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Omega-3 fatty acids in vegetarian and vegan diets: Translating evidence into practice

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ABSTRACT

Vegetarian and vegan diets are consistently associated with reduced cardiometabolic risk, despite providing minimal amounts of long-chain omega-3 polyunsaturated fatty acids (n-3 PUFAs), key precursors of bioactive lipid mediators, raising questions about n-3 PUFA metabolism and requirements in plant-based populations. This review examines current evidence on the metabolic fate of alpha-linolenic acid (ALA), its conversion to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and the implications for n-3 PUFA-derived signaling pathways. Although conversion efficiency is limited, it is influenced by dietary and non-dietary factors and may be supported by adaptive mechanisms that preserve tissue DHA. Individuals following plant-based diets exhibit lower EPA and DHA status, yet maintain favorable health profiles, suggesting that overall dietary context and endogenous regulation may mitigate reduced intake of preformed n-3 PUFAs. Targeted strategies, including optimizing ALA intake and using algae-derived EPA/DHA, effectively improve biomarker status. Understanding these mechanisms may help redefine n-3 PUFA requirements in plant-based populations.

1. Introduction

A plant-based diet (PBD) is a broad term encompassing dietary patterns that emphasize the consumption of whole or minimally processed plant foods. Although often used interchangeably with vegetarian or vegan diets, PBD also includes other dietary patterns such as flexitarian and Mediterranean diets. Vegetarian diets typically exclude meat and fish but may include dairy products and eggs, whereas vegan diets exclude all foods of animal origin, including dairy, eggs, and honey [1]. Well-planned vegetarian and vegan diets confer long-term health benefits, including improved cardiometabolic health, and are linked with a lower risk of major non-communicable chronic diseases, including cardiovascular disease, type 2 diabetes, hypertension, and obesity [2,3]. Recent umbrella reviews further report favorable effects of vegetarian and vegan dietary patterns on several cardiovascular risk factors, including blood pressure, blood lipids, body mass index, and C-reactive protein concentrations [4].

The prevalence of vegetarian and vegan dietary patterns has increased substantially worldwide in recent decades. Current estimates suggest that vegan diets are followed by approximately 1–3% of the population in many Western countries, with substantially higher prevalence in specific regions and younger population groups, while vegetarian dietary patterns may account for approximately 5–10% of the population depending on the country and methodology used [5–7]. In parallel, flexitarian dietary patterns, characterized by a reduced intake of animal-source foods, are also rapidly increasing worldwide [8]. This growing adoption of plant-based dietary patterns has increased scientific and clinical interest in their long-term nutritional adequacy.

Although vegetarian and vegan diets offer substantial health benefits, they can limit the optimal intake of certain nutrients, particularly n-3 PUFAs [9]. Alpha-linolenic acid (ALA; C18:3n-3), the plant-derived n-3 PUFA, is the only one considered essential, since it can be endogenously converted into the longer chain, biologically active forms eicosapentaenoic acid (EPA, C20:5n-3) and docosahexaenoic acid (DHA C22:6n-3). However, the efficiency of this bioconversion is limited and remains controversial [10]. Marine foods, such as fish and shellfish, provide preformed EPA and DHA, provide preformed EPA and DHA and are virtually the only direct source of these long-chain n-3 PUFAs. This review aims to analyze n-3 PUFA metabolism and physiological functions, assess dietary sources and n-3 PUFA status in individuals following vegetarian and vegan diets, and provide evidence-based practical recommendations.

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2. n-3 PUFA metabolism

The metabolism of n-3 PUFAs is a complex, multi-step process primarily occurring in the liver, which serves as the major organ for fatty acid synthesis. This metabolic pathway involves the conversion of the nutritionally essential precursor ALA into longer-chain derivatives like EPA and DHA. This conversion requires alternating reactions of desaturation and elongation, occurring in the endoplasmic reticulum (microsomes), followed by a final step of peroxisomal β-oxidation for DHA synthesis [11].

The enzymes delta-6 desaturase (encoded by the FADS2 gene) and delta-5 desaturase (encoded by the FADS1 gene) catalyze desaturation reactions (the formation of double bonds at the 6th and 5th carbon positions, respectively). Delta-6 desaturase is considered the rate-limiting enzyme in this pathway [11,12]. The elongation reaction consists in the addition of two carbon units to the carboxyl end of the fatty acid chain, and is performed by elongases, specifically ELOVL2 and ELOVL5. ELOVL5 acts on a wide range of C18 and C20 PUFAs, while ELOVL2 is specialized for the elongation of C20 and C22 PUFAs [11].

The final step of the n-3 PUFA bioconversion is the transportation of tetracosahexaenoic acid (THA, 24:6n-3) to peroxisomes for partial β-oxidation, to produce DHA [12]. This step can also be achieved by direct desaturation of THA to DHAby the delta 4-desaturase (encoded by the FADS2 gene) as has been shown in both animals and humans [13,14].

The n-3 PUFAs metabolism pathways and the involved enzymes are summarized in Fig. 1.

3. Factors influencing n-3 PUFA metabolism

In healthy adults, the conversion of ALA to long-chain n-3 PUFAs is limited and highly variable depending on the methodology used and population studied. While earlier estimates suggested conversion rates of approximately 5–10% for EPA and 2–5% for DHA, stable isotope tracer studies generally report substantially lower DHA conversion rates, frequently below 1% [15,16].

Several factors affect the n-3 PUFA elongation and desaturation reactions, which can be divided into non-dietary and dietary.

3.1. Non-dietary factors

3.1.1. Sex

Conversion rates are particularly low in men, whereas women exhibit slightly higher conversion rates [17]. These differences may be attributed to estrogen-enhanced enzymatic activity and the increased physiological demand for EPA and DHA during pregnancy and fetal development [18].

3.1.2. Gene polymorphisms

Evidence from precursor supplementation studies shows that increasing dietary ALA intake consistently elevates blood EPA concentrations, whereas DHA levels remain largely unchanged [19]. The high interindividual variability in response to ALA supplementation may be partly explained by numerous genetic variants in the FADS and ELOVL gene families, which modulate the efficiency of desaturation and elongation steps in the n-3 PUFA metabolic pathway [20].

