Uso de medicamentos no tratamento do transtorno do espectro autista em crianças: revisão narrativa

Use of medications in the treatment of autism spectrum disorder in children: a narrative review

Uso de medicamentos en el tratamiento del trastorno del espectro autista en niños: una revisión narrativa

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How to cite: *Sgorlon MFS, Brand SM, Barbosa AJC, Moreira NM, Zilly A*. Medications for autism in children. REVISA. 2026; 15(4): 16-36. Doi: https://doi.org/10.36239/revisa.v15.n4.p16a36

REVISA

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Recebido: 13/01/2026
Aprovado: 27/03/2026

RESUMO

Objetivo: identificar, na literatura científica, os principais medicamentos utilizados no tratamento de crianças com Transtorno do Espectro Autista (TEA). **Métodos**: revisão narrativa da literatura, de abordagem qualitativa e caráter descritivo-exploratório, realizada nas bases PubMed e SciELO, considerando publicações dos últimos cinco anos. Foram incluídos estudos em português ou inglês relacionados à farmacoterapia em crianças com TEA, contemplando uso, eficácia, segurança ou padrões de utilização de medicamentos. **Resultados**: foram identificados 595 registros e, após remoção de duplicatas, triagem e aplicação dos critérios de elegibilidade, 22 estudos compuseram a síntese final. A farmacoterapia mostrou-se direcionada principalmente ao manejo de sintomas associados e comorbidades. Risperidona e aripiprazol apresentaram evidências mais consistentes para irritabilidade, agressividade e comportamentos desafiadores; metilfenidato, atomoxetina e guanfacina foram identificados no manejo de sintomas relacionados ao TDAH; e a melatonina apresentou resultados favoráveis para distúrbios do sono. Terapias direcionadas aos sintomas centrais do TEA e estratégias emergentes apresentaram resultados heterogêneos ou evidências limitadas. **Conclusão**: não há tratamento farmacológico único para o TEA. A farmacoterapia deve ser individualizada e orientada pelo sintoma-alvo, comorbidades, resposta clínica e perfil de segurança dos medicamentos.

Descritores: Transtorno do Espectro Autista; Farmacoterapia; Medicamentos; Crianças.

ABSTRACT

Objective: to identify, in scientific literature, the main medications used in the treatment of children with autism spectrum disorder (ASD). **Methods:** a narrative review of the literature, with a qualitative approach and a descriptive-exploratory character, carried out in the PubMed and SciELO databases, considering publications from the last five years. Studies in Portuguese or English related to pharmacotherapy in children with ASD were included, including the use, efficacy, safety, or patterns of medication use. **Results:** 595 records were identified and, after removal of duplicates, screening and application of eligibility criteria, 22 studies composed the final synthesis. Pharmacotherapy was shown to be directed mainly to the management of associated symptoms and comorbidities. Risperidone and aripiprazole presented more consistent evidence for irritability, aggressiveness, and challenging behaviors; methylphenidate, atomoxetine, and guanfacine have been identified in the management of ADHD-related symptoms; and melatonin showed favorable results for sleep disorders. Therapies targeting core symptoms of ASD and emerging strategies have shown heterogeneous results or limited evidence. **Conclusion:** there is no single pharmacological treatment for ASD. Pharmacotherapy should be individualized and guided by the target symptom, comorbidities, clinical response, and drug safety profile.

Descriptors: Autism Spectrum Disorder; Pharmacotherapy; Medications; Children.

RESUMEN

Objetivo: identificar, en la literatura científica, los principales medicamentos utilizados en el tratamiento de niños con Trastorno del Espectro Autista (TEA). **Métodos**: una revisión narrativa de la literatura, con un enfoque cualitativo y un carácter descriptivo-exploratorio, realizada en las bases de datos PubMed y SciELO, considerando publicaciones de los últimos cinco años. Se incluyeron estudios en portugués o inglés relacionados con farmacoterapia en niños con TEA, incluyendo el uso, eficacia, seguridad o patrones de uso de medicación. **Resultados**: Se identificaron 595 registros y, tras la eliminación de duplicados, el cribado y la aplicación de criterios de elegibilidad, 22 estudios compusieron la síntesis final. Se demostró que la farmacoterapia se dirige principalmente al manejo de los síntomas y comorbilidades asociadas. La risperidona y el aripiprazol presentaron evidencia más consistente de irritabilidad, agresividad y conductas desafiantes; se han identificado metilfenidato, atomoxetina y guanfacina en el manejo de síntomas relacionados con el TDAH; y la melatonina mostró resultados favorables para los trastornos del sueño. Las terapias que abordan los síntomas centrales del TEA y las estrategias emergentes han mostrado resultados heterogéneos o evidencia limitada. **Conclusión**: no existe un tratamiento farmacológico único para el TEA. La farmacoterapia debe individualizarse y guiarse por el síntoma objetivo, las comorbilidades, la respuesta clínica y el perfil de seguridad del medicamento.

Descriptores: Trastorno del Espectro Autista; Farmacoterapia; Medicamentos; Niños.

REVIEW

Introduction

Autism spectrum disorder (ASD) is a highly complex neurodevelopmental condition characterized by persistent deficits in social interaction and communication, together with restricted, repetitive behaviors, interests, or activities[1]. Given its multifactorial biological origins and etiopathogenic mechanisms that have yet to be fully elucidated, the term "spectrum" is used to represent the marked variability in symptoms, differing levels of clinical impairment, and heterogeneous individual responses to therapeutic interventions[2].

The DSM-5 classification divides ASD into three severity levels based on the degree of support required in social communication and interaction, as well as restricted and stereotyped behaviors. Level 1 refers to individuals requiring support; level 2 is characterized by the need for substantial support; and level 3 applies to cases requiring very substantial support[3]. The main clinical manifestations typically emerge in early childhood, commonly by three years of age, and include reduced or absent eye contact, delayed or absent development of verbal language, motor stereotypies such as hand flapping, difficulty adhering to social conventions, gaze avoidance, absence of early vocalizations, and unusual sensory sensitivity[4].

Global statistics suggest that the disorder affects approximately 1% of the world's population, while recent surveys in the United States estimate a diagnosis rate of 1 in 36 eight-year-old children. In Brazil, data from the 2022 Population Census indicated that approximately 2.4 million people reported having an ASD diagnosis, representing nearly 1.2% of the country's population, with a higher concentration of diagnoses among children aged 5–9 years and a clear predominance among males[5,6].

