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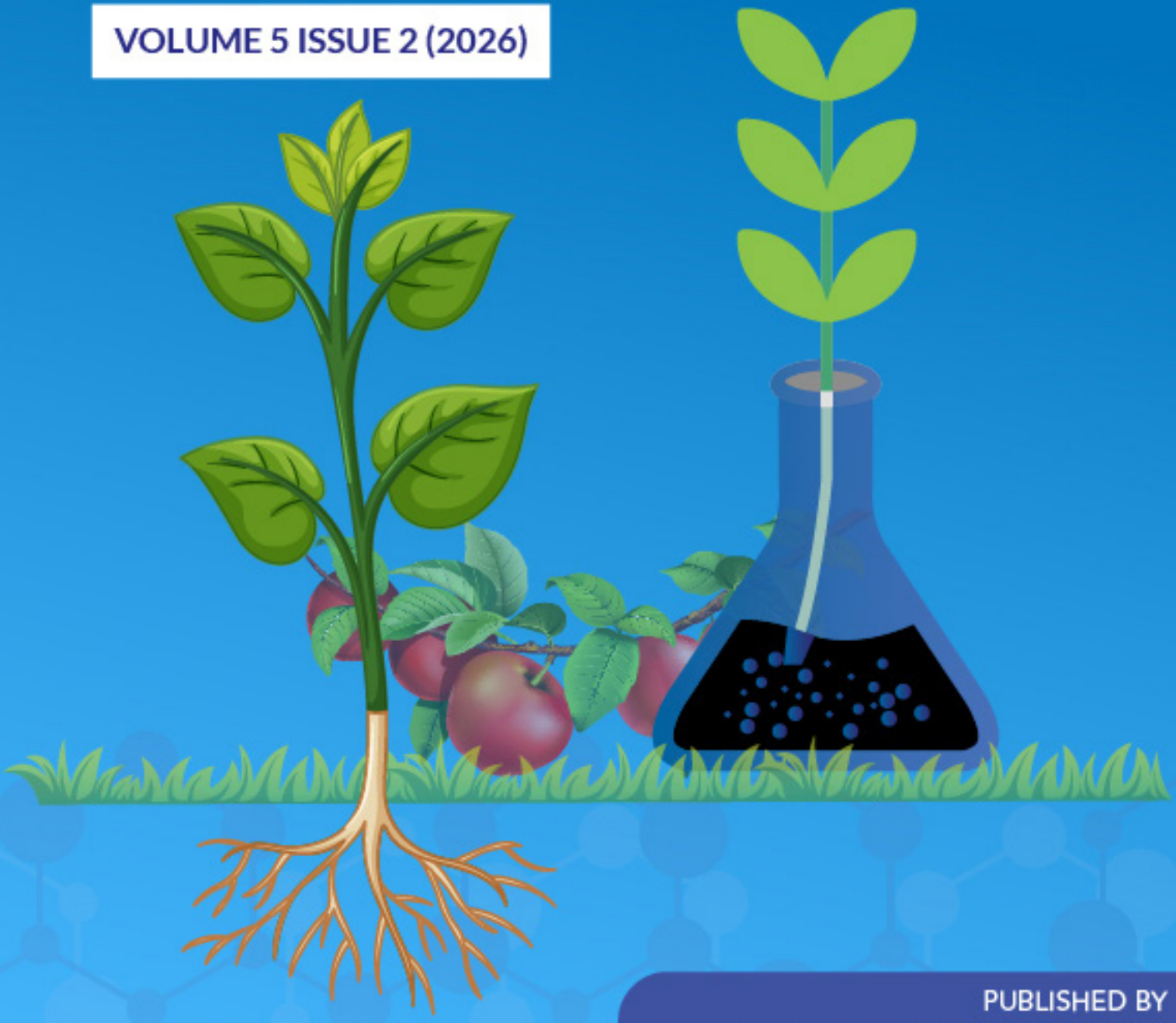

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Substitute for Casein Protein in Cow's Milk of Children with Autism Spectrum Disorder: A Review