3.1.3. Age

There is strong evidence and biological plausibility for age-related decline in desaturase and elongase activity, but this knowledge arises mostly from animal models [21,22]. Primary human studies directly measuring enzyme activity across age groups are essentially absent from the literature, because direct measurement of desaturase and elongase enzyme activity requires tissue biopsies (typically liver) and in vitro enzyme assays with microsomes, an invasive procedure not justified in healthy ageing populations.

Interestingly, circulating EPA and DHA concentrations have been reported to increase with age in some observational studies. However, these findings may be influenced by age-related differences in dietary habits and lifestyle factors, including a potentially higher fish intake among older adults, rather than reflecting enhanced endogenous conversion efficiency [23,24].

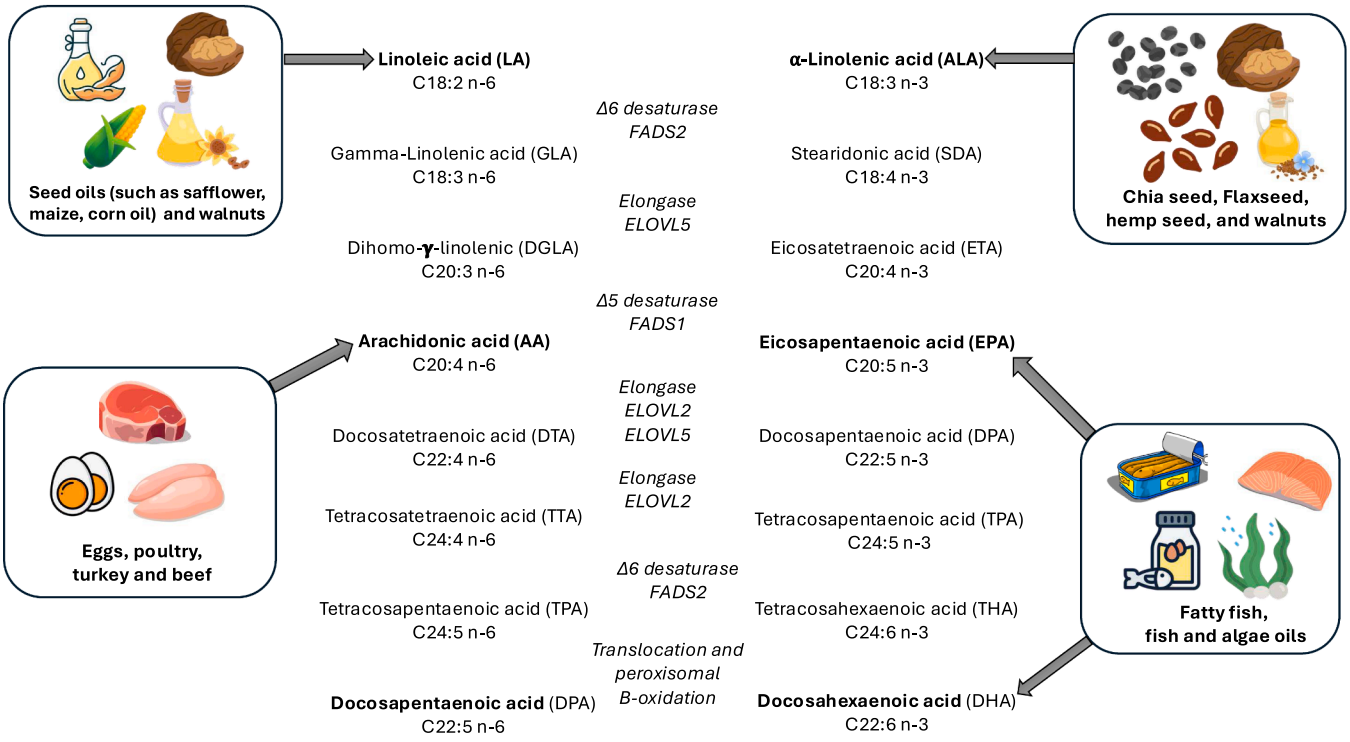


Fig. 1. n-3 and n-6 PUFAs bioconversion pathways.

3.1.4. Smoking

Smoking has been consistently associated with lower erythrocyte EPA and DHA levels in epidemiological studies, with reductions ranging from approximately 6% to 17% compared with non-smokers [24]. These differences may partly reflect dietary patterns, including lower fish consumption among smokers [25]. However, smoking may also directly affect n-3 PUFA metabolism through multiple mechanisms, including the induction of oxidative stress, which promotes PUFA peroxidation and degradation, as well as the inhibition of Δ5-desaturase activity [26, 27].

3.1.5. Obesity, insulin resistance and diabetes

Several studies have indirectly estimated desaturase activity by measuring product to precursor ratios in plasma (AA[20:4n-6]:dihomo-γ-linolenic acid [DGLA, 20:3n-6] ratio for delta-5 desaturase activity, and gamma-linolenic acid [18:3n-6]:LA[18:2n-6] for delta-6 desaturase) [28]. Using these approaches, some studies have reported increased estimated desaturase activity in individuals with type 2 diabetes. For example, one study examining plasma PUFA profiles in 396 patients with type 2 diabetes found higher plasma concentrations of DHA, AA, and DGLA, together with a higher AA/DGLA ratio compared with non-diabetic controls [29].

Nevertheless, the actual hepatic capacity to synthesize these fatty acids from precursors appears to be impaired in insulin-resistant states, despite what plasma ratios might suggest. Direct measurement of liver enzyme activity in patients with obesity revealed lower delta-6 and delta-5 desaturase activity [30].

Therefore, plasma fatty acid ratios may not accurately reflect true enzymatic activity under altered metabolic conditions. The elevated DHA levels observed in diabetic patients likely reflect dietary intake, altered clearance, or redistribution from tissues rather than enhanced endogenous synthesis. Hepatic fat accumulation, dyslipidemia and increased oxidative stress may all contribute to the discrepancy between circulating biomarkers and actual hepatic desaturase function [28,31].