The clinical presentation of ASD becomes even more challenging because of the high prevalence of co-occurring psychiatric and medical conditions, observed in approximately 70% of affected individuals. Conditions with a major impact on pharmacotherapeutic decisions include attention-deficit/hyperactivity disorder (ADHD), anxiety and mood disorders, episodes of hostility and aggression, sleep disturbances, and epilepsy. These associated manifestations substantially compromise functional performance, learning, and the overall well-being of individuals and their families[7,8].

Despite scientific advances, no pharmacological agents have yet been approved to alleviate the core symptoms of ASD, and current medication-based interventions remain limited to managing specific behavioral manifestations. In this context, only risperidone and aripiprazole have formal regulatory approval to reduce aggressive behavior and marked irritability in the pediatric population on the autism spectrum[9,10]. Other medication classes, including psychostimulants, antidepressants, mood stabilizers, and melatonin, are commonly used off-label, although the scientific evidence supporting several of these therapies is considered limited or conflicting[11,12].

The individual characteristics of each pediatric patient on the autism spectrum, together with interindividual pharmacokinetic differences, pose considerable challenges to establishing universal treatment guidelines[13]. Important clinical questions also remain regarding the long-term effectiveness and safety of various routinely prescribed agents, and identifying the medications most frequently used in healthcare services is therefore warranted. From this perspective, this study undertakes a narrative review of scientific publications from the past five years to identify the pharmacological agents most commonly used in the therapeutic management of children with ASD.

Objective

To identify, through a literature search, the main medications used in the treatment of children with autism spectrum disorder (ASD).

Methods

This study is a narrative literature review with a qualitative approach and a descriptive and exploratory design. The methodology was structured to gather and analyze the available scientific evidence on medication-based treatment for children with autism spectrum disorder (ASD).

Studies were searched for in the PubMed and SciELO databases, considering articles published within the past five years. The search used the terms "medicamentos and/or transtorno do espectro autista" and "crianças autistas and/or medicamentos".

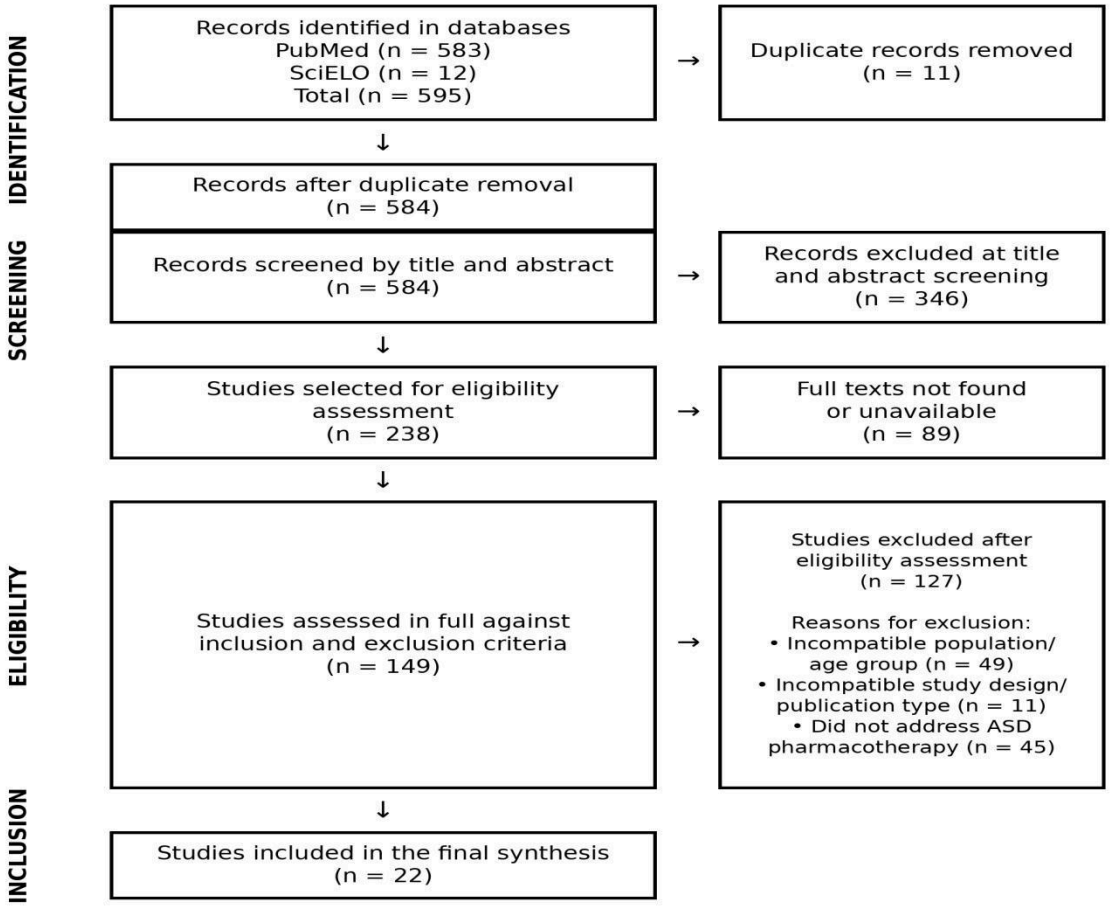
Articles published in Portuguese or English within the specified period and related to the research topic were included. Eligible studies also had to involve children diagnosed with ASD and address aspects of medication use, efficacy, safety, or prescribing. Duplicate articles, studies involving populations or age groups other than those defined for the review, studies that did not directly address medication-based treatment in ASD, and articles whose full text was unavailable for analysis were excluded.

Titles and abstracts were initially screened to identify studies related to the topic. The selected articles were then read in full to assess their relevance to the research question and compliance with the established criteria. Books and scientific materials available on digital platforms were also consulted to supplement the search.

Because this study was based exclusively on the analysis of previously published literature, without direct human participation or access to individual participant information, submission to a Research Ethics Committee was not required.

Results

The initial search of the specified databases yielded 595 references. After 11 duplicate articles were identified and removed, 584 records remained for screening.



Source: prepared by the authors (2026).

