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Review paper

Omega 3 Fatty Acid-Rich Nutraceuticals: Current Trends and Future Perspective of Managing Autism Spectrum Disorder

Mansi Vats [1#], Pranya Dutta [1#], Swastika Maiti [1], Soumi Chakraborty [*1]

[1] *Amity Institute of Food Technology, Amity University, Noida, Uttar Pradesh, India*
[#] *Both authors have contributed equally for drafting this manuscript*

KEYWORDS

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ABSTRACT

Autism Spectrum Disorder is a complex neurodevelopmental condition characterised by challenges in social interaction, communication and repetitive behaviours, with a multifactorial aetiology involving genetic, environmental and neurological factors. The global prevalence of Autism Spectrum Disorder is maximum in Europe and Western Pacific countries (250 to 263 per 10000 population) compared to the Eastern Mediterranean countries (153 per 10000 population) has risen, reflecting variations in dietary practices, since the healthcare resources are comparatively better in the Europe and Western Pacific countries. Recently it has been highlighted that maternal consumption of polyunsaturated fatty acids helps in child's brain development, microglial activity and neuroinflammatory pathways. It is believed that polyunsaturated fatty acids metabolism is aberrant or insufficient in children with Autism Spectrum Disorder, which results in increased oxidative stress, proinflammatory cytokine production and imbalance in neurotransmitter synthesis and activity. These essential polyunsaturated fatty acids (PUFAs), including eicosapentaenoic acid and docosah-exaenoic acid, are vital for brain function and inflammation modulation. Recent research suggests that Omega-3 supplementation, particularly docosahexaenoic acid, may improve neurodevelopmental processes and alleviate core Autism Spectrum Disorder symptoms. Evidence from clinical trials, animal models and case studies indicates that Omega-3s may enhance social communication and reduce repetitive behaviours, underscoring their potential as a complementary therapeutic approach. In various clinical trials and case studies, Omega-3 fatty acid-rich nutraceuticals, particularly fish oil or fish capsules containing eicosapentaenoic acid and docosahexaenoic acid, have been administered to children with Autism Spectrum Disorder. The typical dosages range from 1.5 to 3 grams per day, with treatment durations spanning from 6 weeks to over 8 months. Evidence from these studies suggests that Omega-3 supplem-entation may enhance social communication, reduce repetitive behaviours and serve as a promising adjunct to conventional Autism Spectrum Disorder therapies. This review aims to analyse all the recent case studies as well as human clinical trials in order to highlight the relationship between omega 3 fatty acids-rich nutraceuticals and Autism Spectrum Disorder. The study would conclude whether in addition to normal medical therapy and psychological interventions the omega 3 fatty acid-rich nutraceuticals have any role in controlling the Autism Spectrum Disorder symptoms or not. The aim is to provide a comprehensive overview of the potential benefits and limitations of Omega-3 fatty acids in the management of Autism Spectrum Disorder and suggest directions for future research.

1. Introduction

Autism Spectrum Disorder is a complex neurodevelopmental condition characterised by difficulties in social interaction, communication challenges and repetitive behaviours. The aetiology of Autism Spectrum Disorder is multifactorial, involving genetic, environmental and neurological components. Autism Spectrum Disorder is highly heritable and most Autism Spectrum Disorder risk genes are expressed in prenatal life and fall into two major groups, broadly expressed regulatory genes and brain-specific ones. Broadly expressed regulatory risk genes are the majority of Autism Spectrum Disorder risk genes. In combination with brain-specific risk genes, they drive aberrant proliferation, neurogenesis, cell fate and migration in Epoch-1. A different set of broadly expressed and brain-specific risk genes disrupt synaptogenesis and cortical wiring in Epoch-2 (Courchesne et al., 2020). According to WHO, as of 2023, the global prevalence of Autism Spectrum Disorder is approximately 1 in 100 children, which equates to 1% of the global child population. This increase in prevalence highlights significant variations in diagnostic practices, awareness and healthcare resources across different regions. The core symptoms of Autism Spectrum Disorder primarily involve challenges in social communication and interaction. These may include reduced or lack of eye contact, difficulties in interpreting and responding to social cues such as body language and facial expressions and struggles with forming and maintaining friendships or relationships. Individuals with Autism Spectrum Disorder often find it hard to engage in reciprocal social interactions, which can lead to misunderstandings and social isolation (Lord et al., 2018).

Autism Spectrum Disorder is frequently linked with neuroinflammation, oxidative stress and disruptions in lipid metabolism, all of which play a role in the disorder's complex pathophysiology. (Gorrindo et al., 2013). These biological abnormalities contribute to the characteristic behavioural and cognitive impairments observed in Autism Spectrum Disorder. Challenges associated with Autism Spectrum Disorder extend beyond the core symptoms, as many individuals also face comorbid conditions, including anxiety, depression and attention-deficit hyperactivity disorder (ADHD). (Mulder et al., 2018) Additionally, gastrointestinal issues are prevalent among individuals with Autism Spectrum Disorder, with studies indicating a higher incidence of conditions such as constipation, diarrhoea and abdominal pain (Madra et al., 2021).

As the search for effective interventions for Autism Spectrum Disorder continues, the field of nutraceuticals has emerged as a promising area of exploration. Nutraceuticals, derived from food sources, offer health benefits that extend beyond basic nutrition, encompassing dietary supplements, functional foods and medicinal formulations aimed at promoting health and preventing disease (Puri et al., 2022). Among these, Omega-3 fatty acids have gained significant attention for their potential role in neurodevelopmental disorders, particularly Autism Spectrum Disorder. (Posar and Visconti, 2016). Omega-3 fatty acids are essential polyunsaturated fatty acids (PUFAs) crucial for maintaining overall health. The primary types of Omega-3s include eicosapentaenoic acid, docosahexaenoic acid and alpha-linolenic acid (alpha-linolenic acid), each with distinct roles in human physiology (Simopoulos, 2016). While eicosapentaenoic acid and docosahexaenoic acid, found predominantly in marine sources like fatty fish, are vital for brain function and reducing inflammation, alpha-linolenic acid, found in plant-based sources, serves as a precursor to eicosapentaenoic acid and docosahexaenoic acid, though its conversion in the body is limited (Brenna et al., 2015).