3.2. Dietary factors

3.2.1. N-6 PUFA intake

Both linoleic acid (LA [18:2n-6], the main dietary n-6 PUFA) and ALA share the same enzymatic pathway for elongation and desaturation, as can be seen in Fig. 1. Even though the desaturase and elongase enzymes have differential substrate affinity, preferring n-3 to n-6 PUFAs [12,32], high LA intake can competitively inhibit the conversion of ALA to EPA and DHA, thereby reducing endogenous synthesis of long- chain n-3 PUFAs [12]. Consequently, the dietary ratio of n-6 to n-3 fatty acids (n-6:n-3 ratio) plays a crucial role in determining the conversion efficiency of ALA to EPA and DHA. Ratios below 10:1, and ideally between 2:1 and 4:1, are considered optimal for maximizing ALA conversion and maintaining a favorable long-chain n-3 PUFA status [33].

3.2.2. Long-chain n-3 PUFAs intake

Desaturase and elongate activity are also influenced through feedback regulation by products of the n-3 PUFA metabolic pathway. Intake of preformed EPA and/or DHA inhibits this pathway at the level of both gene expression and enzyme activity, thus reducing ALA desaturation and elongation [34].

3.2.3. Protein intake

Evidence in both animals and humans suggests that higher protein intake may enhance desaturase activity, while protein-deficient diets appear to impair this process. However, these findings should be interpreted cautiously due to several methodological limitations, including differences in body weight between groups, the indirect estimation of desaturase activity using blood fatty acid profiles, and the concomitant reduction in total energy intake observed in protein-restricted diets [13, 35].

3.2.4. Micronutrient deficiencies

Several minerals (especially zinc, magnesium and iron) as well as vitamins such as niacin, pyridoxine and ascorbic acid act as cofactors in the desaturation and elongation reactions. Deficiencies in these micronutrients may impair the activity of desaturase and elongase enzymes, thereby reducing the endogenous synthesis of long-chain n-3 PUFA [13, 32].

3.2.5. Alcohol

Animal and in vitro studies suggest that alcohol exposure promotes lipid accumulation and alters desaturase activity, potentially contributing to lower n-3 PUFA levels [36–38]. However, the mechanisms underlying the relationship between alcohol intake and n-3 PUFAs in humans remain incompletely understood. In most studies, the association between alcohol consumption and n-3 PUFA levels in humans is either negative or neutral [24]. Wine consumption appears to be a possible exception, as some epidemiological studies have reported positive associations with n-3 PUFA status. Nevertheless, these findings may be influenced by residual confounding factors, including overall dietary patterns and lifestyle behaviors. The apparent discrepancy between the potentially harmful effects of alcohol on n-3 PUFA metabolism and the favorable associations observed with wine intake raises the possibility that non-alcoholic compounds present in wine, particularly polyphenols, may contribute to these observations [39,40]. These findings suggest that factors other than ethanol itself, including wine polyphenols or broader dietary patterns, may partly explain the observed associations.

4. Emerging evidence regarding n-3 PUFA metabolism

Emerging evidence suggests that the n-3 PUFAs biosynthetic pathway is more dynamic than previously assumed. Recent isotope tracer studies indicate that intermediates such as EPA and docosapentaenoic acid (DPA) may contribute substantially to endogenous DHA synthesis, with DPA potentially acting as a metabolic reservoir within the pathway [41]. In contrast, retroconversion of DHA back to EPA in humans appears to be minimal under most physiological conditions [42]. These findings suggest that long-chain n-3 PUFA metabolism involves bidirectional interconversion and intermediary storage pools rather than a simple linear conversion pathway from ALA to DHA, revealing a more complex metabolic regulation than previously recognized.

Taken together, dietary intake of ALA within current recommended ranges appears sufficient to sustain the formation of long-chain n-3 PUFAs. The hepatic capacity for ALA conversion, together with peripheral tissue PUFA synthesis and potential metabolic adaptations, may contribute to maintaining physiologically relevant EPA and DHA concentrations in some individuals, although the extent to which these mechanisms fully meet long-term human requirements remains uncertain [43].

5. Biological functions of n-3 PUFAs

The most widely recognized biological effect of n-3 PUFAs is their anti-inflammatory activity. This involves multiple mechanisms, including inhibition of the conversion of arachidonic acid (AA, the end product of n-6 PUFAs metabolism) to pro-inflammatory eicosanoids such as prostaglandin E2 and leukotriene B4, as well as the synthesis of specialized pro-resolving mediators such as resolvin E1, protectin D1, and maresin [44].

Beyond their immunomodulatory effects, n-3 PUFAs, mainly EPA and DHA, have direct cardiovascular and metabolic actions. These fatty acids are incorporated into plasma membranes, where they influence properties such as fluidity and ion channel activity, thereby modulating cardiomyocyte membrane excitability and conductivity [45,46]. At the intracellular level, n-3 PUFAs exert anti-inflammatory and antifibrotic

activities by modulating pathways, including nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) signaling, NOD-like receptor family pyrin domain containing 3 (NLPR3) inflammasome, and the activation of peroxisome proliferator-activated receptor (PPAR) alpha and gamma [47,48]. Furthermore, n-3 PUFAs display antiplatelet properties through increased prostaglandin E3 formation and reduced thromboxane A2 synthesis [49]. They also contribute to lipid regulation by lowering serum triglycerides and remnant cholesterol concentrations via inhibition of VLDL synthesis and reduced apolipoprotein C-III activity [44]. n-3 PUFAs also play a critical role in neurological health. DHA is the most abundant n-3 PUFA in the central nervous system, modulating key biophysical properties of neuronal membranes and contributing to neurogenesis and synaptogenesis. DHA is also concentrated in the retina, where it is essential for the optimal activation and signaling of photoreceptors [50].