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ABSTRACT

Children with Autism Spectrum Disorder (ASD) are frequently affected by gastrointestinal disturbances, selective eating behaviors, and sensitivity to cow's milk casein, increasing the demand for nutritionally appropriate milk substitutes in casein-free dietary management. This review aimed to look at the possible substitute to cow milk with focus given to nutritional composition, digestibility, allergenicity, environmental sustainability, and particularly to children living with ASD. To meet the objectives, a review of 39 studies published between 2003 and 2025 was conducted by searching Google Scholar, PubMed, Scopus, and ScienceDirect using specific keywords.The findings identified several alternative animal milks, including human, goat, camel, and sheep milk, as well as diverse plant-based milk categories such as cereal-based (oat, rice, corn and spelt milks), legume-based (soy, peanut, lupine and pea milks), nut-based (almond, coconut, hazelnut, pistachio, walnut and cashew milks), seed-based (sesame, flax, hemp and sunflower milks) and pseudo-cereal based (quinoa, teff, amaranth and buckwheat milks). Soy and pea-based milks were found to provide comparatively higher protein content. Nutritional deficiencies may be mitigated through calcium-rich foods such as sesame, almonds, beans, lentils, chickpeas, and tofu; vitamin D sources including fatty parts of fish, egg yolk, mushrooms, and sun exposure; and vitamin B12 sources such as purple laver, seaweeds, fermented foods, wheatgrass, and fenugreek juice and also the raw plant-based diet. Simultaneously, food-processing techniques including cooking, fermentation, sprouting, and hydrolysis were also identified as beneficial for improving nutrient bioavailability and digestibility. Taste acceptability among children with ASD may be enhanced through natural flavoring agents such as honey, jaggery, stevia, cinnamon, and sweet fruits. Careful dietary planning with professional supervision, alongside further research on more substitute milk sources and their acceptability, is recommended.

INTRODUCTION

As of recent estimates, approximately 1 in 100 children globally, which equates to about 1% of the worldwide population, are diagnosed with autism spectrum disorder (ASD). Many parents of children with ASD implement a gluten-free and casein-free (GFCF) diet for their children, hoping to alleviate their maladaptive symptoms. Numerous therapies are available to assist in reducing these maladaptive symptoms, enabling individuals to pursue a more typical and independent lifestyle.

Casein-free Milk and Diet

The casein-free diet represents a nutritional approach that may be advantageous for certain individuals with autism, especially in alleviating gastrointestinal symptoms and particular behavioral challenges. This diet entails the removal of casein, a protein predominantly present in the liquid component of cow's milk and its derived products (such as milk, cheese, yogurt, ice cream, etc. (Baspinar & Yardimci, 2020). Similar to the gluten-free diet (GFD), the casein-free diet is founded on hypotheses proposing a connection between dietary proteins and the manifestations of autism symptoms (Piwowarczyk *et al.*, 2018).

Rationale for Cow's milk Casein-free Diet in Autism

Leader *et al.* (2022) demonstrated some people with autism have an increased sensitivity or allergy to casein. This can lead to digestive issues and inflammation, which can worsen symptoms of autism. Whilst digesting, casein can produce peptides that act like opioids (known as casomorphins), just like gluten. These peptides can potentially enter the brain and influence function and behavior in autism spectrum disorder (Thiruvengadam *et al.*, 2021). The theory of the "gut-brain axis" proposes that the health of the gut is strongly linked to the health of the brain, and casein could be involved in this process. Casein can make the gut irritated, increasing the permeability of the gut, known as "leaky gut", and allow substances to enter the bloodstream and cause changes in the brain and behaviour (Alharth *et al.*, 2022). Therefore, alternative (casein-free diets) should be considered. These aim to prevent casein from reaching the bloodstream, which may alleviate the behavioural and cognitive issues associated with autism (Adamczyk *et al.*, 2022).

To narrow the scope of this review, the focus will be on plant-derived milk products to counteract the limited research in this area. Dairy substitutes derived from

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plants include milk, yogurt, cream, ice cream, butter and cheese (Adamczyk *et al.*, 2022). These dairy substitutes are sourced from one of five main categories of plants: grains, legumes, vegetables, seeds and nuts (Bridges, 2018). The nutritional value and healthiness of plant dairy substitutes are debated (Clark *et al.*, 2022). It is well known that dairy products are a good source of a range of nutrients such as protein, vitamin D, calcium and magnesium (Bridges, 2018). But in terms of children's nutrition, it is argued that plant-based dairy alters may contain more of these nutrients, and in a more bioavailable form than dairy products (Adamczyk *et al.*, 2022). Overall, many health professionals argue that while dairy is the better choice, plant-based dairy could still be part of a balanced diet (Poe & Belarmino, 2022). Given that children are the future generation, they play a critical role in the world (Demagistris & Uldemolins, 2022). As such, to encourage a more sustainable future, it's essential to teach them about following dietary principles that prioritise plant-based foods.