Emerging research has begun to elucidate the potential benefits of Omega-3 supplementation in managing Autism Spectrum Disorder. These studies suggest that Omega-3s, particularly docosahexaenoic acid, play a critical role in neurogenesis, synaptic plasticity and the overall health of neuronal membranes, which are essential processes in brain development and function (Dyall, 2015) Furthermore, eicosapentaenoic acid contributes to brain health by modulating inflammatory pathways, which are often dysregulated in individuals with Autism Spectrum Disorder (Bazinet and Layé, 2014). The integration of Omega-3 fatty acids as a nutraceutical intervention in Autism Spectrum Disorder management represents a promising avenue for mitigating symptoms and improving quality of life. Recent meta-analyses have highlighted the positive impact of Omega-3 supplementation on social communication and repetitive behaviours in Autism Spectrum Disorder, reinforcing the potential of these fatty acids as a complementary therapeutic strategy (Zhang et al., 2023). As research in this area continues to advance, the role of Omega-3s in supporting neurodevelopment and managing Autism Spectrum Disorder symptoms may become increasingly pivotal in clinical practice.

2. Scope of this Review

This review delves into the intricate relationship between Omega-3 fatty acids and Autism Spectrum Disorder, exploring a comprehensive range of studies and evidence. It encompasses in-depth analyses of human clinical

*Corresponding author: Soumi Chakraborty

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trials, animal models and case studies that have investigated the effects of Omega-3 supplementation on Autism Spectrum Disorder symptoms. Additionally, the review highlights the underlying biological mechanisms, such as the modulation of neuroinflammation and synaptic plasticity, that contribute to the observed therapeutic effects.

The findings presented in this review underscore the potential benefits and limitations of Omega-3 fatty acids as a nutraceutical intervention for Autism Spectrum Disorder. By critically evaluating the current literature, this review aims to provide a nuanced understanding of how Omega-3s may contribute to the management of Autism Spectrum Disorder and what future research directions may further elucidate their role in neurodevelopmental disorders.

3. Objective of the Study

This review aims to critically evaluate and synthesize the current evidence on the role of Omega-3 fatty acids as a nutraceutical intervention in the management of Autism Spectrum Disorder. The focus is to elucidate the underlying mechanisms by which Omega-3 fatty acids may influence neurodevelopmental and behavioural outcomes in individuals with Autism Spectrum Disorder. By examining studies published in the last 15-20 years, this review will explore both the biological rationale for Omega-3 supplementation, including its anti-inflammatory and neuroprotective properties and the clinical evidence supporting its therapeutic use in Autism Spectrum Disorder.

The review will delve into various types of research, including human trials, case studies and experimental models, to provide a comprehensive analysis of the efficacy, safety and potential of Omega-3 fatty acids in improving Autism Spectrum Disorder symptoms. Furthermore, this review highlights advancements in nutraceutical science, emphasizing the growing interest in Omega-3 fatty acids as a promising, non-pharmacological approach to managing Autism Spectrum Disorder. By synthesizing the available literature, the review seeks to offer a nuanced understanding of the benefits and limitations of Omega-3 supplementation, identify gaps in the current research and suggest directions for future investigations. This comprehensive overview will contribute to the broader discourse on the role of nutraceuticals in neurodevelopmental disorders, particularly Autism Spectrum Disorder and their potential in advancing personalized and integrative approaches to treatment.

4. Methodology

On Scopus, we used the medical subject heading words "Autism," "Autism Spectrum Disorders," and "Omega 3 supplements" to search for articles between the years 2024 and 2014 initially. Since the data was insufficient, we extended the number of years by another 10 years to 2004. This search yielded 69 papers that were all in English. We have excluded the papers with other dietary management (like keto diet, Mediterranean diets, Gluten-free diet etc.) and included the paper only on omega-3 fatty acid nutraceuticals. In total, we have included 56 papers, including literature reviews, case-control studies, meta-analysis studies and surveys, those are relevant to our topic of interest and removed all the duplicate papers and essays.

5. Exploring Omega-3 Fatty Acids as a Therapeutic Avenue for Autism Spectrum Disorder

5.1 Chemical Structure of Omega-3 Fatty Acids

PUFAs are one of the primary components of phospholipids, which play a crucial role in cell membrane structure and function. These 3 fatty acids are majorly considered as omega-3 fatty acids, such as linoleic acid (18:2*n*-6, LA), α-linolenic acid (18:3*n*-3, alpha-linolenic acid) and their metabolic products, arachidonic acid (20:4*n*-6, AA), eicosapentaenoic acid (20:5*n*-3; EPA) and docosahexaenoic acid (22:6*n*-3; DHA) (Fig. 1).