In addition to serving as a metabolic precursor of EPA and DHA, ALA itself exerts protective effects that should not be overlooked. ALA is incorporated into cell membranes, modulating their structural and functional properties, and can be converted into lipid mediators with anti-inflammatory and antihypertensive effects [10]. Evidence from randomized trials shows beneficial effects of ALA on lipid profile, blood pressure, and inflammation biomarkers. Moreover, findings from both epidemiological studies and RCTs suggest potential benefits of ALA consumption for cardiovascular and cognitive health [51].

6. Dietary n-3 PUFA recommendations across life stages

Recommendations for n-3 PUFA intake vary among health authorities, reflecting the differences in methodological approaches and target populations (Table 2). The World Health Organization and Food and Agriculture Organization (WHO/FAO) define a population nutrient intake range for n-3 PUFAs of 1–2% of total daily energy intake, unless otherwise specified [52]. The Institute of Medicine (IOM) establishes the Adequate Intake (AI) for ALA in adults as 1.6 g/day for men and 1.1 g/day for women. Given the lack of sufficient evidence to define a Recommended Dietary Allowance (RDA) for n-3 PUFAs, the Institute of Medicine (IOM) sets the AI based on the highest median intake of ALA among United States adults, a population in which deficiency is virtually nonexistent among non-institutionalized individuals [53]. In the case of infants, where DHA plays a critical role in brain and retina development, the requirements for ALA are based on the amount of n-3 PUFAs provided by human milk. This results in an AI of 0.5 g/day for infants, corresponding to approximately 1% of total daily energy intake. The European Food Safety Authority (EFSA) establishes that there is insufficient scientific data to derive an Average Requirement, a Lower Threshold Intake, or a Population Reference Intake for ALA [54]. Therefore, the EFSA set an AI for ALA at 0.5% of total energy intake, based on the lowest estimated mean intakes from various population groups across several European countries, where no overt symptoms of ALA deficiency were observed. In contrast to the WHO and IOM, the EFSA establishes an AI of 250 mg for EPA+DHA for healthy adults as primary prevention of cardiovascular risk. Additionally, it is recommended to add 100 to 200 mg of preformed DHA during pregnancy and lactation, while intakes of 50 to 100 mg per day in older infants are recommended for adequate visual function during the complementary feeding period. The Academy of Nutrition and Dietetics (AND) advises an intake of ALA at 0.6–1.2% of total energy intake, including 250–500 mg of EPA+DHA [55]. None of these dietary guidelines provides differentiated recommendations specifically for individuals following vegetarian diets. In this regard, the AND established that, in the absence of consistent evidence from intervention trials on EPA/DHA dosages in individuals following a vegetarian and vegan diet, recommendations for healthy adults should emphasize regular intake of ALA-rich plant foods.

It has been proposed that the current ALA AI for individuals following a vegetarian and vegan diet should be increased to ensure a daily intake of at least 2.2 g/day (and up to 4.4 g/day), aiming for an n-6:n-3 ratio between 2:1 - 4:1, which is optimal for the endogenous conversion of ALA to EPA and DHA [33]. A lower n-6:n-3 ratio is also associated with lower all-cause, cardiovascular and cancer mortality, and a lower risk of stroke [56,57]. However, the clinical validity and practical relevance of this ratio remain controversial, and no official recommendations have been established regarding its optimal value for health outcomes [58,59]. Further research is warranted to clarify these relationships.

7. Plant-based sources of n-3 PUFAs

The primary dietary sources of ALA are plant-based and include flaxseed, chia seeds, walnuts, hemp seeds, and oils such as canola and soybean oil. Table 3 presents the major plant-based sources of ALA, along with their LA content. Obtaining sufficient ALA intake without a concurrent increase in LA intake can be challenging, as most ALA-rich foods also contain considerable amounts of LA. However, choosing foods with a low n-6:n-3 ratio, such as flaxseed, flaxseed oil, chia seeds, hemp seeds, or canola oil, may facilitate meeting ALA recommendations while limiting excessive LA intake [60]. Commonly consumed vegetable oils in Western dietary patterns, such as sunflower, corn, and safflower oils, are rich in LA but contain minimal amounts of ALA [61]. Therefore, vegetarian and vegan diets predominantly based on these oils may still result in high dietary n-6 PUFA exposure, potentially limiting endogenous conversion of ALA into long-chain n-3 PUFAs despite an otherwise plant-based dietary pattern.

Some microalgae, such as *Nannochloropsis salina, Nannochloropsis* sp., and *Nannochloropsis* sp. *CCNM 1081*, as well as certain seaweeds, including *Codium fragile* and *Palmaria palmata*, are also important sources of EPA [62]. In contrast, the primary sources of EPA and DHA are animal-based, with notable examples including salmon, sardines, herring, and oysters [63]. Smaller amounts may also be found in n-3 enriched eggs and grass-fed dairy and meat products [64,65].

8. Effect of vegetarian and vegan diets on n-3 PUFA status

Traditionally, n-3 PUFA status has been evaluated through measurements of plasma or serum levels. However, this approach has several limitations, as these levels can fluctuate significantly based on recent dietary intake, reflecting only short-term n-3 PUFAs status [63]. The Omega-3 Index (O3I) assesses n-3 PUFAs status by measuring the proportion of EPA and DHA in erythrocyte membranes, serving as a reliable indicator of long-term intake over approximately the previous 120 days [66]. Optimal O3I values for cardiovascular protection are considered to be above 8%, with values between 4% and 8% regarded as adequate, while values below 4% are associated with an increased risk of cardiovascular disease due to insufficient n-3 PUFA intake [67] Previous studies have shown that individuals following a vegan diet exhibit a significantly lower O3I score than individuals following omnivorous diets, with both groups having values below the optimal threshold (Table 4). Similarly, in individuals following a vegan diet, a slightly lower mean O3I has been observed in females compared to males (3.9% vs. 4.0%), along with an age-related increase from the youngest to the oldest age groups (3.5%vs. 4.0%) [68]. In endurance athletes following a vegan diet, higher O3I values have been reported (4.1%), although still below the proposed optimal threshold for cardiovascular protection [69].