Usefulness and Implementation of a Casein-free Milk and Diet

Transitioning to a diet free of casein necessitates thorough preparation to maintain adequate nutrition. This approach excludes all sources of casein like milk, cheese, yogurt, butter, and various dairy products, along with hidden forms found in processed foods (Maríbauset *et al.*, 2014). Caregivers may use casein-free alternatives such as almond milk, soy milk, rice milk, coconut milk, and cheese substitutes without casein to sustain a well-rounded diet. Parents and guardians have noted a decrease in hyperactivity, irritability, and repetitive actions (Pennesi & Klein, 2012). For certain individuals diagnosed with ASD, following a casein-free diet may improve overall well-being through better health and symptom control. Moreover, findings from supporting studies suggest that implementing a gluten-free and casein-free diet in children diagnosed with Autism Spectrum Disorder notably lessens the occurrence of maladaptive symptoms. Research conducted by Herbert *et al.*, 2013; Knivsberg *et al.*, 2003; Pedersen *et al.*,2014 and Whiteley *et al.*,2010 shows considerable declines in maladaptive symptoms utilizing various behavioral assessment techniques.

Certain targeted dietary changes, including the removal of specific foods, can help some individuals with autism by identifying and eliminating possible allergens or irritants, which may assist in alleviating gastrointestinal symptoms and some behavioral problems. Thus, dietary modifications and treatments are essential in enhancing the health and quality of life for those with ASD (Hartman & Patel, 2020). This review aims to conduct an overview of Substitute for Cow's Milk, including nutrient composition (macronutrients and micronutrients), allergens, market sales, environmental sustainability and reality.

MATERIALS AND METHODS

Study Design

This review was conducted following the principles of the PRISMA guidelines (Figure-1) to ensure transparent identification, screening, eligibility assessment, and inclusion of studies related to substitutes for casein protein in cow's milk among children with Autism Spectrum Disorder (ASD). A narrative review approach was adopted because of the heterogeneity of study designs, interventions, and outcome measures across the included literature.

Search Strategy

A comprehensive literature search was carried out using the electronic databases Google Scholar, PubMed, Scopus, and Science Direct. Articles published between 2003 and 2025 were searched and screened. The following keywords and Boolean combinations were used: Autism Spectrum Disorder OR "ASD", casein-free diet, cow milk protein, casein protein, milk substitutes, plant-based milk alternatives, plant based milk, nutritional composition, digestibility, allergenicity; reference lists of relevant studies were also manually screened to identify additional eligible articles.

Inclusion Criteria

The following studies were selected:

- Articles that mentioned Autism Spectrum Disorder (ASD) and dietary management were selected.
- Cow's milk replacements and/or casein-free milk replacements were tested.
- The article identified nutritional, GI, behavioral, allergenic, or environmental impact of Cow's milk replacement.
- They were peer-reviewed articles published in journals, review, clinical trials or observations
- The article was published in the English language within the years of 2003 to 2025.

Data Extraction

Relevant information was extracted from eligible studies including: Author and publication year, study objectives, type of milk substitute, nutritional composition, digestibility and allergenicity findings, gastrointestinal and behavioral outcomes, environmental and sustainability considerations; the extracted findings were narratively synthesized and categorized into nutritional, health, environmental, and practical perspectives of cow's milk substitutes.

Quality control

The risk of bias is obvious in nearly all systematic reviews so the study took steps to avoid the risks in the manner illustrated in Table 1. Information was taken from appropriate databases and journals.

Data analysis

The literature review followed content and abstract synthesis using spreadsheets, as these methods minimize researcher intervention when capturing large amounts of data. This enabled qualitative and quantitative examination of the text data. Substitute components for the casein