Figure 1 – Flowchart of the literature search and the identification, screening, eligibility assessment, and inclusion of selected studies

The search of the PubMed and SciELO databases initially identified 595 records, including 583 from PubMed and 12 from SciELO. Eleven duplicate records were removed, and 584 studies underwent title and abstract screening. At this stage, 346 records unrelated to the topic or research question were excluded, leaving 238 studies selected for eligibility assessment. Of these, 89 full texts could not be located, were unavailable, or were incomplete, allowing 149 studies to be assessed in full.

After full-text assessment, 127 studies were excluded, mainly because they involved an incompatible population or age group (n = 49), did not address pharmacotherapy in autism spectrum disorder (ASD) (n = 45), or had an incompatible study design or publication type (n = 11). At the end of the literature selection process, 22 studies met the defined criteria and were included in the final synthesis.

The studies analyzed addressed different aspects of medication-based treatment for children and adolescents with ASD, particularly the use of medications to control irritability and aggressive behaviors, manage ADHD-related symptoms, sleep disturbances, and other manifestations or comorbidities associated with ASD. Some studies also evaluated pharmacological treatments that remain under investigation, while others examined prescribing patterns and psychotropic medication use in this population.

Among the most frequently investigated medications were risperidone and

aripiprazole, primarily for controlling irritability, aggression, and challenging behaviors. Medications used for ADHD-related symptoms, including methylphenidate, atomoxetine, and guanfacine, were also identified, as was melatonin for managing sleep disturbances. Other medications and substances, such as valproic acid, memantine, and propranolol, were also addressed. Among investigational alternatives, studies examined intranasal oxytocin, balovaptan, folinic acid, phytocannabinoids, metformin, and N-acetylcysteine (NAC), with varying results regarding efficacy and adverse effects.

Table 1 presents the main characteristics of the 22 studies included in the review, bringing together information on methodological aspects and the pharmacological treatments evaluated:

Author/year	Study title	Design/sample	Medication(s)/focus	Main findings
Lalanne et al. (2021)	Melatonin: From Pharmacokinetics to Clinical Use in Autism Spectrum Disorder	Review of the clinical use and pharmacokinetics of melatonin in pediatric ASD.	Melatonin – sleep disorders.	Reports benefits primarily for sleep onset latency and sleep quality, with good tolerability, supporting its use in managing sleep disorders in children and adolescents with ASD.
Sikich et al. (2021)	Intranasal Oxytocin in Children and Adolescents with Autism Spectrum Disorder	Phase 2 randomized, placebo-controlled clinical trial, 24 weeks; 290 participants aged 3–17 years.	Intranasal oxytocin – social functioning.	No significant difference between oxytocin and placebo in the primary outcome of social withdrawal; adverse events were similar between groups.
Popow et al. (2021)	Practitioner's review: medication for children and adolescents with autism spectrum disorder (ASD) and comorbid conditions	Clinical review; children and adolescents with ASD and comorbidities.	Various psychotropic medications – ADHD, behavior, sleep, and other comorbidities.	Emphasizes that pharmacotherapy primarily targets comorbidities and associated symptoms when nonpharmacological interventions are insufficient.
Kloosterboer et al. (2021)	Risperidone plasma concentrations are associated with side effects and effectiveness in children and adolescents with autism spectrum disorder	Prospective observational study, 24 weeks; 42 participants aged 6–18 years.	Risperidone – behavioral problems/irritability.	Higher exposure was associated with greater effectiveness, but also with higher BMI, sedation, and prolactin levels, reinforcing the need for monitoring.
Wang et al. (2021)	The efficacy and safety in attention deficit hyperactivity disorder of second-generation antipsychotics and other medications for hyperactivity in children and adolescents with autism: a meta-analysis	Meta-analysis of 13 double-blind randomized trials; 712 children and adolescents with ASD.	Second-generation antipsychotics and ADHD medications – hyperactivity.	Both groups reduced hyperactivity but increased adverse events; somnolence with antipsychotics and decreased appetite with ADHD medications were prominent.

Author/year	Study title	Design/sample	Medication(s)/focus	Main findings
Wiggins et al. (2021)	Many Young Children with Autism Who Use Psychotropic Medication Do Not Receive Behavior Therapy: A Multisite Case-Control Study	Multisite case-control study; 763 children with ASD aged 2–5 years.	Various psychotropic medications – behavioral symptoms.	Psychotropic medications were used by 8.1%, and 3.7% had started medication by age 3; a substantial proportion of users had not received behavioral therapy.
Batebi et al. (2021)	Folinic Acid as Adjunctive Therapy in Treatment of Inappropriate Speech in Children with Autism: A Double-Blind and Placebo-Controlled Randomized Trial	Randomized, double-blind, placebo-controlled trial; 55 children with ASD, mean age 13.4 years.	Folinic acid combined with risperidone – inappropriate speech and behavioral symptoms.	Significant improvement in inappropriate speech, stereotypies, and hyperactivity/noncompliance; no significant difference in social withdrawal or irritability. Preliminary evidence.
Siafis et al. (2022)	Pharmacological and dietary-supplement treatments for autism spectrum disorder: a systematic review and network meta-analysis	Systematic review and network meta-analysis; 125 RCTs, 7,450 children/adolescents; 41 medications and 17 supplements.	Risperidone, aripiprazole, atomoxetine, bumetanide, and others.	Some agents showed benefits in specific domains, but confidence in the estimates was generally low or very low; does not support routine prescribing for core symptoms.
Maniram et al. (2022)	Pharmacological Management of Core Symptoms and Comorbidities of Autism Spectrum Disorder in Children and Adolescents: A Systematic Review	Systematic review; 33 studies.	Risperidone, aripiprazole, methylphenidate, guanfacine, atomoxetine, and others.	Identified options for insomnia, hyperactivity, irritability/aggression, and other comorbidities; agents targeting core symptoms remain under investigation.
Hollander et al. (2022)	Balovaptan vs Placebo for Social Communication in Childhood Autism Spectrum Disorder: A Randomized Clinical Trial	Phase 2 randomized, double-blind, placebo-controlled clinical trial; 339 participants aged 5–17 years.	Balovaptan – socialization and communication.	No significant benefit versus placebo in socialization/communication outcomes at 24 weeks; generally well tolerated.
Kompella et al. (2022)	Impact of Antipsychotic Use on Readmission Rates in Children and Adolescents With Autism Spectrum Disorder and Irritability	Multicenter retrospective study; 2,375 patients aged 6–17 years.	Antipsychotics, primarily risperidone and aripiprazole – irritability.	Antipsychotic use was associated with reduced readmissions at 30 and 90 days; risperidone and aripiprazole showed similar results.