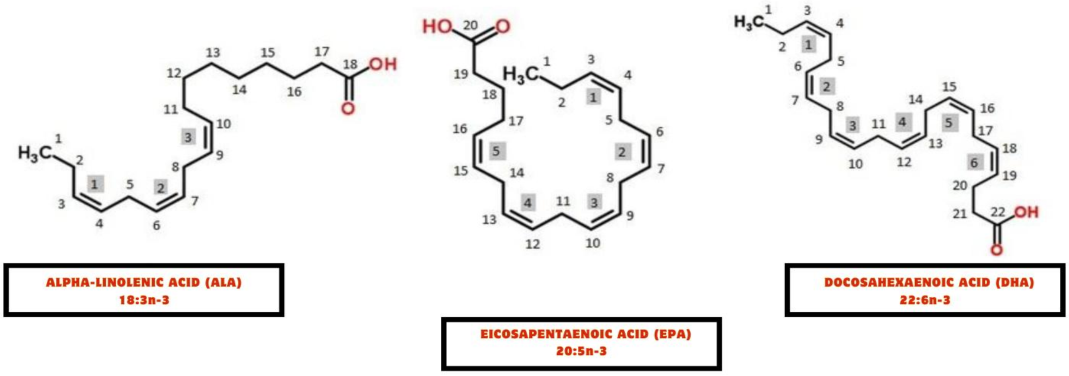

Fig. 1 Chemical Structure of Omega-3 Fatty Acids. (Roke, 2016)

Emerging research has highlighted that the metabolism of polyunsaturated fatty acids (PUFAs), including Omega-3 fatty acids, is often deficient or abnormal in children with Autism Spectrum Disorder. This deficiency is believed to trigger a cascade of negative outcomes, including the overproduction of proinflammatory cytokines, increased oxidative stress and disturbances in neurotransmitter balance (Veselinovic et al., 2021). Given the potential role of these disruptions in the manifestation of Autism Spectrum Disorder symptoms, Omega-3 fatty acids have garnered attention as a possible intervention. Omega-3 fatty acids, particularly eicosapentaenoic acid, docosahexaenoic acid are known for their anti-inflammatory properties and their ability to modulate brain function. (Calder, 2017). These fatty acids have been shown to reduce the production of proinflammatory cytokines and oxidative stress markers, which are elevated in individuals with Autism Spectrum Disorder, potentially improving neuroinflammation and overall brain health. (Bazinet and Layé, 2014)

In clinical studies, Omega-3 supplementation has been explored as a means to alleviate these pathological processes and enhance the overall functioning of individuals with Autism Spectrum Disorder. For example, supplementation has been linked with improvements in social communication, reductions in repetitive behaviours and better cognitive outcomes. (Ooi et al., 2015) These findings suggest that Omega-3 fatty acids could play a therapeutic role in managing Autism Spectrum Disorder by targeting the underlying biological mechanisms that contribute to the disorder (Fig. 2).

Furthermore, ongoing research is exploring the optimal dosages, forms and combinations of Omega-3 supplements that could maximize therapeutic benefits while minimizing potential side effects. As nutraceuticals continue to advance, the refinement of Omega-3-based interventions may offer a promising avenue for improving the quality of life for individuals with Autism Spectrum Disorder. The potential for Omega-3 fatty acids to serve as a nutraceutical intervention in Autism Spectrum Disorder highlights the importance of continued research in this area, with a focus on translating these findings into practical, evidence-based treatments.

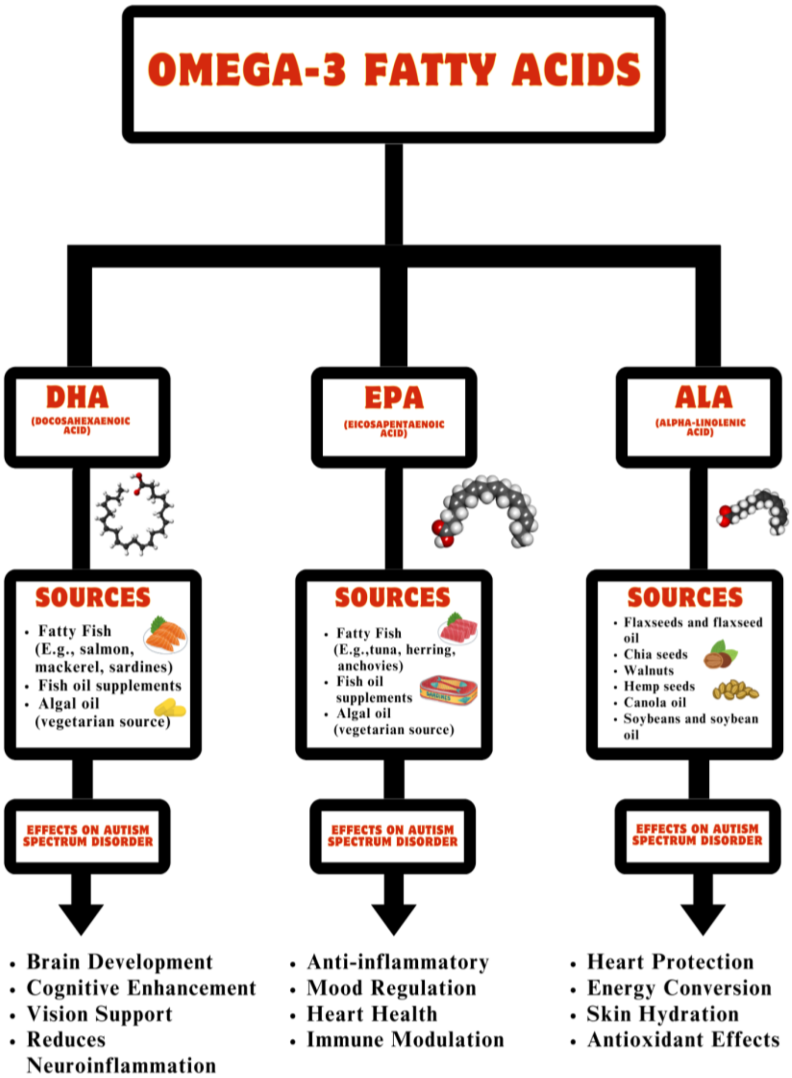

Fig. 2 Types and Sources of Omega-3 Fatty Acids and Effects of Different Omega-3 Fatty Acids on Autism Spectrum Disorder (Bent et al., 2009; Doaei et al., 2021)