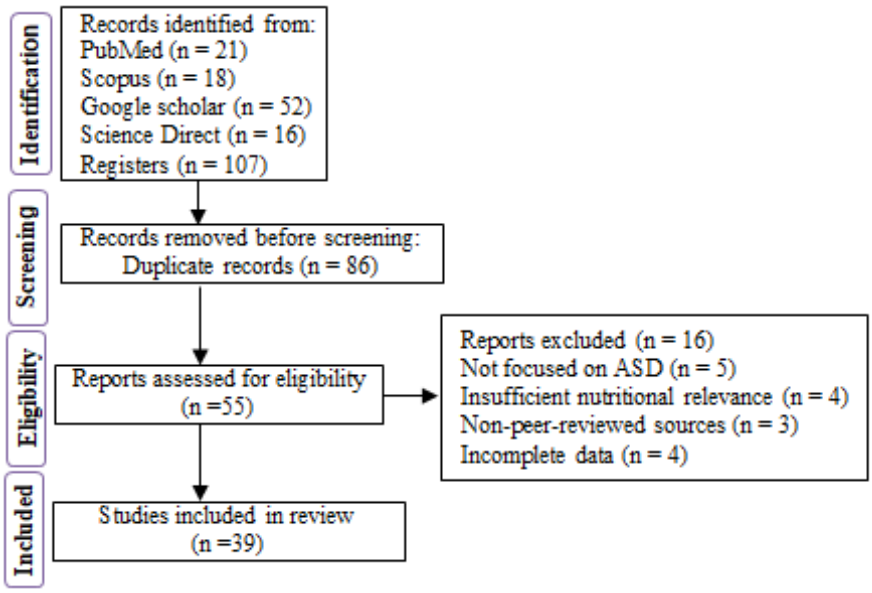

Figure 1: PRISMA flow chart of the review

Table 1: Measures implemented for quality control during the study

Quality control guide adopted during the literature review	O The study ensured research questions were realistic and answerable
	O A clear eligibility criterion was formulated and peer reviewed
	O Prior to the search, the researchers checked again with online repositories to determine if the research questions had already been asked
	O All literature sought from appropriately referenced, and deemed to be sufficient sources
	O The research team ensured there was no conflict of interest
	O Each case assessed on the merits of the individual case

protein in cow's milk were researched, antecedents were found and the gaps in the research identified. This method was chosen as it adequately furnished all of the research questions with sufficiently sound and complete answers.

RESULTS AND DISCUSSION

Sources with Nutritional Value of Substitute for Cow's Milk

They consist of aqueous extracts derived from legumes, grains, pseudo grains, oilseeds, vegetables, and nuts. The demand for Plant-Based Milk Alternatives (PBMAs) continues to grow as an increasing number of individuals transition from dairy to plant-based diets, viewing them as nutritious, environmentally friendly, free from casein proteins, and produced without harm to animals. The categorization according to different groups is provided in Table 2.

Protein is an essential macronutrient, here may be a lot of protein in milk, but that doesn't mean that it doesn't exist anywhere else. It does! And vegans simply do what elephants, bison and rhinos do. So, it's important to be aware of what plant-based milks are protein-rich, and

Table 2: Classification of Plant Based Milk Alternatives based on categories

Category	**Sources**	**Protein (%)**
Cereal Based	Corn milk, Spelt milk, Rice milk, Oat milk	7-14
Legume Based	Soy milk, Peanut milk, Lupin milk, Cowpea milk	36-40
Nut Based	Almond milk, Coconut milk, Hazelnut milk, Pistachio milk, Walnut milk	15-30
Seed Based	Sesame milk, Flax milk, Hemp milk, Sunflower milk	15-30
Pseudo Based	Quinoa milk, Teff milk, Amaranth milk	30-35

to include a variety of plant-based milk proteins in your meals. Above issues do the clear that-

All essential amino acid: Cow's milk protein contains all the essential amino acids, on the other hand plant proteins vary widely in concentration and amino acid balance. Legumes are rich in lysine but low in methionine, while cereals show the opposite trend. Combining these sources achieves a complementary amino acid profile similar to animal proteins that we need. Interestingly, Quinoa contains all nine essential amino acids (Alsaleem *et al.*, 2024)

Bioactive Components: Plant proteins contain naturally occurring compounds such as polyphenols, phytosterols, dietary fiber, and antioxidants, which contribute cardio-metabolic and anti-inflammatory benefits for children with ASD.

Different Prospective of Substitute for Cow's Milk

Nutritional Prospective of Substitute for Cow's Milk

Yang *et al.* (2012) emphasized the components of autistic children's blood and tissue reveals they have lower levels of important nutrients, such as: Vitamins B12, Vitamin C, Vitamin D, Calcium, Iron, Magnesium, and Zinc.