9. n-3 PUFAs intake in individuals following vegetarian and vegan diets

Intake of n-3 PUFAs varies considerably among individuals following vegetarian and vegan diets. The largest study to assess n-3 PUFA intake in vegetarians and vegans was the Adventist Health Study-2, which included a total of 71,751 participants: 33,664 non-vegetarians, 4042 semi-vegetarians, 6583 pesco-vegetarians, 21,799 lacto-ovo-

vegetarians, and 5694 vegans. In this study, only total n-3 PUFA and DHA intakes were reported [70]. Total n-3 PUFA intake was sufficient and similar in all groups, with vegans having the lowest (mean total n-3 PUFA of 2 g/day) and pescovegetarians the highest (mean of 2.4 g/day). Pescovegetarians had a mean DHA intake of 187 mg/d, contrasting with non-vegetarians, vegetarians and vegans, whose average DHA intake was very low (below 35 mg/d). Notably, in this study, neither ALA nor EPA intake was reported, so intake of those specific types of n-3 PUFA intake could not be assessed [70].

More recently, a study from the same cohort compared n-3 PUFAs intake in 300 individuals following non-vegetarian, pescovegetarian, vegetarian and vegan diets [71]. Pescovegetarians reported the greatest average EPA+DHA intake (158 mg/d), followed by non-vegetarians (117 mg/d), vegetarians (17.9 mg/d) and vegans (9.5 mg/d) (Table 5). In line with these findings, a study from the EPIC—Norfolk cohort reported that participants who regularly consumed fish had an average EPA+DHA intake of approximately 320 mg/day in men and 260 mg/day in women, while non–fish-eaters (including vegetarians, vegans, and meat-eaters who did not consume fish) had negligible intakes, averaging <40 mg/day [72]. This suggests that, without consuming supplements, meeting the EFSA recommendation of 250 mg/day of EPA+DHA is feasible mainly among regular fish eaters [54].

A recent systematic review including 12 studies found that average n-3 PUFA intake was higher in vegans (2.69 g/d) compared with vegetarians (1.36 g/d), and meat-eaters (1.08 g/d), primarily due to a greater consumption of ALA. As expected, the intake of EPA and DHA was considerably lower in vegetarians (16 mg/d and 31 mg/d, respectively) and virtually negligible in vegans (27 mg/d and 4 mg/d). Meat-eaters (including fish-eaters) had greater average intake (94 mg/d for EPA and 172 mg/d for DHA) [9].

While these intake data provide useful context, their physiological relevance depends on how dietary n-3 PUFAs availability translates into downstream metabolic pathways and lipid mediator production.

10. Vegetarian and vegan diets, n-3 PUFA status, and health outcomes

As described in the previous sections, in individuals following vegetarian and vegan diets, intake of ALA is often higher, while circulating levels of EPA (and especially DHA) tend to be lower. This finding can be due to the limited conversion of ALA to long-chain n-3 PUFA, as well as nutritional factors that may influence this process, such as inadequate intake or status of protein, zinc or iron. For example, vegetarians and vegans show a lower zinc status and higher deficiency rates, reaching up to 30% in vegans [9]. This potential limitation can be overcome through appropriate dietary planning, including the use of supplementation strategies when necessary.

Vegetarian and vegan diets are characterized by a lower intake of long-chain n-3 PUFAs yet are consistently associated with a reduced risk of several chronic conditions, including cardiovascular disease and cancer [2,3,73]. Several factors may contribute to this apparent discrepancy, including the benefits of vegetarian and vegan diets that could offset a lower n-3 PUFA status, possible physiological adaptations to low EPA and DHA intake, and methodological limitations to the available evidence.

Animal studies indicate that n-3 PUFA deprivation can prolong DHA half-life in the brain by reducing its catabolism [74]. This adaptive mechanism, in conjunction with the well-documented health-promoting properties of plant-based diets, may partially account for the favorable long-term neurological outcomes observed in vegetarian and vegan diets, despite their comparatively lower intake of DHA [75]. However, the translational relevance of these adaptive mechanisms to long-term human neurological outcomes remains incompletely understood.

Individuals following vegan diets, despite higher ALA intake, exhibit significantly lower DHA levels in plasma, erythrocytes, and spermatozoa compared to omnivores [76,77]. However, a systematic meta-analysis found no significant differences in standard semen parameters—including count, concentration, motility, and morphology—between vegetarians and omnivores [78]. Although conventional semen quality parameters appear preserved, the long-term physiological implications of reduced sperm DHA levels remain unclear and warrant further investigation.

A higher EPA/AA ratio, associated with lower systemic inflammatory status and reduced cardiovascular risk, has been described in Japanese vegetarians, despite having lower n-3 PUFA intake [79]. The lower energy and fat content typically observed in vegetarian and vegan diets may enhance Sterol Regulatory Element-Binding Protein 1 (SREBP-1) activity, thereby promoting delta-5 and delta-6 desaturase expression, and therefore EPA and DHA synthesis [79]. However, the efficiency of this bioconversion is strongly influenced by FADS gene polymorphisms and by other metabolic and dietary factors that affect desaturase activity (Table 1).

Properly planned vegetarian and vegan diets are characterized by a favorable macronutrient profile, being rich in unsaturated fats and plant protein, and low in saturated and trans fats, sodium, and animal protein, while also providing abundant dietary fiber, vitamins, minerals, and a wide range of antioxidant and phytochemical compounds [3]. This composition leads to lower levels of atherogenic lipoproteins, blood pressure, body fat, systemic inflammation, and higher insulin sensitivity. Consequently, vegetarian and vegan diets are consistently associated with a greater longevity and a reduced risk of cardiovascular and cerebrovascular disease, type 2 diabetes, obesity, chronic kidney disease, dementia, and cancer [2,3,73].

