁰¹ In a clinical trial, curcumin supplementation significantly reduced Childhood Autism Rating Scale and Social Responsiveness Scale (SRS) scores in children with ASD.¹⁰² While these results are promising, curcumin's low bioavailability remains a challenge.¹⁰³ New formulations using liposomes, nanoparticles, or exosomes are being investigated to improve delivery across the blood–brain barrier.^{104,105} Despite these encouraging findings (Table 1), larger and more rigorous clinical studies are needed to confirm curcumin's therapeutic role in ASD.

4. Conclusion and future perspectives

Neuroinflammation is increasingly recognized as a key contributor to the pathogenesis of ASD, influencing synaptic connectivity, neuronal development, and immune signaling. Curcumin, through its anti-inflammatory, antioxidant, and mitochondrial-protective actions, has shown potential to counter these mechanisms. Preclinical studies consistently report improvements in oxidative stress, mitochondrial function, and behavioral deficits, while early clinical data indicate reductions in autism severity scores.

Despite these encouraging findings, significant challenges remain. The poor oral bioavailability of curcumin limits its clinical translation. Advances in delivery systems, including nanoparticles, liposomes, and exosomes, may improve pharmacokinetics and enhance their therapeutic potential. Furthermore, existing human studies are limited in scale and methodological rigor, making it premature to draw firm conclusions.

Future research should prioritize large, well-controlled clinical trials to establish efficacy, optimal dosing, and long-term safety. Investigations into curcumin's interactions with conventional therapies and its role in modulating gut–brain communication may also provide valuable insights. Overall, curcumin represents a promising adjunctive approach for reducing neuroinflammation and

improving behavioral outcomes in ASD, but robust clinical validation is still required before its widespread use can be recommended.

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Conflict of interest

The authors declare that they have no competing interests.

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