6. Exploring the Mechanisms of Omega-3 Fatty Acid-Rich Nutraceuticals in Autism Spectrum Disorder Management

6.1 Neuroinflammation and the Role of Omega-3 Fatty Acids

Neuroinflammation is increasingly recognized as a key factor in the pathophysiology of Autism Spectrum Disorder, contributing to both behavioural and cognitive deficits (Masi et al., 2017). Studies have shown that individuals with Autism Spectrum Disorder exhibit elevated levels of pro-inflammatory cytokines and activated microglia, indicating chronic neuroinflammation in the brain (Vargas et al., 2015). This persistent inflammatory state can disrupt neuronal function and synaptic plasticity, leading to the behavioural manifestations seen in Autism Spectrum Disorder (Estes and McAllister, 2015).

Omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid have been shown to modulate neuroinflammatory pathways by reducing the production of pro-inflammatory cytokines and inhibiting microglial activation (Calder, 2017). In the context of Autism Spectrum Disorder, supplementation with omega-3 fatty acids has been associated with reduced levels of neuroinflammation, which may contribute to improvements in cognitive and behavioural outcomes (Ghezzo et al., 2018). Studies have also found that altered PUFA metabolism leads to increased production of proinflammatory cytokines, increased oxidative stress and an imbalance in the formation and action of neurotransmitters in individuals with Autism Spectrum Disorder (Veselinovic et al., 2021). So, by targeting these inflammatory processes, omega-3 fatty acids offer a potential therapeutic approach for managing Autism Spectrum Disorder symptoms, particularly those related to neuroinflammation.

6.2 Impact of Omega-3 Fatty Acids on Neurotransmitter Function in Autism Spectrum Disorder

Neurotransmitters are chemical messengers that transmit signals across synapses from one neuron to another, playing a critical role in regulating brain functions such as mood, cognition, behaviour and overall neuronal communication. Key neurotransmitters include gamma-aminobutyric acid (GABA), glutamate, serotonin, dopamine, norepinephrine and epinephrine. The balance and function of these neurotransmitters are vital for normal brain functioning and are often disrupted in neurological conditions such as Autism Spectrum Disorder. Omega-3 fatty acids, classified as nutraceuticals due to their health-promoting properties beyond basic nutrition, have garnered attention for their potential to modulate neurotransmitter activity in the brain. Omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid have been shown to influence the synthesis, release and function of various neurotransmitters. This modulation can help restore balance in neurotransmitter systems that are often altered in Autism Spectrum Disorder, contributing to improved cognitive function, behaviour and overall neurological health. In addition to the commonly studied neurotransmitters, acetylcholine and histamine also play significant roles in cognitive processes and behavioural regulation and their modulation by Omega-3 fatty acids further highlights the potential therapeutic effects of these nutraceuticals in managing Autism Spectrum Disorder symptoms (Table 1).

Table 1 Effect of Omega-3 Fatty Acids on the Neurotransmitter Levels of Autism Spectrum Disorder

Effect of Omega-3 Fatty Acids on the Level of Neurotransmitters	Observed Outcomes in Autism Spectrum Disorder Patients	References
GABA (Gamma-Aminobutyric Acid) Increased GABAergic activity	Enhanced inhibitory neurotransmission, reduced anxiety and improved mood stability.	Healy-Stoffel and Levant, 2018
Glutamate Decreased glutamate levels	Reduced excitotoxicity, leading to improved neural function and decreased hyperactivity.	Aryal et al., 2019
Serotonin Increased serotonin synthesis and release	Improved mood, social behaviour and reduced depressive symptoms.	Patrick et al., 2015
Dopamine Modulated dopamine production	Enhanced cognitive function, attention and reward processing.	Healy-Stoffel and Levant, 2018
Norepinephrine Balanced norepinephrine levels	Improved attention, focus and reduction in anxiety.	Monahan et al., 2004
Epinephrine Stabilized epinephrine levels	Better stress response, regulation of arousal and elimination of stress-induced cortisol increase.	Giles et al., 2015
Acetylcholine Enhanced acetylcholine function	Improved learning, memory and cognitive flexibility.	Tavarapruk and Song, 2010
Histamine Modulated histamine activity	Regulation of sleep-wake cycles, appetite, cognitive processes, neurogenesis and neuroinflammation.	Mandecka and Regulska-Ilow, 2022; Thomas et al., 2024

7. Mitochondrial Function and the Impact of Omega-3 Fatty Acids

7.1 Mitochondrial Dysfunction in Autism Spectrum Disorder

Mitochondrial dysfunction has been increasingly recognized as a contributing factor in Autism Spectrum Disorder. Mitochondria play a crucial role in energy production and their dysfunction can lead to impaired cellular energy metabolism, which is often observed in individuals with Autism Spectrum Disorder (Frye et al., 2017). Studies have shown that children with Autism Spectrum Disorder exhibit abnormalities in mitochondrial function, including decreased oxidative phosphorylation and increased oxidative stress, which can contribute to neurodevelopmental issues (Giulivi et al., 2016).

These mitochondrial abnormalities may manifest as reduced ATP production and increased production of reactive oxygen species (ROS), leading to cellular damage and exacerbation of Autism Spectrum Disorder symptoms (Rossignol and Frye, 2014). Additionally, mitochondrial DNA mutations and deletions have been identified in individuals with Autism Spectrum Disorder, further supporting the role of mitochondria in the disorder. A 2018 study identified mitochondrial DNA mutations and deletions in individuals with Autism Spectrum Disorder, reinforcing the notion that mitochondrial dysfunction plays a critical role in the disorder (Varga et al., 2018).