Lastly, limited exposure contrast in studies evaluating n-3 PUFA status between vegetarian and vegan diets compared to omnivorous diets should be considered. In most Western countries, n-3 PUFA status is suboptimal, as reflected by low O3I values. For example, a large study of 160,000 adults showed a mean O3I of 4.7%, and the Framingham Offspring Study found an average of 5.7% [80]. As described previously, individuals following vegetarian and vegan diets generally show even lower O3I values (Table 4). However, the difference in n-3 PUFA status between dietary groups may not be enough to generate a sufficient contrast to identify significant differences in clinical outcomes. In other words, most comparisons are made between individuals with low n-3 PUFA status (omnivores) and those with an even lower status (vegetarians and vegans). To date, no study has directly compared long-term health outcomes in individuals on vegetarian and vegan diets with low (<4%) versus optimal (>8%) O3I levels, a design that would be necessary to clarify the clinical relevance of these differences.

Table 1
Factors that may reduce the bioconversion pathway of ALA to EPA and DHA.

Non-modifiable factors	Clinical conditions	Dietary factors	Lifestyle factors
Male sex [17,18]	Obesity, insulin resistance and diabetes [28–31]	n-6:n-3 ratio > 4:1 (especially > 10:1) [12,32,33]	Smoking [24, 27]
Older age [23,24]		Lack of vitamin and mineral cofactors, especially zinc, magnesium, niacin, pyridoxine and vitamin C [13]	Alcohol consumption [24,39,40]
FADS and ELOVL gene polymorphisms [19,20]			

FADS = Fatty Acid Desaturase. ELOVL = Elongation of Very Long Chain Fatty Acids.

Table 2
Summary of of n-3 PUFA recommendations.

WHO/FAO [52]	Adults: 1–2% of total energy n-3 PUFAs
IOM [53]	Pregnancy: 1.4 g/day of ALA Lactation: 1.3 g/day of ALA 0–12 months: 0.5 g/day of ALA (AI) 1–3 years: 0.7 g/day of ALA 4–8 years: 0.9 g/day of ALA 9–13 years: 1.2 g/day (boys) and 1.0 g/day of ALA (girls) >14–18 years: 1.6 g/day (men) and 1.1 g/day of ALA (women)
EFSA [54]	Pregnancy and lactation: 0.5% of total energy of ALA 250 mg/day of EPA+DHA + 100–200 mg/day DHA 7–24 months: 0.5% of total energy of ALA / 100 mg/day of DHA 2–18 years: 0.5% of total energy of ALA/ 250 mg/day of *EPA+DHA*. Adults: 0.5% of total energy of ALA/ 250 mg/day of *EPA+DHA*
AND [55]	0.6–1.2% of total energy as ALA; 500 mg EPA+DHA/day

LA, Alpha-linolenic acid; AND, Academy of Nutrition and Dietetics; DHA, Docosahexaenoic acid; EFSA, European Food Safety Authority; EPA, Eicosapentaenoic acid; FAO, Food and Agriculture Organization; IOM, Institute of Medicine; PUFA, Polyunsaturated fatty acids; WHO, World Health Organization.

Table 3
Plant-based sources of α-linolenic acid and linoleic acid.

Food	LA (g)	ALA (g)	n-6/n-3 ratio	Amount needed for men (1.6 g ALA/d)	Amount needed for women (1.1 g ALA/d)
Canola oil	17.80	7.50	2.37	21.3	14.7
Chia seeds*	5.80	17.80	0.33	9.0	6.2
Corn oil	51.9	1.04	49.9	153.8	105.8
Edamame	1.80	0.36	5.00	444.4	305.6
Flaxseed	5.26	19.40	0.27	8.2	5.7
Flaxseed oil	14.30	53.40	0.27	3.0	2.1
Hempseed hulled	1.30	8.90	0.15	18.0	12.4
Soybean	2.80	0.40	7.00	400.0	275.0
Soybean oil*	50.90	6.60	7.71	24.2	16.7
Sunflower oil	20.6	0.16	126.4	1000	687.5
Walnuts*	38.10	9.10	4.19	17.6	12.1

Values are expressed per 100 g of food. Data are extracted from the US Department of Agriculture Nutrient Database, except.
* which were extracted from [33]. A-Linolenic Acid (ALA) and Linoleic Acid (LA).

11. Plant-based n-3 PUFA supplements

As described above, both n-3 PUFA intake and status are lower among individuals following vegetarian and vegan diets compared to omnivorous or pescovegetarian diets. Consequently, it has been suggested that individuals adhering to vegetarian or vegan diets may benefit from n-3 PUFA supplements. n-3 PUFA supplements derived from fish oil are widely consumed, and many large clinical trials, systematic reviews and meta-analyses have been conducted assessing their health effects, mostly regarding cardiovascular health, with conflicting results [81,82]. Nevertheless, since this review focuses on people following vegetarian and vegan diets, and fish oil supplements are derived from fish, this type of supplements will not be discussed. In this section we summarize the current evidence regarding different forms of plant-based n-3 PUFA supplements, focusing on their relevance in vegetarian and vegan diets.

11.1. ALA supplements (flaxseed oil, chia oil)

Flaxseed oil is one of the richest plant-based sources of ALA, providing a more concentrated and bioavailable formulation compared with whole flaxseed, as the oil matrix facilitates absorption and incorporation into circulating lipids [83]. This is particularly relevant in plant-based diets, where efficient utilization of ALA is critical to maintain an adequate n-3 PUFA status. Evidence from clinical trials indicates that flaxseed oil supplementation increases circulating ALA and enhances the conversion to long-chain n-3 PUFAs, leading to higher levels of EPA and DPA but without affecting DHA [84].

Flaxseed supplementation has been investigated not only for its effects on fatty acid status but also for its influence on inflammatory and endothelial markers associated with n-3 PUFA intake. A meta-analysis of

Table 5
Reported daily intake of n-3 PUFAs by diet group in the Adventist Health Study-2.

	NV	PV	LOV	VGN
ALA (g)	1.40 ± 0.5	1.6 ± 1.0	1.5 ± 0.7	1.5 ± 0.9
EPA (mg)	32.0 ± 26.6	54.4 ± 107.8	4.9 ± 15.6	2.8 ± 11.5
DHA (mg)	85.1 ± 66.5	103.6 ± 174.5	13.0 ± 38.4	6.7 ± 28.2
EPA+DHA (mg)	117.1 ± 91.1	158.1 ± 278.5	17.9 ± 53.8	9.5 ± 39.5

Adapted from [71]. NV = Non-vegetarians. PV = Pescovegetarians. VGN = Vegans. LOV = Lacto-ovo-vegetarians. Values are expressed as means ± standard deviation.