Author/year	Study title	Design/sample	Medication(s)/focus	Main findings
Alsayouf et al. (2022)	Core Signs and Symptoms in Children with Autism Spectrum Disorder Improved after Starting Risperidone and Aripiprazole in Combination with Standard Supportive Therapies: A Large, Single-Center, Retrospective Case Series	Retrospective case series; 82 children aged 2–13 years.	Risperidone or aripiprazole combined with supportive therapies.	Reported substantial clinical improvement, with asymptomatic hyperprolactinemia and excessive weight gain among the main adverse effects; the observational design limits causal inference.
Mellahn et al. (2022)	Understanding the Diversity of Pharmacotherapeutic Management of ADHD With Co-occurring Autism: An Australian Cross-Sectional Survey	Cross-sectional study of caregivers of 505 children aged 2–18 years; ADHD, ASD, and ADHD+ASD groups.	Stimulants, nonstimulants, antipsychotics, antidepressants, and melatonin.	The ADHD+ASD group used a broader range of medication classes, reinforcing the need for individualized treatment in the presence of comorbidities.
Alenezi et al. (2022)	Psychotropic Medications Use among Children with Autism in Saudi Arabia	Cross-sectional study of 293 parents of children with ASD.	Risperidone, methylphenidate, valproic acid, and other psychotropic medications.	Current medication use was reported by 39.08%; among users, risperidone (53%), methylphenidate (30%), and valproic acid (9%) were most frequently reported.
Brignell et al. (2022)	Memantine for autism spectrum disorder	Cochrane systematic review; 3 RCTs, 204 participants; children/adolescents, mean age 9.4 years.	Memantine – core and associated symptoms.	No clear evidence of benefit for core or associated symptoms; certainty of evidence was very low.
Sadeh et al. (2023)	Adherence to treatment and parents' perspective about effectiveness of melatonin in children with autism spectrum disorder and sleep disturbances	Retrospective pediatric cohort and caregiver survey.	Melatonin – sleep disorders.	Caregivers reported improvements in sleep onset, duration, and nighttime awakenings; reported adverse events were mainly mild.

Author/year	Study title	Design/sample	Medication(s)/focus	Main findings
Guastella et al. (2023)	The effect of oxytocin nasal spray on social interaction in young children with autism: a randomized clinical trial	Randomized, double-blind, placebo-controlled clinical trial; 87 children aged 3–12 years.	Intranasal oxytocin – social responsiveness and interaction.	No significant overall effect; an exploratory signal suggested possible benefit in younger children, without consistent confirmation in other outcomes.
Ibsen and Thomsen (2024)	Cannabinoids as alleviating treatment for core symptoms of autism spectrum disorder in children and adolescents: a systematic review	Pediatric systematic review; 5 studies, including 2 RCTs and 3 cohorts.	Cannabinoids/CBD – core and behavioral symptoms.	Evidence for core symptoms was inconclusive and predominantly at high risk of bias; possible behavioral benefits were described, but safety and long-term effects remain uncertain.
London et al. (2024)	High-Dose Propranolol for Severe and Chronic Aggression in Autism Spectrum Disorder: A Pilot, Double-Blind, Placebo-Controlled, Randomized Crossover Study	Randomized, double-blind, crossover pilot trial; 6 participants aged 12–19 years.	Propranolol – severe/chronic aggression.	Approximately 50% reduction in CGI-I and 37% in ABC-C/I versus placebo; the very small sample limits generalizability.
Maniram et al. (2024)	An Overview of Pharmacotherapy in the Management of Children with Autism Spectrum Disorder at a Public Hospital in KwaZulu-Natal	Retrospective quantitative study; 181 children with ASD.	Risperidone, methylphenidate, melatonin, sodium valproate, carbamazepine, and others.	Risperidone was the most frequently prescribed medication (88%); other medications were used primarily for comorbidities. Improvement was documented in some medical records.
Bazrafshan et al. (2025)	Metformin efficacy and safety as an adjunctive treatment for irritability in children with autism spectrum disorder: A randomized, double-blind, placebo-controlled trial	Randomized, double-blind, placebo-controlled trial, 10 weeks; 55 children with ASD.	Metformin as an adjunct to risperidone – irritability.	Metformin significantly reduced irritability versus placebo and showed signs of benefit for hyperactivity and inappropriate speech; the authors recommend confirmation before widespread use.
Williams et al. (2025)	Glutathione, Vitamin C, and Cysteine Use in Autistic Children With Disruptive Behavior: A Double-Blind, Placebo-Controlled Crossover Pilot Study	Randomized, double-blind, crossover pilot trial; 24 children aged 5–16 years.	Glutathione alone or combined with vitamin C and N-acetylcysteine (NAC) – disruptive behavior.	No difference between treatment and placebo in behavioral or biological outcomes; no significant adverse effects attributable to the interventions were observed.

Fonte: elaborado pelos autores (2026), com base nos registros recuperados e triados no Rayyan.
***Nota metodológica:** foram retirados da versão anterior os estudos com população mista ou faixa etária ampliada que dificultavam atribuir os resultados à população pediátrica. As substituições foram feitas por registros presentes no conjunto de 584 referências da busca atual, preservando a rastreabilidade da seleção. O ensaio de ácido folínico de Panda et al. (2024) não foi incluído por ter sido retratado em 2026; o ensaio de Batebi et al. (2021) é uma publicação distinta.

Analysis of the 22 selected studies indicated that medication-based treatment for children and adolescents with ASD primarily focuses on managing associated symptoms and comorbidities. The evidence identified in the literature also showed varying levels of consistency, depending on the medication used and the outcomes evaluated in each study.

Among the medications analyzed, the second-generation antipsychotics risperidone and aripiprazole stood out; these are used primarily to control irritability, aggression, and behavioral disturbances. The studies also indicated benefits from methylphenidate, atomoxetine, and guanfacine in managing ADHD-related symptoms. For sleep disturbances and insomnia, melatonin showed favorable results, including reduced sleep onset latency, increased total sleep duration, and improved sleep quality.