These deficiencies, often stemming from selective eating habits, sensory sensitivities, and GI issues, can exacerbate the core symptoms of ASD and lead to additional health complications. The overall protein, fat, and nutrient profile depend on the base ingredient. Fat content varies across both dairy and plant-based milks. Soy and pea milks tend to contain higher protein levels comparable to cow's milk, whereas almond, rice, oat, and coconut milks often provide minimal protein and energy.

Oat milk is a more affordable source of zinc and riboflavin but is lower in protein, calcium, and potassium. Other side, Almonds and sesame milk are naturally rich in calcium, zinc, potassium, and magnesium (Table-3). Besides plant milk also contains fiber and omega-3 which is very rare in liquid parts of cow's milk; Fiber plays a crucial role in maintaining bowel regularity by promoting bulk formation and stool softening (Yang *et al.*, 2012) and omega-3 fatty acid to improve neuronal function, lower inflammation, and balance neurotransmitters to help control the immunological response in the brain of child with ASD (Bent *et al.*, 2011)

Table 3: Average nutrients in dairy and plant-based milks (USDA, 2019)

Item, 240ml (products)	Protein (g)	Ca# (mg)	Ma# (mg)	P# (mg)	K# (mg)	Se# (mcg)	Z# (mg)	Ch# (mg)	Ri# (mg)	Vit-D (mcg)	Fiber (gm)	Omega-3 -
Daily Value	50	1,300	420	1,250	4,700	55	11	550	1.3	20	-	0.2
Dairy milk	8.2*	309**	29	252**	387	4.8	1.1	44	.33**	2.7*	Nil	0.05
Almond milk	1.0	449**	15	22	163	.2	.1	8	.002	2.4*	.5	
Cashew milk	1.8	116	ND	ND	69	ND	ND	ND	ND.	0.0	1	0.02
Coconut milk	0.5	459**	0	0	46	.0	.0	0	.00	2.4*	0	0.01
Hemp milk	2.3	204*	54*	199**	101	ND	0.6	ND	.42**	2.5*	1	0.1
Oat milk	2.7	248*	ND	170*	184	ND	1.0	ND	.55**	2.3*	2	0.1
Pea milk	7.5*	385**	0	ND	421	ND	ND	ND	ND	2.5*	4	0.1
Rice milk	0.7	288**	27	137*	66	5.4	0.3	5	0.35**	2.4*	0.3	0.01
Soy milk	6.1*	294**	33	176*	280	5.2	0.5	44	0.45**	2.7*	1	0.2

#Ca=Calcium, Mg=Magnesium, P=Phosphorus, K= potassium, Se=Selenium, Z=Zinc, Ch=Choline, Ri=Reboflavine
*** meets 20% Daily Value, * meets 10% Daily Value, ND = no data available*

Health Prospective

Digestive Tolerability and Behavioral Considerations in autism

The Lefter *et al.*, 2022 study reports that as much as 70% of those with ASD have GI symptoms such as stomach pain, constipation, diarrhoea, bloating and gastroesophageal reflux (GERD). These have been reported to be more frequent and severe in ASD compared to a non-ASD population.

Casein, being a gut irritant, may lead to leaky gut (firstly in the gut then in the brain) and the release of toxins - which subsequently impact on behaviour (Alharthi *et al.*, 2022). GI problems may worsen ASD-related behavioural symptoms, such as irritability, aggression, and repetitive behaviours (Fulceri *et al.*, 2016).

Addressing these GI issues are important in improving the quality of life and health outcomes of people with ASD, as the conditions may require individualised treatment, with a consideration for their sensory and dietary preferences.

Lactose Intolerance of Children with ASD

Lactose intolerance is a common problem affecting the digestion of lactose. Autistic children generally present with a higher tendency towards lactose intolerance than neurotypical children. In a recent study, the Lactase Deficiency rate was 58% in children with autism under 5 years, and 65% in older people with autism (Kushak et al, 2011). This can lead to a number of gastrointestinal symptoms, including gas, bloat and constipation. These issues can exacerbate abdominal pain which is a major issue for many children on the autism spectrum. Excluding lactose from the diet of a child with autism may improve not only gastrointestinal symptoms, but may also improve traits of autism.

Pus

Many dairy cows suffer from mastitis, or a bacterial infection of the udder, causing painful swelling or hardness. This painful disease is commonly associated with dirty, inadequate and poorly ventilated housing. There can be as many as 70 cases of mastitis per 100 cows per year in the UK (NADIS, 2025).