Table 4
Comparison of Omega-3 Index values between vegan and omnivorous diets.

Authors	Country	Population	O3I with vegan diet	O3I with vegetarian diet	O3I with omnivorous diet
Sanders et al. 1978 [103]	British	Individuals following vegan diet (n = 22) and omnivorous diet (n = 22)	2.0%*	-	6.4%*
Agren et al. 1995 [104]	Finnish	Individuals following strict raw vegan diet (n = 8) and omnivorous diet (n = 11)	3.8%*	-	8.1%*
Fokkema et al. 2000 [105]	Dutch	Individuals following vegan diet (n = 12) and omnivorous diet (n = 76)	2.3%*	-	4.5%*
Kornsteiner et al. 2008 [106]	Austrian	Individuals following vegan diet (n = 37) and omnivorous diet (n = 23)	1.5%*	2.0%	2.9%*
Sarter et al. 2015 [68]	USA	Men following vegan diet (n = 40) and omnivorous diet (n = 78).	3.5%	-	3.5%
Pinto et al. 2017 [107]	UK	Individuals following vegan diet (n = 23) and omnivorous diet (n = 24). Age and BMI matched.	2.7%	-	5.4%
Craddock et al. 2022 [69]	Australian	Endurance athletes following vegan diet (n = 12) and omnivorous diet (n = 8)	4.1%	-	5.4%
Klein et al. 2025 [108]	Germany	Healthy individuals following a vegan diet (n=57) and an omnivorous diet (n=62)	2.6%*	3.2%	4.0%*
Harris et al. 2025 [71]	USA	Individuals following vegan diet (n = 69), vegetarian diet (n = 65) and omnivores diet (n = 54)	3.7%	3.9%	5.0%

* indicates that the Omega-3 Index was not reported and was calculated as [(EPA + DHA) / Total fatty acids in erythrocytes] × 100 [68]. O3I, Omega-3 Index; USA, United States; UK, United Kingdom.

40 randomized controlled trials reported significant reductions in C-reactive protein (CRP), interleukin-6 (IL-6), and VCAM-1, with IL-6 reductions observed specifically with flaxseed oil and CRP reductions with whole flaxseed, suggesting formulation-specific anti-inflammatory effects [85]. In addition, in a retrospective study of patients with type 2 diabetes mellitus and coronary heart disease, flaxseed oil supplementation (1 g/day, providing 400 mg ALA) was associated with greater decreases in serum insulin and high-sensitivity CRP compared with fish oil [86]. These findings collectively suggest that flaxseed oil may confer cardiometabolic and anti-inflammatory benefits through mechanisms not strictly dependent on DHA enrichment, supporting its use as a complementary n-3 PUFA source in plant-based dietary patterns.

Chia oil is another concentrated plant-based source of ALA, and supplementation has been shown to effectively increase circulating ALA levels. However, evidence from human studies regarding its conversion to long-chain n-3 PUFAs such as EPA and DHA remains limited [87]. Interestingly, a study comparing whole versus milled chia seeds found that plasma ALA increased by 58% and EPA by 39% in the milled chia seed group, whereas nonsignificant changes were observed in the whole seed and placebo groups [88]. Despite these increases in fatty acid levels, no significant changes were detected in body composition, inflammation markers, blood pressure, or lipoproteins. Moreover, in a supplementation trial with Chilean mothers, daily intake of 16 mL chia oil from the third trimester of pregnancy through the first six months of nursing increased erythrocyte ALA and EPA and transiently elevated milk DHA during the first three months of lactation, without affecting arachidonic acid or long-term DHA levels [89]. These findings suggest that mechanical processing of chia seeds may enhance the bioavailability of ALA and its partial conversion to EPA, although the clinical relevance of these changes for cardiometabolic outcomes requires further investigation.

Regarding clinical outcomes, current evidence suggests potential cardiovascular benefits of ALA, including reductions in atherogenic lipoproteins, blood pressure, and inflammatory markers. However, findings remain inconsistent across studies due to variations in study design, ALA dosage, intervention duration, background diet, and participant characteristics. Further research is needed to clarify the role of ALA in CVD prevention and management. Evidence for effects on type 2 diabetes, metabolic syndrome, and obesity remains inconclusive, while data on cognitive function appear promising but are still preliminary [51,82].

11.2. Algae-based supplements

Since fish are not the primary producers of DHA but rather accumulate it through the marine food chain, algae are the primary source of this fatty acid [90]. Algal oil supplements therefore provide a direct, plant-based alternative source of DHA that may help overcome the limited endogenous conversion of ALA to DHA observed in humans [91]. Evidence from intervention and cohort studies demonstrates that algal oil supplementation effectively increases DHA concentrations in plasma, serum, platelets, and red blood cells, as well as the O3I, in vegetarian and vegan populations [92,93]. Reported increases include 55–82% in the O3I and up to 246% in serum and platelet phospholipid DHA [68,94]. Comparisons between algal DHA and fish oil supplementation have shown no significant differences in bioavailability, suggesting comparable efficacy between sources [95]. Moreover, algal DHA supplementation may also increase EPA concentrations through retro-conversion, which is particularly relevant in vegetarian populations with lower baseline EPA status [96]. A recent systematic review shows that microalgal DHA intake effectively improves DHA status in erythrocyte membrane and plasma, particularly during pregnancy and lactation in women following vegan diets [93].

Further large-scale, well-controlled trials are warranted to establish clinically meaningful recommendations for algal DHA use in plant-based populations and to determine whether such supplementation provides additional cardiometabolic benefits beyond those already associated with vegetarian diets.