Studies evaluating medication use profiles found a high frequency of psychotropic prescribing among children and adolescents with ASD. Alenezi et al. (2022) observed that 39.08% of the participants assessed were receiving medication treatment, with risperidone being the most frequently reported medication, followed by methylphenidate and valproic acid. Similarly, Maniram et al. (2024) identified risperidone as the most frequently prescribed medication (88%) in the medical records analyzed.

Regarding treatment safety and tolerability, the studies identified several important adverse effects. For risperidone, better treatment responses were observed in individuals with higher drug concentrations in the body; however, these individuals also experienced increased body mass index (BMI), somnolence, and elevated prolactin levels. Other studies likewise observed significant weight gain and increased prolactin associated with antipsychotic use.

For treatments that remain under investigation or have limited supporting evidence, the review identified studies on memantine, propranolol, intranasal oxytocin, balovaptan, folinic acid, cannabinoids, metformin combined with other medications, and N-acetylcysteine, with varying results. While some studies reported benefits for specific symptoms or aspects, others found no significant differences compared with placebo or provided low-level evidence, limiting firm conclusions about efficacy.

Overall, the studies selected for this review show that medications are frequently prescribed to control symptoms associated with ASD, including aggression, irritability, hyperactivity, ADHD symptoms, and sleep disturbances. In contrast, pharmacological treatments targeting the core symptoms of ASD continue to show limited or inconclusive results, indicating the need for further studies to establish their efficacy and safety.

Discussion

The main finding of this review is that medication-based treatment for children with ASD primarily targets associated symptoms and comorbidities, including aggression, irritability, agitation, ADHD-related symptoms, and sleep disturbances[14-17]. The variety of medications identified reinforces the need to consider each patient's symptoms and clinical characteristics when selecting treatment. Medications should be used primarily when associated symptoms significantly interfere with school performance, development, or the quality of life of the child and family; behavioral and educational interventions therefore remain fundamental to the care of children and adolescents with ASD[14,16,18].

The selected studies clearly highlighted risperidone and aripiprazole for controlling irritability, physical or verbal aggression, and challenging behaviors[16,19]. The results demonstrate benefits from these antipsychotics in managing behavioral disturbances, although the different study designs and methods must be considered. In a retrospective study[19], atypical antipsychotic use was associated with reduced readmissions among

children and adolescents with ASD and severe irritability, with no important differences between risperidone and aripiprazole; however, the retrospective design does not allow a direct causal relationship to be established. Favorable outcomes were also observed when these medications were combined with conventional rehabilitation and supportive therapies[14], but the observational nature of the evidence prevents precise determination of how much of the improvement can be attributed exclusively to medication treatment.

Beyond the observed benefits, the potential adverse effects of antipsychotic use must be considered, particularly in pediatric patients. The most commonly reported effects include weight gain, metabolic changes, somnolence, and increased prolactin levels[14,20]. Studies indicate that higher risperidone concentrations in the body may be associated both with a better clinical response and with increased BMI, somnolence, and elevated prolactin[20]. These findings reinforce the need to assess treatment benefits alongside potential risks, requiring regular follow-up to allow individualized dose adjustment throughout treatment.

For controlling hyperactivity and ADHD symptoms associated with ASD, the studies reported the use of stimulant and nonstimulant medications, particularly methylphenidate, atomoxetine, and guanfacine[16,17,21]. A meta-analysis[29] showed that both atypical antipsychotics and ADHD medications contributed to reduced hyperactivity in children and adolescents with ASD, although benefits were accompanied by adverse effects, primarily somnolence among patients receiving antipsychotics and decreased appetite among those receiving ADHD medications[29]. Accordingly, the studies do not identify a single treatment as the most appropriate for all patients; medication selection should consider presenting symptoms, comorbidities, individual treatment response, and potential associated risks[16,21].

Studies evaluating prescribing patterns also highlighted the need for individualized treatment. Different medication classes were identified for managing ASD-associated symptoms, including antipsychotics, stimulants, and other agents used to treat co-occurring conditions[9]. Studies of prescribing patterns demonstrated a wide range of medications used by children with ASD[17]. This diversity was even greater among children with both ASD and ADHD, reflecting the need to treat different symptoms and associated conditions[21]. These findings reinforce that medication treatment should be determined by each patient's needs and characteristics, with no single therapeutic regimen suitable for all children with ASD.

Data on psychotropic use also show that these medications are common in clinical practice. In one study based on information provided by family members and caregivers, 39% of participants were taking medications, with risperidone being the most frequently reported drug, followed by methylphenidate and valproic acid. These findings demonstrate the use of different medication classes in the care of children with ASD and reinforce that pharmacotherapy primarily targets behavioral symptoms and associated conditions, rather than solely treating ASD as a whole[33].

For sleep disturbances, melatonin showed favorable results and good tolerability in the studies analyzed. Improvements were observed mainly in reduced sleep onset latency, increased sleep duration and quality, and fewer nighttime awakenings, with generally mild adverse effects[22,23]. Because sleep problems can affect both the child's behavior and family quality of life, these findings reinforce the importance of identifying and treating such disturbances as part of the care of children with ASD.

Treatments investigated to improve the core symptoms of ASD, however, showed less consistent evidence. Balovaptan showed no significant difference from placebo in social interaction or communication[15]. Similarly, intranasal oxytocin did not produce significant clinical improvement in social functioning[24,25], although exploratory analyses

suggested possible benefits in younger children[25]. Taken together, these results remain insufficient to recommend the routine use of these substances in clinical practice.

Similarly, memantine and cannabinoids had limited supporting evidence. For memantine, studies showed no clear benefits for core or associated ASD symptoms, and the quality of evidence was considered very low[26]. For cannabinoids, results remain inconsistent and inconclusive, with methodological limitations, risk of bias, and uncertainty about long-term safety[27]. Thus, although some studies report improvements in certain behavioral aspects, the available evidence remains insufficient to confirm the efficacy and safety of these medications in children with ASD.

Among complementary approaches still under investigation, high-dose propranolol showed positive results in controlling severe, persistent aggression in a pilot study[28]. However, the small number of participants limits generalizability, and studies with larger samples are needed to confirm the observed benefits. This finding illustrates a common feature of treatments in the early stages of investigation: despite promising results, more consistent evidence is required before their application in clinical practice.