7.2 The Role of Omega-3 in Enhancing Mitochondrial Health

Omega-3 fatty acids, particularly docosahexaenoic acid and eicosapentaenoic acid, have shown promise in improving mitochondrial function and health. These fatty acids are integral components of mitochondrial membranes, where they influence membrane fluidity and the efficiency of the electron transport chain (ETC), thus optimizing ATP production (Lalia et al., 2017).

Studies have demonstrated that supplementation with omega-3 fatty acids can improve mitochondrial function in various conditions, including neurodevelopmental disorders like Autism Spectrum Disorder (Politi et al., 2018). Omega-3 fatty acids have also been shown to enhance the activity of mitochondrial enzymes and reduce mitochondrial membrane potential depolarization, which are key factors in maintaining healthy mitochondrial function (Herbst et al., 2014). These effects may contribute to the reduction of oxidative stress and neuroinflammation in Autism Spectrum Disorder, thereby improving cellular and neurological outcomes (Yui et al., 2016).

In a 2018 human trial, supplementation with omega-3 fatty acids in children with Autism Spectrum Disorder was associated with improved mitochondrial function, as evidenced by enhanced mitochondrial enzyme activity and decreased mitochondrial membrane depolarization (Pallejà et al., 2018). Furthermore, Omega-3 fatty acids have been linked to the regulation of neurotransmitter systems, which are often dysregulated in Autism Spectrum Disorder. By supporting mitochondrial health and function, Omega-3s may help to restore balance in neurotransmitter synthesis and release, offering additional benefits for managing Autism Spectrum Disorder symptoms.

8. Effects of Omega-3 Fatty Acids on the Behavioural Changes of Autism Spectrum Disorder

Omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid, have been studied for their potential benefits on behavioural symptoms in Autism Spectrum Disorder. Several clinical trials and observational studies suggest that omega-3 supplementation may lead to improvements in core Autism Spectrum Disorder symptoms, including social interaction, communication and repetitive behaviours (Gao et al., 2016). A meta-analysis found that omega-3 supplementation was associated with reduced anxiety symptoms in children with Autism Spectrum Disorder, likely due to its effects on neurotransmitter function and inflammation (Table-2) (Cheng et al., 2017).

9. Omega-3 Fatty Acids in Social Responsiveness

This pilot study conducted in Singapore aimed to evaluate the effectiveness and safety of omega-3 fatty acid supplementation in children and adolescents with Autism Spectrum Disorder. The study involved 41 participants, aged 7 to 18 years, who received omega-3 supplements over a 12-week period. Significant improvements were observed in social responsiveness and attention-related behaviours, as measured by the Social Responsiveness Scale and the Child Behaviour Checklist. These improvements were linked to changes in blood omega-3 levels, suggesting that these fatty acids may serve as a biomarker for treatment efficacy.

The study also highlighted that baseline omega-3 levels could predict the degree of symptom improvement, offering insights into individualized treatment approaches. Importantly, the supplementation was well-tolerated, with no serious adverse effects reported, indicating its safety for use in this population. While the results are promising and suggest potential benefits of omega-3s in managing Autism Spectrum Disorder symptoms, the study calls for further research. Specifically, larger randomized controlled trials with longer follow-up periods and blood fatty acid measurements are needed to better understand the long-term efficacy and safety of omega-3 supplementation in Autism Spectrum Disorder management. **(Ooi et al., 2015)**

Table 2 Summary of case studies evaluating the behavioural effects of Omega-3 fatty acids supplementation in individuals with Autism Spectrum Disorder

Dose and Duration of Omega-3	Patient Information	Observed Behavioural Outcomes	Conclusion	References
3 g/day (540 mg eicosapentaenoic acid) over 8 months	11-year-old child, diagnosed with autism at 2.5 years	Complete elimination of anxiety and agitation after 1 week, with stable improvement over 8 months.	Omega-3 fatty acids can have a significant positive impact on anxiety and agitation in Autism Spectrum Disorder patients.	Bent et al., 2019
Varying doses over at least 6 months	Nine children with autism	General health, behaviour and various outcomes improved as reported by parents.	Omega-3 supplementation appears to have a positive effect on overall health and behaviour in Autism Spectrum Disorder children.	Bertoglio et al., 2009
1.5 g/day for 6 months	Children aged 2-5 years	Worsening scores on BASC-2 externalizing problems; no significant changes in adaptive function or language	No significant change in autism composite scores & Autism Spectrum Disorder symptoms.	Mankad et al., 2015
2000 mg/day (600 mg eicosapentaenoic acid, 1200 mg docosahexaenoic acid) for 12 weeks	31 children with Autism Spectrum Disorder, aged 2-8 years	Significant improvements in social communication skills, reduction in hyperactivity; no significant changes in irritability or stereotypy.	Omega-3 supplementation may be beneficial as an adjunct therapy in managing behavioural symptoms in Autism Spectrum Disorder.	Mazahery et al., 2019
Two fish oil capsules per day for 6 weeks	19 young adults with severe autism (CARS >40), aged 18-40	No significant improvement in problematic behaviours during or post-treatment.	Omega-3 fatty acids may not be effective in improving behaviour in severe cases of autism.	Politi et al., 2008
Omega-3 fatty acids supplement in autistic children; 1.5 g/day of omega-3 fatty acids (0.84 g/deicosapentaenoic acid (eicosapentaenoic acid) + 0.7 g/daydocosahexaenoic acid (docosahexaenoic acid) for six week	13 (5–17 years of age);	Improved symptoms (hyperactivity and stereotypy)	Supplementation with 1.5 g/day of omega-3 fatty acids for 6 weeks in autistic children (aged 5–17 years) led to improvements in behavioural symptoms.	Amminger et al., 2007