In response to mastitis, a cow's body produces more "policemen" (white blood cells) to fight infection, which ends up in the milk. These are known as somatic cells or pus. The greater number of somatic cells, the greater the risk of udder infection. Since mastitis is common in dairy cows it cannot be completely eliminated, and the EU legal limit for pus in milk (consumed by people) is 400,000 cells per liter (AHDB, 2025).

New infectious threats to health

Livestock production is now a source of new infectious disease risks, which can result in human epidemics and pandemics at any time. Antibiotic use in animal farming plays a major role in the rise of antibiotic-resistant infections, which again pose a threat to human health. It's now understood internationally we need to switch to a plant-based diet to maintain health in both humans and the environment. Hana Kahleova, MD, PhD, who is the director of clinical research at the Physicians Committee for Responsible Medicine and the lead author of the study, stated that eating acid-producing foods (such as meat, dairy and eggs) can raise dietary acid load (amount of acid consumed) which in turn results in inflammation (Kahleova *et al.*, 2024).

Environmental Sustainability

A significant investigation conducted by Oxford University evaluated the ecological consequences of the most frequently consumed food items from 40,000 diverse farms in 119 nations. The research revealed that the carbon emissions associated with producing cow's milk are threefold compared to those from any plant-based milk. Additionally, it indicated that dairy production requires substantially more land and a considerable amount of water an astonishing 22 times more than the water needed for soya milk (Poore & Nemecek, 2018). Moreover, one of the primary researchers, Joseph Poore stated: "Refraining from consuming animal products yields considerably greater environmental advantages than opting for sustainable meat and dairy." Therefore, plant-based milk is the most environmentally-friendly option - including almond milk, despite its high water usage.

Marketing Prospective of Substitute for Cow's Milk

The market for plant-based milks has grown phenomenally over the past 10 years and has rapidly become a multi-billion-dollar industry in the United States and across the globe (Jeski *et al.*, 2017, Bridges, 2018). One of the factors fuelling this growth has been the perception among consumers that these alternatives to milk offer similar (or even better) nutritional qualities to cow milk (Singhal *et al.*, 2017). This perception is heavily influenced by the term milk as part of labels and placement of these products next to cow milk in dairy aisles in supermarkets. So, it seems that everything that cows can provide, plants can provide even more of.

Reality: The White Truth of Cow Milk

Dr. Biswaroop Roy Chowdhury (www.biswaroop.com), he is best known for developing the popular research based D.I.P. Diet plan, describes that, Human is the only species that drinks milk all life long and human is the only animal who drinks milk of other animals! Never seen a tiger drinking a cow's milk! Humans have infringed the nature by consuming milk which was intended for child of that animal. It's not that surprising that humans are the only animals who suffer from diabetes, heart diseases, cancer and various other deadly diseases.

"Myth 1 claims dairy is essential for strong bones, but the truth shown here is that countries with high dairy intake (Finland, Sweden, Denmark) still have osteoporosis, while Vietnam and Thailand with low dairy intake have fewer bone diseases. Myth 2 says dairy is full of nutrition and calcium; truth: calcium ultimately comes from plants, cows get it from greens, and humans can obtain nutrition from plant sources, with milk not being necessary. Myth 3 asserts that milk promotes growth; truth: cow milk contains growth hormones much higher than human milk, and very rapid growth isn't necessarily good, with some links claimed between high dairy consumption and cancer. The piece also promotes a "3 Weeks Drop Dairy Challenge" promising dramatic health improvements, though such claims should be viewed with skepticism"

In addition, large dietetic association globally, such as the British Dietetic Association (BDA) in the United Kingdom has stated that a 100% plant-based diet can provide all the nutritional requirements for the life cycle from infancy to adulthood (BDA, 2026). A recent study was done by (Jaeger *et al.*, 2024) in New Zealand among 143 individuals and 18 PBMA samples. An exploratory analysis was performed to investigate the relationship between energy, protein, fat and carbohydrate content, but found no difference.

These aforementioned facts have made the use of plant-

based milks (vegetables, pulses, fruits, legumes, seeds, and cereals) increase due to several reasons, such as attitudes of the environmentally conscious attitude, abhorrence to animal cruelty and maintenance of a healthy diet. Therefore, the growth of plant-based dairy products has grown up to 61 % from 2012 (Reyesjurado *et al.*, 2023).

Challenges and Mitigation of Substitute for Cow Milk

A potential challenge with substitute for cow's milk or diets is the lack of important macro and micronutrients compared to cow's milk, such as essential protein, calcium, vitamins D, B12 and, along with the problems of more anti-nutrients, allergens and tastelessness. But the comforting thing is that alternative and emerging technologies can overcome these challenges in table-4.