Another finding requiring cautious interpretation concerns folinic acid. A controlled clinical study[30] found that its combination with risperidone was associated with improvements in inappropriate speech, stereotyped behaviors, hyperactivity, and resistance to change. However, no significant differences were found in social withdrawal or irritability[30]. These results suggest possible benefits for specific symptoms but do not yet establish folinic acid as effective for different ASD manifestations; further studies are needed before broader use can be recommended.

Another relevant finding was the use of metformin combined with risperidone, which significantly reduced irritability compared with placebo and showed possible benefits for hyperactivity and speech disturbances. Despite these favorable results, the study included only 55 participants and lasted ten weeks, limiting the applicability of its findings to larger populations and longer periods[31]. Additional studies are therefore needed to confirm these findings and better assess its effects. Based on the evidence analyzed in this review, metformin should be considered an investigational option rather than an established treatment for irritability in children with ASD.

Not all investigational treatments showed positive results. Glutathione, either alone or combined with vitamin C and N-acetylcysteine (NAC), showed no significant differences from placebo in the behavioral or biological outcomes assessed in children with severe behavioral disturbances. Although no serious adverse effects were recorded, the absence of significant benefits demonstrates that a plausible biological rationale for using a substance is insufficient to establish its efficacy in clinical practice[32].

Differences among the results identified in this review also highlight the gap between medications supported by more consistent evidence and treatments still in the early stages of investigation. While risperidone and aripiprazole have stronger evidence for controlling irritability, aggression, and challenging behaviors, melatonin has shown favorable results for treating sleep disturbances. Other substances, however, show more variable results and less consistent evidence[10,16,22,23].

A systematic review with network meta-analysis[10] reinforces this distinction by showing that, although some medications provide benefits for specific symptoms, the quality of evidence remains low for several interventions, particularly those targeting the core symptoms of ASD.

Another aspect warranting attention is the frequency of psychotropic medication use among children and adolescents with ASD. The studies included in this review show that these medications are part of clinical practice and that their use may begin in childhood[18], a situation requiring attention. A large proportion of prescriptions target

specific symptoms and associated conditions, and both benefits and adverse effects may vary among patients[16,17]. Medication treatment should therefore begin with a clear definition of the target symptom, taking into account potential benefits, risks, and each child's individual response. Pharmacotherapy must also be integrated with behavioral interventions and multidisciplinary follow-up, which continue to play an important role in the care of children and adolescents with ASD.

Variation in study methods also makes direct comparison among treatments difficult. Included studies comprised randomized clinical trials, prospective and cohort studies, surveys based on questionnaires completed by parents or caregivers, retrospective studies, systematic reviews, and meta-analyses. These studies differed substantially in participant numbers and ages, follow-up duration, and outcomes assessed. Some investigational treatments were examined in small samples, while other studies used caregiver-reported information or medical record data. These methodological differences must be considered when interpreting the findings, as the level of evidence is not the same for all medications analyzed.

Overall, the studies evaluated show that no single medication can comprehensively treat ASD, as pharmacological treatment in childhood primarily targets specific symptoms and associated conditions. Risperidone and aripiprazole have more consistent evidence for managing irritability, aggression, and difficult-to-control behaviors. Methylphenidate, atomoxetine, and guanfacine show benefits for managing ADHD-related symptoms, while melatonin has demonstrated favorable results for sleep disturbances.

Conversely, substances such as folinic acid, metformin, propranolol, intranasal oxytocin, balovaptan, memantine, cannabinoids, and antioxidants continue to show variable or inconclusive results, requiring further studies to better clarify their efficacy and safety. The findings of this review therefore reinforce the importance of individualized medication treatment, determined by each patient's symptoms and needs and based on the best available evidence, while consistently weighing benefits against potential adverse effects.

Conclusion

This review provided an overview of the main medication-based treatments used in children and adolescents with ASD. The findings show that pharmacotherapy primarily targets associated symptoms and comorbidities rather than treating ASD comprehensively. Medication selection should therefore be individualized, considering each patient's clinical characteristics, presenting symptoms, and needs.

Among the treatments analyzed, the antipsychotics risperidone and aripiprazole had more consistent evidence for controlling irritability, aggression, and challenging behaviors. Despite the observed benefits, their use requires attention to potential adverse effects, including weight gain, metabolic changes, somnolence, and hormonal changes. These risks reinforce the importance of regular medical follow-up during treatment to assess clinical response and identify potential unwanted effects.

For children with ASD who also have ADHD-related symptoms, medications such as methylphenidate, atomoxetine, and guanfacine demonstrated benefits, although response and tolerability may vary among patients. For sleep disturbances, melatonin showed favorable results in the studies analyzed. In contrast, treatments targeting the core symptoms of ASD and some investigational alternatives, such as oxytocin, balovaptan, memantine, and cannabinoids, showed less consistent results. The available evidence is therefore still insufficient to recommend routine use of these substances in clinical practice.

Overall, the findings of this review reinforce that medication treatment should be part of individualized, multidisciplinary care, taking into account the symptoms that most interfere with quality of life, associated conditions, clinical course, and each patient's response to medication. Despite advances in the literature, questions remain regarding the efficacy and safety of some interventions. Further studies with greater methodological rigor, larger samples, and longer follow-up periods are therefore needed, particularly focusing on children and adolescents with ASD.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgments

This study was self-funded by the authors.

References

1. Paditz E, Renner B, Koch R, Schneider BM, Schlarb AA, Ipsiroglu OS. The pharmacokinetics, dosage, preparation forms, and efficacy of orally administered melatonin for non-organic sleep disorders in autism spectrum disorder during childhood and adolescence: a systematic review. Children (Basel). 2025;12(5):648. Disponível em: https://www.mdpi.com/2227-9067/12/5/648. Acesso em: 02 jul. 2026.

2. Sauer AK, Stanton JE, Hans S, Grabrucker AM. Autism spectrum disorders: etiology and pathology. In: Grabrucker AM, editor. Autism Spectrum Disorders [Internet]. Brisbane (AU): Exon Publications; 2021 [cited 2025 Dec 12]. Chapter 1. Available from: NCBI Bookshelf

3. Waizbard-Bartov E, Fein D, Lord C, Amaral DG. Autism severity and its relationship to disability. Autism Res. 2023;16(4):685-696. Disponível em: https://onlinelibrary.wiley.com/doi/abs/10.1002/aur.2898. Acesso em: 22 jul. 2026.