10. Omega-3 PUFA and Gut Microbiota in Autism Spectrum Disorder

It has been reported that intake of omega-3 PUFA has a significant positive association with *Lactobacillus* group abundance in faeces samples (Wang et al., 2016). The increase in omega-3 PUFA improves transepithelial resistance and thereby improves epithelial barrier integrity. These results suggest a link between PUFA types and their different effects on the faecal microbiota. Dietary supplementation with Bifidobacteria has been shown to increase tissue levels of eicosapentaenoic acid and docosahexaenoic acid in mice and dietary supplementation with parent omega-3 PUFA alpha-linolenic acid combined with *Bifidobacterium breve* resulted in higher liver eicosapentaenoic acid and brain docosahexaenoic acid levels. It has been observed that probiotic bacteria (e.g., *Bifidobacterium* and *Akkermansia*) and omega-3 fatty acids may have synergistic health benefits in treating patients with Autism Spectrum Disorder (Kelly et al., 2017).

11. Impact of Omega-3 Fatty Acids on Autism Spectrum Disorder Severity

In a study analyzing the effects of various nutraceuticals on Autism Spectrum Disorder severity, Omega-3 fatty acids emerged as a significant supplement, with a reported positive impact on Autism Spectrum Disorder symptoms. Among 123 nutraceuticals studied, Omega-3 fatty acids were one of the most commonly used treatments, with 15% of respondents utilizing them. The analysis included 276 responses related to Omega-3 supplementation, encompassing different forms such as fish oil and krill oil.

A notable positive change in Autism Spectrum Disorder severity was statistically associated with Omega-3 supplementation. The effect was particularly evident in patients with more severe baseline Autism Spectrum Disorder symptoms, indicating that Omega-3 fatty acids might be more beneficial for those with higher initial severity levels. In the review conducted, it was found that Omega-3 fatty acids demonstrated a significant impact on various symptoms. Among the 188 respondents using Omega-3 supplements, a substantial portion reported general benefits, with 59% noting improvements across multiple symptoms. Specific areas of improvement included cognition (26%), attention (25%) and language/communication (10%). Adverse effects were minimal, with only a small percentage reporting issues like gastrointestinal problems (1%) and anxiety (5%). Overall, the study highlights Omega-3 fatty acids as a potentially effective intervention in managing Autism Spectrum Disorder symptoms, especially in cases of severe autism (Adams et al., 2021).

12. Market Scenario of Omega 3 Rich Nutraceuticals

The cost of buying omega-3 supplements depends on a range of factors including the type of supplement, the quantity you buy, the supplier, delivery charges etc. We found a wide range of suppliers providing omega-3 supplements for a wide range of prices when we did an online search on 9 May 2018. Prices varied from £2.87 for 120 tablets to £75 for 250 tablets (Smith & Jones, 2018).

In the UK, it is sometimes possible to obtain free NHS prescriptions for specific dietary supplements if you have certain medical conditions (such as diabetes) or you are a member of an exempt group (such as being under 16 or over 65). In India, the cost of Omega-3 supplements varies depending on factors such as the brand, the concentration of eicosapentaenoic acid and docosahexaenoic acid (the active components of Omega-3), the form of the supplement (e.g., capsules, syrups, or oils) and the retailer. A market survey conducted in 2023 showed that prices for Omega-3 supplements in India ranged from INR 300 for a bottle of 60 capsules to INR 2,000 for more premium products containing higher concentrations of eicosapentaenoic acid and docosahexaenoic acid (Sharma et al., 2019).

Popular brands such as WOW Life Science, Himalaya Wellness and Nordic Naturals are leading the market with products tailored to different age groups and health needs, including formulations specifically designed for children with ASD. A comparative study conducted in 2020 analyzed the efficacy of different Omega-3 supplement brands in India on children with ASD. The study found that while all brands offered benefits, those with higher DHA concentrations, like Nordic Naturals, showed more pronounced improvements in cognitive and behavioural symptoms (Suman et al., 2020).

13. Dose and Duration Of Nutraceuticals

The amount of time it takes to use omega-3 supplements will depend on a number of factors including the overall length of treatment, the frequency of treatments and the time taken to administer a single dose, as well as the needs of the person undertaking it (Kendall et al., 2014). Most Omega-3 supplements are designed to be taken once or twice daily, preferably with meals to enhance absorption . This routine not only supports the consistent delivery of these fatty acids to the body but also helps in maintaining stable plasma levels of eicosapentaenoic acid and docosahexaenoic acid, which are essential for their neuroprotective effects.

Studies suggest that for Omega-3 fatty acids to exhibit their full therapeutic effects, they need to be administered daily over an extended period. A typical recommendation is a minimum of 3 to 6 months of continuous use. For instance, a study highlighted that consistent supplementation with 600-1,200 mg/day of combined EPA and DHA over 12 weeks led to measurable improvements in behavioural symptoms in children with ASD (Bent et al. 2014). However, adherence to a supplementation regimen can be challenging, particularly in young children who may resist taking capsules or liquids due to taste or texture. In such cases, alternative delivery forms such as flavoured syrups or chewable gummies are often recommended to improve compliance (Johnson et al., 2017).

It is crucial to monitor the use of Omega-3 supplements regularly with a healthcare professional. Excessive intake over prolonged periods, especially without professional oversight, may lead to adverse effects such as gastrointestinal disturbances or bleeding risks. Therefore, regular consultations with a dietitian or healthcare provider are recommended to tailor the dose according to the individual's response and to adjust the regimen as needed.