Table 4: Challenge with substitute for cow's milk of children with Autism and their Mitigation plan

Challenges	Mitigation plan
Substitute for casein free of cow' milk and Plant based Essential amino acids	**Others animal milks**: Cow milk contains too much the autistic and allergenic-caseins others animal such as human, goat, camel, sheep milk is lacks the autistic and allergenic-caseins, so others animal milks is a good option for children with ASD (Shabo *et al.*, 2005). Plant milks: Soy and pea milks tend to contain higher protein levels comparable to cow's milk, whereas almond, rice, oat, and coconut milks often provide minimal protein (USDA, 2019). Plant based essential amino acids: A balanced diet that includes both whole grains and legumes (beans, peas, nuts) will provide us with all the amino acids we need (Clem *et al.*, 2021). Interestingly, Quinoa, a grain-like seed, is a fantastic source of protein and contains all nine essential amino acids (Alsaleem *et al.*, 2024). **Recycling of Protein**: The human body is capable of recycling more than 70% of its protein, so excess protein is not necessary (Ethel, 1994).
Calcium	**Seeds, Nuts and Legumes**: High intrinsic calcium content in seeds (sesame, poppy) and Almond nut (Grembecka *et al.*, 2022). Besides, Beans, lentils, and chickpeas contribute meaningful amounts and soy products such as tofu are especially rich sources of calcium (Messina, 2014)
Vitamin D	**Animal Sources**: Such as fatty fish (salmon, sardines, herring, and mackerel), liver, egg yolk, and fatty part of milk (cream). Plant Sources: Mushrooms are the only significant natural plant-based source of vitamin D (Phillips *et al.*, 2011). Sunlight: Vitamin D is mainly made in our skin after sun exposure.
Vitamin B12	**Plant-based sources**: According to peer-reviewed journal literature, Watanabe *et al.*, 2014 identified dried purple laver (Porphyra species) containing measurable amounts of vitamin B_{12}. Another Systematic Review found that Seaweeds, mushrooms, fermented foods contain B12 (Marques *et al.*, 2023). Other side, Eissa *et al.*, 2020 emphasized, the concentrations of B1, B2, B3, B6, B9 and B12 in wheatgrass juice samples were found to be 201.8, 1.28, 34.47, 4.66, 7.4 and 28.9 µg/ml respectively. Fermentations: The juice of fenugreek (Trigonella foenum graecum) leaves enriched with B12 (12.5 µg/100 mL) by certain lactic fermentations (Watanabe *et al.* 2013). Auto Producing B12: People who eat whole food plant raw forms automatically produce B12 by bacteria in the small intestine (Biswaroop, 2025).
Anti-nutrients, and allergens	Thermal processing (boiling, frying, pressure cooking) reduces trypsin inhibitors and lectins. Fermentation improves amino acid availability, reduces anti-nutrients, and enhances flavor. Germination (sprouting) activates endogenous enzymes that improve digestibility and bioavailability of nutrients. Enzymatic hydrolysis increases solubility and digestibility by breaking peptide bonds.
Tastelessness	Honey, jaggery, stevia, cinnamon powder and sweet fruits etc. can be added to substitute milks to enhance the taste for children with ASD.

CONCLUSION

So, which is better in these reviews: substitute or cow's milk? The reality is that a substitute for cow milk requires fewer resources to produce, has a smaller environmental footprint, and is allergen-free, casein-free, and lactose-free, making it suitable for children, especially children with ASD. However, transitioning to a casein-free milk or diet requires careful planning to ensure nutritional adequacy. A balanced diet combining whole grains and legumes provides all the essential protein. On the other hand, cooking reduces inhibitors, fermentation enhances nutrients, sprouting activates enzymes, and hydrolysis boosts digestibility. It is a good step to minimize anti-nutrient and allergen properties. Overall, it is true to say that dairy products are not an essential part of our diet and whether dairy products should be considered 'nutritional value' is debatable. As a result, caregivers need to be informed about alternatives to cow's milk for

organizing meals, shopping for groceries and cooking dishes that fulfill the dietary requirements of those with ASD. Organizations ought to provide training focused on alternatives to cow's milk. Regulatory agencies should establish guidelines regarding this matter, in addition to researchers needing to investigate this field.

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