4. Tomiyama S, Yoshida K, Tani H, Uchida H. Pharmacological treatment of autism spectrum disorder: a systematic review of treatment guidelines. Pharmacopsychiatry. 2025;58(3):100-116. Disponível em: https://www.thieme-connect.com/products/ejournals/abstract/10.1055/a-2514-4452. Acesso em: 05 ago. 2026.

5. Seize MM, Borsa JC. Questionário para Rastreio de Sinais Precoces do Transtorno do Espectro Autista: evidências de validade e consistência interna. J Bras Psiquiatr. 2022;71(3):176-185. Disponível em: https://www.scielo.br/j/jbpsiq/a/h66FRPSd6kp963Tmp4WGWwd/abstract/?lang=en. Acesso em: 01 ago. 2026.

6. Pereira DA, Cheidde L, Megiolaro MDR, Camargo AEF, Weba ETP, Soares VG, et al. Efficacy and safety of cannabinoids for autism spectrum disorder: an updated systematic review. Cureus. 2025;17(3):e80725. Disponível em:

https://assets.cureus.com/uploads/review_article/pdf/347254/20250417-283611-m7dvqf.pdf. Acesso em: 01 ago. 2026.

7. World Health Organization. Autism [Internet]. Geneva: World Health Organization; 2025 Sep 17 [cited 2026 Aug 18]. Disponível em: https://www.who.int/en/news-room/fact-sheets/detail/autism-spectrum-disorders. Acesso em: 15 ago. 2026.

8. Mano-Sousa BJ, Pedrosa AM, Alves BC, Galduróz JCF, Belo VS, Chaves VE, et al. Effects of risperidone in autistic children and young adults: a systematic review and meta-analysis. Curr Neuropharmacol. 2021;19(4):538-552. Disponível em: https://www.ingentaconnect.com/content/ben/cn/2021/00000019/00000004/art00009. Acesso em: 21 ago. 2026.

9. Maniram J, Karrim SBS, Oosthuizen F, Wiafe E. Pharmacological management of core symptoms and comorbidities of autism spectrum disorder in children and adolescents: a systematic review. Neuropsychiatr Dis Treat. 2022; 18:1629-1644. Disponível em: https://www.tandfonline.com/doi/full/10.2147/NDT.S371013. Acesso em: 03 29. jul. 2026.

10. Siafis S, Çıray O, Wu H, Schneider-Thoma J, Bighelli I, Krause M, et al. Pharmacological and dietary-supplement treatments for autism spectrum disorder: a systematic review and network meta-analysis. Mol Autism. 2022;13(1):10. Disponível em: https://link.springer.com/article/10.1186/s13229-022-00488-4. Acesso em: 19 ago. 2026.

11. Manter MA, Birtwell KB, Bath J, Friedman ND, Keary CJ, Neumeyer AM, et al. Pharmacological treatment in autism: a proposal for guidelines on common co-occurring psychiatric symptoms. BMC Med. 2025;23(1):11. Disponível em: https://link.springer.com/article/10.1186/s12916-024-03814-0. Acesso em: 30 jul. 2026.

12. Trinari E, Noronha NJ, Papola D, Devji T, Navarro T, Kraus de Camargo O, et al. Selective serotonin reuptake inhibitors for children with autism spectrum disorder: a systematic review and meta-analysis. Clin Med Insights Pediatr. 2026;20:1-15. Disponível em: https://journals.sagepub.com/doi/abs/10.1177/11795565261442820. Acesso em: 18 ago. 2026.

13. Salloum-Asfar S, Zawia N, Abdulla SA. Retracing our steps: a review on autism research in children, its limitation and impending pharmacological interventions. Pharmacol Ther. 2024;253:108564. Disponível em: https://www.sciencedirect.com/science/article/pii/S0163725823002280. Acesso em: 13 ago. 2026.

14. Alsayouf HA, Talo H, Biddappa ML. Core signs and symptoms in children with autism spectrum disorder improved after starting risperidone and aripiprazole in combination with standard supportive therapies: a large, single-center, retrospective case series. Brain Sci. 2022;12(5):618. Disponível em: https://www.mdpi.com/2076-3425/12/5/618. Acesso em: 13 ago. 2026.

15. Hollander E, Jacob S, Jou R, McNamara N, Sikich L, Tobe R, et al. Balovaptan vs placebo for social communication in childhood autism spectrum disorder: a randomized

clinical trial. JAMA Psychiatry. 2022;79(8):760-769. doi:10.1001/jamapsychiatry.2022.1717.

16. Popow C, Ohmann S, Plener P. Practitioner's review: medication for children and adolescents with autism spectrum disorder (ASD) and comorbid conditions. Neuropsychiatr. 2021;35:113-134. Disponível em: https://link.springer.com/article/10.1007/s40211-021-00395-9. Acesso em: 01 ago. 2026.

17. Maniram J, Oosthuizen F, Karrim SBS. An overview of pharmacotherapy in the management of children with autism spectrum disorder at a public hospital in KwaZulu-Natal. Child Psychiatry Hum Dev. 2024;55:1655-1663. Disponível em: https://link.springer.com/article/10.1007/s10578-023-01514-z. Acesso em: 19 jul. 2026.

18. Wiggins LD, Nadler C, Rosenberg S, Moody E, Reyes N, Reynolds A, et al. Many young children with autism who use psychotropic medication do not receive behavior therapy: a multisite case-control study. J Pediatr. 2021;232:264-271. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0022347621000779. Acesso em: 22 ago. 2026.

19. Kompella S, Vittori A, Kroin J, Kaushal S, Khan S, Neuhut S. Impact of antipsychotic use on readmission rates in children and adolescents with autism spectrum disorder and irritability. Cureus. 2022;14(2):e22361. Disponível em: https://assets.cureus.com/uploads/original_article/pdf/75558/20240724-319105-90s0pf.pdf. Acesso em: 30 jul. 2026.