14. Risk and Hazard Related to Omega-3 Rich Nutraceuticals

The quality of Omega-3 supplements can vary significantly depending on the specific product, manufacturer, ingredients and production process. While Omega-3 supplements are generally considered safe, it is crucial to consult with a healthcare professional before beginning any new supplement regimen. It's also advisable to adhere to the recommended daily intake guidelines, such as the Reference Intakes (RIs) set by the UK's Food Standards Agency or the Recommended Dietary Allowances (RDAs) provided by the USA's Office of Dietary Supplements (Mahan et al., 2020).

15. Key Precautions

Toxin Avoidance

Be cautious of contaminants like mercury, hormones, dioxins and polychlorinated biphenyls (PCBs), which are often found in fish oil supplements. Opt for products that have been purified through molecular distillation and are labelled as pharmaceutical grade.

Vitamin A Toxicity

Fish oil supplements often contain vitamin A, which can be toxic at high doses. Ensure that your total intake of vitamin A remains within the safe limits recommended by the UK Department of Health, considering all sources of this vitamin.

Allergen Awareness

Check for any ingredients that might trigger allergies or hypersensitivity in you, your child, or your client before taking a supplement.

Dosage Caution

Be cautious with doses exceeding 1000 mg (1 gram) of Omega-3 per day.

Impact on Blood Sugar

Fish oil supplements can affect blood sugar regulation, which is particularly important for individuals with diabetes.

Blood Thinning Effects

High levels of fish oil supplementation can thin the blood, potentially posing risks for individuals who bruise easily, self-harm, have bleeding disorders, or are on blood-thinning medications.

16. Potential Side Effects of Omega-3 Supplements

The potential side effects of Omega-3 supplements may include burping, heartburn, diarrhoea and headaches. Although Omega-3 supplements have few contraindications, it's important to note that they can interact with medications. According to the National Institutes of Health (2017), high doses of Omega-3s can increase the risk of bleeding when taken with anticoagulant medications like warfarin. In summary, while Omega-3 rich nutraceuticals offer numerous health benefits, it is essential to be mindful of potential risks and consult with a healthcare provider to ensure safe and effective use.

17. Discussion

Overall, we have explored the multifaceted roles of Omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid, in addressing the complex neurodevelopmental and behavioural challenges associated with Autism Spectrum Disorder (Gao et al., 2016). The evidence suggests that Omega-3 fatty acids, as a form of nutraceutical intervention, hold considerable promise in mitigating Autism Spectrum Disorder symptoms through their impact on neuroinflammation, oxidative stress, neurotransmitter function and mitochondrial health (Bazinet and Layé, 2014; Calder, 2017). The modulation of neurotransmitter systems, including GABA, glutamate, serotonin, dopamine, norepinephrine and epinephrine, further underscores the therapeutic potential of Omega-3s in restoring alpha-linolenic acids in disrupted neurochemical pathways in Autism Spectrum Disorder (Healy-Stoffel and Levant, 2018).

Additionally, the positive effects on mitochondrial function suggest that Omega-3 fatty acids may address some of the cellular energy deficits associated with Autism Spectrum Disorder (Giulivi et al., 2016; Frye and Rossignol, 2011). The findings from clinical studies and meta-analyses provide support for the efficacy of Omega-3 supplementation in improving social communication, reducing repetitive behaviours and enhancing overall quality of life in individuals with Autism Spectrum Disorder (Bent et al., 2019; Mazahery et al., 2019). The open-label pilot study from Singapore offers promising preliminary data, demonstrating significant improvements in Autism Spectrum Disorder symptoms and a favourable safety profile for Omega-3 supplementation. However, it is clear that further research is necessary to confirm these findings through larger, well-designed randomized controlled trials with extended follow-up periods (Ghezzo et al., 2018). As the field of nutraceuticals advances, Omega-3 fatty acids represent a noteworthy example of how dietary supplements can be integrated into therapeutic strategies for managing neurodevelopmental disorders. The ongoing exploration of Omega-3s highlights the potential of nutraceuticals to offer non-pharmacological interventions that complement traditional treatments, paving the way for more holistic and personalized approaches to Autism Spectrum Disorder management (Frye and Rossignol, 2017).

A study has been found on the rating (out of 1) of Omega 3 rich Nutraceuticals based on the Ability to redress the symptoms of Autism Spectrum Disorder (Adams et al., 2021), such as general benefit (no one particular symptom): 0.74; Cognition: 0.43; attention: 0.29 and language/communication: 0.25.

Comparative effectiveness studies with other therapeutic interventions will also be crucial in establishing the role of Omega-3s within a broader treatment framework (Lord et al., 2020). In summary, the integration of Omega-3 fatty acids as a nutraceutical intervention for Autism Spectrum Disorder reflects significant advancements in the field of nutraceuticals, offering a potential avenue for improving the lives of individuals with Autism Spectrum Disorder through innovative, evidence-based approaches. The continued exploration and refinement of Omega-3 supplementation will contribute to a deeper understanding of its role in neurodevelopmental disorders and support the advancement of personalized, integrative treatment strategies (Aryal et al., 2019; Cheng et al., 2017).

18. Inconclusive Studies on this Area

Although several studies have highlighted the potential health benefits of Omega-3 fatty acids in managing Autism Spectrum Disorder (Autism Spectrum Disorder), the evidence remains inconclusive. Notably, one small randomized controlled trial involving 13 participants *(n = 13)* reported non-significant improvements in hyperactivity and stereotypy. This suggests that while Omega-3 supplementation may offer benefits, the findings are not uniformly consistent across all studies, particularly those with smaller sample sizes. Therefore, further research with larger, well-designed trials is necessary to establish more definitive conclusions regarding the efficacy of Omega-3 fatty acids in Autism Spectrum Disorder management (James et al., 2011).

19. Strengths of this Study

This review serves as a valuable resource for scientists, clinicians, dietitians and other healthcare professionals, offering insights into the efficacy of Omega-3 fatty acid-rich nutraceuticals in managing Autism Spectrum Disorder (ASD). By focusing on specific Omega-3-rich foods such as walnuts, soybean oil, flaxseed, tuna and sardines, our analysis highlights the potential benefits these dietary interventions can offer to individuals with Autism Spectrum Disorder. The findings support the development of personalized dietary recommendations and underscore the importance of including Omega-3 polyunsaturated fatty acids in the diets of those with ASD. This review lays the groundwork for future research and dietary strategies, emphasizing the need for long-term studies to further explore the impact of Omega-3 supplementation on the social and behavioral challenges associated with Autism Spectrum Disorder.

20. Limitations of this Study

The primary limitation of this review stems from the nature of the available literature, which restricted our ability to assess feasibility, acceptability and equity comprehensively. Additionally, the study design did not allow for longitudinal evaluation or the establishment of a cause-and-effect relationship. The conclusions are drawn from a relatively small pool of studies that met our inclusion criteria and were identified through our search strategy. This limitation underscores the need for more robust research designs in future studies, including larger sample sizes, standardized methodologies, long-term follow-ups and the inclusion of control groups.

21. Future Prospects

21.1 Further Clinical Trials and Longitudinal Studies

There is a need for larger-scale, double-blind, randomized controlled trials (RCTs) with extended follow-up periods to better understand the long-term effects and safety of omega-3 fatty acids in managing Autism

Spectrum Disorder (Autism Spectrum Disorder). Current studies often have small sample sizes and limited duration, which can impact the generalizability of the findings. Comprehensive trials should focus on varying dosages, different formulations and specific subpopulations within Autism Spectrum Disorder to establish more robust evidence (Gao et al., 2016).

21.2 Exploration of Omega-3 Fatty Acid Mechanisms in Depth

Future research should delve deeper into the specific biological mechanisms through which omega-3 fatty acids exert their effects on Autism Spectrum Disorder. This includes investigating their impact on neuroinflammation, oxidative stress, neurotransmitter modulation and mitochondrial function at a more granular level. Understanding these mechanisms will help to tailor treatments more effectively and identify biomarkers that predict treatment response (Calder, 2017).

21.3 Personalized Medicine Approaches for Autism Spectrum Disorder

Integrating omega-3 supplementation into personalized medicine approaches could enhance its effectiveness. Future research should focus on identifying genetic or metabolic profiles that predict which individuals with Autism Spectrum Disorder are most likely to benefit from omega-3 supplementation. Personalized interventions based on individual biomarkers could lead to more targeted and effective treatments (Frye and Rossignol, 2011).

21.4 Comparative Effectiveness with Other Therapies of Autism Spectrum Disorder

Research should also explore the comparative effectiveness of omega-3 fatty acids relative to other therapeutic interventions for Autism Spectrum Disorder. This includes evaluating omega-3s alongside conventional treatments like behavioural therapy, medications and other dietary supplements. Such comparative studies will help establish the role of omega-3s within a broader therapeutic context (Zhang et al., 2023).

21.5 Understanding Gut-Brain Interaction

Researchers indicated that understanding gut brain interaction would be an excellent approach to reveal the exact mechanism of the PUFA on Autism Spectrum Disorder and thereby to treat mood and behavioural disorders (Mazahery et al., 2019).

21.6 Dose and Duration of Omega-3 Fatty Acid-rich Nutraceuticals to Redress Autism Spectrum Disorder

Future research should focus on elucidating the specific biological mechanisms through which Omega-3 fatty acids exert their effects, exploring optimal dosages and formulations and identifying biomarkers that predict individual responses to supplementation (Dyall, 2015; Lalia et al., 2017).

22. Conclusion

In the context of advancing nutraceuticals, Omega-3 fatty acids have emerged as a significant area of interest in the management of Autism Spectrum Disorder. The evidence suggests that Omega-3 fatty acids, as a form of nutraceutical intervention, hold considerable promise in mitigating Autism Spectrum Disorder symptoms through their impact on neuroinflammation, oxidative stress, neurotransmitter function and mitochondrial health. Overall, alpha-linolenic acid intake of omega3 -rich and nutraceutical could delay the onset and progression of Autism Spectrum Disorder. Clinical trials and case studies have demonstrated improvements in social communication and reductions in repetitive behaviours in children with Autism Spectrum Disorder who received Omega-3 supplementation, typically in doses ranging from 1.5 to 3 grams per day over periods of 6 weeks to 8 months.

The findings also suggest that Omega-3 fatty acids may complement traditional medical and psychological interventions, offering a holistic approach to Autism Spectrum Disorder management. While the results are encouraging, the review underscores the need for further research, particularly large-scale, randomised controlled trials with longer follow-up periods, to confirm the long-term efficacy and safety of Omega-3 supplementation in Autism Spectrum Disorder. Additionally, understanding the specific mechanisms through which Omega-3s exert their effects and identifying biomarkers for treatment response could lead to more personalised and effective treatment strategies.

Overall, Omega-3 fatty acids represent a valuable addition to the therapeutic toolkit for Autism Spectrum Disorder, with the potential to improve the quality of life for individuals affected by this complex neurodevelopmental disorder. Continued exploration in this area is essential to fully harness the benefits of Omega-3s and integrate them into comprehensive treatment plans for Autism Spectrum Disorder.

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Conflict of Interests

Authors are declaring that there is no conflict of interest.

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