20. Kloosterboer SM, de Winter BCM, Reichart CG, Kouijzer MEJ, de Kroon MMJ, van Daalen E, et al. Risperidone plasma concentrations are associated with side effects and effectiveness in children and adolescents with autism spectrum disorder. Br J Clin Pharmacol. 2021;87:1069-1081. Disponível em: https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bcp.14465. Acesso em: 25 jul. 2026.

21. Mellahn OJ, Knott R, Tiego J, Kallady K, Williams K, Bellgrove MA, et al. Understanding the diversity of pharmacotherapeutic management of ADHD with co-occurring autism: an Australian cross-sectional survey. Front Psychiatry. 2022;13:914668. Disponível em: https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2022.914668/full. Acesso em: 01 set. 2026.

22. Lalanne S, Fougerou-Leurent C, Anderson GM, Schroder CM, Nir T, Chokron S, et al. Melatonin: from pharmacokinetics to clinical use in autism spectrum disorder. Int J Mol Sci. 2021;22(3):1490. Disponível em: https://www.mdpi.com/1422-0067/22/3/1490. Acesso em: 17 jul. 2026.

23. Sadeh H, Meiri G, Zigdon D, Ilan M, Faroy M, Michaelovski A, et al. Adherence to treatment and parents' perspective about effectiveness of melatonin in children with autism spectrum disorder and sleep disturbances. Child Adolesc Psychiatry Ment Health. 2023;17: 123. Disponível em: https://link.springer.com/article/10.1186/s13034-023-00669-w. Acesso em: 28 ago. 2026.

24. Sikich L, Kolevzon A, King BH, McDougle CJ, Sanders KB, Kim SJ, et al. Intranasal

oxytocin in children and adolescents with autism spectrum disorder. N Engl J Med. 2021;385(16):1462-1473.

25. Disponível em: https://www.nejm.org/doi/abs/10.1056/NEJMoa2103583. Acesso em: 28 agp. 2026.

26. Guastella AJ, Boulton KA, Whitehouse AJO, Song YJ, Thapa R, Gregory SG, et al. The effect of oxytocin nasal spray on social interaction in young children with autism: a randomized clinical trial. Mol Psychiatry. 2023;28:834-842. Disponível em: https://www.nature.com/articles/s41380-022-01845-8. Acesso em: 21 ago. 2026.

27. Brignell A, Marraffa C, Williams K, May T. Memantine for autism spectrum disorder. Cochrane Database Syst Rev. 2022;(8):CD013845. Disponível em: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013845.pub2/abstract. Acesso em: 20 ago. 2026.

28. Ibsen EWD, Thomsen PH. Cannabinoids as alleviating treatment for core symptoms of autism spectrum disorder in children and adolescents: a systematic review. Nord J Psychiatry. 2024;78(7):553-560. Disponível em: https://www.tandfonline.com/doi/full/10.1080/08039488.2024.2381541. Acesso em: 02 jul. 2026.

29. London EB, Zimmerman-Bier BL, Yoo JH, Gaffney JW. High-dose propranolol for severe and chronic aggression in autism spectrum disorder: a pilot, double-blind, placebo-controlled, randomized crossover study. J Clin Psychopharmacol. 2024;44:462-467. Disponível em: https://pmc.ncbi.nlm.nih.gov/articles/PMC11460740/. Acesso em: 23 jul. 2026.

30. WANG, F.; WEN, F.; YU, L.; YAN, J.; LIU, J.; LI, Y.; CUI, Y. The efficacy and safety in attention deficit hyperactivity disorder of second-generation antipsychotics and other medications for hyperactivity in children and adolescents with autism: a meta-analysis. International Clinical Psychopharmacology, v. 36, n. 3, p. 109-116, 2021. Disponível em: https://www.ovid.com/jnls/intclinpsychopharm/abstract/10.1097/yic.0000000000000349~the-efficacy-and-safety-in-attention-deficit-hyperactivity?redirectionsource=fulltextview . Acesso em: 01 set. 2026.

31. BATEBI, N.; SANJARI MOGHADDAM, H.; HASANZADEH, A.; FAKOUR, Y.; MOHAMMADI, M. R.; AKHONDZADEH, S. Folinic Acid as Adjunctive Therapy in Treatment of Inappropriate Speech in Children with Autism: A Double-Blind and Placebo-Controlled Randomized Trial. Child Psychiatry & Human Development, v. 52, n. 5, p. 928-938, 2021. Disponível em: https://link.springer.com/article/10.1007/s10578-020-01072-8. Acesso em: 15 ago. 2026.

32. BAZRAFSHAN, Z.; MOHAMMADI, P.; HASANZADEH, A.; SANJARI MOGHADDAM, M.; KABIRI, M.; SANJARI MOGHADDAM, H.; ABDOLGHAFFARI, A. H.; MOHAMMADI, M.-R.; AKHONDZADEH, S. Metformin efficacy and safety as an adjunctive treatment for irritability in children with autism spectrum disorder: A randomized, double-blind, placebo-controlled trial. Journal of Psychopharmacology, v. 39, n. 3, p. 214-222, 2025. Disponível em:

https://journals.sagepub.com/doi/abs/10.1177/02698811241303593. Acesso em: 22 ago. 2026.

33. WILLIAMS, P. G.; SEARS, L.; WATSON, W. H.; GUNARATNAM, B.; FEYGIN, Y.; WRIGHT, S. P.; SULLIVAN, J. E. Glutathione, Vitamin C, and Cysteine Use in Autistic Children With Disruptive Behavior: A Double-Blind, Placebo-Controlled Crossover Pilot Study. Journal of Developmental & Behavioral Pediatrics, v. 46, n. 1, p. e17-e24, 2025. Disponível em: https://www.ovid.com/jnls/jrnldbp/abstract/10.1097/dbp.0000000000001334~glutathione-vitamin-c-and-cysteine-use-in-autistic-children?redirectionsource=fulltextview. Acesso em: 10 ago. 2026.

34. ALENEZI, S.; ALNEMARY, F.; ALAMRI, A.; ALBAKR, D.; ABUALKHAIR, L.; ALNEMARY, F. Psychotropic Medications Use among Children with Autism in Saudi Arabia. Children, v. 9, n. 7, p. 966, 2022. Disponível em: https://www.mdpi.com/2227-9067/9/7/966. Acesso em: 01 set. 2026.

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