11.3. Stearidonic acid supplements

Stearidonic acid (SDA, C18:4 n-3), obtained from plant sources such as *Echium plantagineum, Buglossoides arvensis, Ribes* sp., and genetically modified soybeans, is emerging as a novel plant-derived n-3 PUFAs source. The conversion of SDA to EPA is more efficient than that of ALA, since SDA lies downstream of the first delta-6-desaturase reaction, which is strongly influenced by genetic and dietary factors (Table 1) [62]. Nevertheless, SDA supplements do not appear to significantly increase DHA levels, indicating that while it may improve EPA status, its effect on the overall long-chain n–3 PUFA pool remains limited.

12. Recommendations

The main dietary strategies to optimize n-3 PUFAs status in individuals following vegetarian and vegan diets are summarized in Fig. 2.

12.1. Ensuring adequate ALA intake

ALA remains the essential n–3 PUFA precursor in plant-based diets. Individuals following vegetarian or vegan patterns should have a regular consumption of ALA-rich foods, including flaxseed, chia seeds, walnuts, soybeans, hemp seeds, and their oils, to support endogenous synthesis of EPA and DHA. Adequate ALA intake represents the minimum requirement for maintaining n–3 PUFA status. As discussed above, in people following vegetarian or vegan diets, it is reasonable to consume higher amounts of ALA to meet an optimal n-6:n-3 ratio of $< 10{:}1$ (ideally $<4{:}1$) [97,98].

12.2. Dietary sources first

Whole foods should be prioritized over supplements, as they provide additional benefits from fiber, antioxidants, proteins, vitamins and minerals. A diverse intake of ALA-rich foods maximizes the potential for endogenous EPA synthesis and contributes to an overall favorable cardiometabolic profile.

12.3. Be mindful about n-6 PUFA sources

Since several studies show that most people following vegetarian and vegan diets have an unbalanced n-6:n-3 ratio, reducing LA while increasing ALA intake seems to be the most rational approach [33]. In order to maintain a low n-6:n-3 ratio (closer to 2–4:1), it may be reasonable to replace concentrated sources of n-6 PUFAs (eg. sunflower and corn oils, and salad dressings) with oils high in monounsaturated fatty acids, such as olive, canola, hemp, avocado and high-oleic variants. It should be noted that this recommendation aims at optimizing ALA conversion to EPA and DHA, and it is not based on n-6 PUFA-rich oils having an intrinsic deleterious effect on health. In fact, evidence from large epidemiological studies and clinical trials have reported benefits of higher LA consumption (across the range of normal dietary intakes) in cardiovascular and metabolic outcomes [59].

12.4. ALA or SDA supplements

Supplementation with ALA-rich oils (e.g., flaxseed, chia) or a concentrated source of SDA (such as Echium) may be considered when dietary intake is insufficient or in populations with reduced conversion efficiency, including individuals with certain FADS gene polymorphisms, older adults, or those consuming low-fat diets. These supplements should complement, rather than replace, dietary sources. However, while these supplements effectively increase EPA status, they do not seem to improve DHA levels [93,99,100].

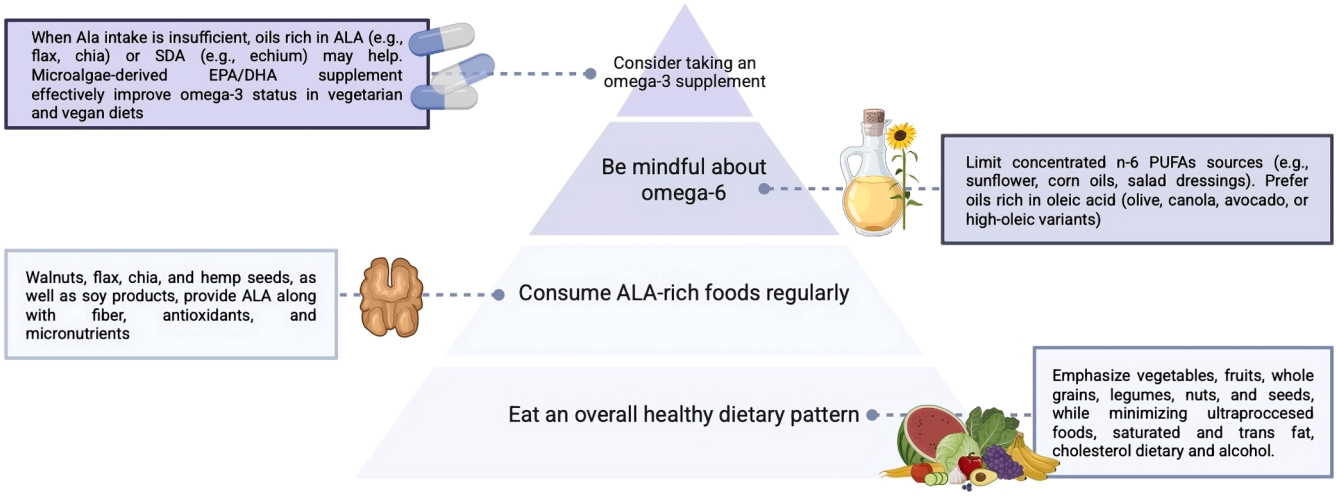


Fig. 2. Recommendations for optimizing n-3 PUFAs status in individuals following vegetarian and vegan diets.

12.5. Microalgae-derived DHA and EPA supplements

For direct increases in DHA and EPA status and to improve the O3I, microalgae-based supplements are a reliable source of preformed long-chain n–3 PUFAs [101,102]. These supplements are particularly recommended for:

- Vegetarians and vegans with low baseline O3I (<4%).
- Pregnant and lactating women.
- Individuals for whom optimization of DHA and EPA status may be clinically relevant.

13. Future research directions

Despite growing evidence regarding n-3 PUFA metabolism in plant-based diets, several important questions remain unresolved. Current evidence is largely derived from observational studies, mechanistic data, and surrogate biomarkers, and should not be interpreted as definitive evidence regarding long-term clinical EPA/DHA requirements in vegetarian and vegan populations. Long-term prospective studies and well-controlled intervention trials are needed to determine the optimal EPA and DHA requirements in vegetarian and vegan populations. Future research should also evaluate the role of genetic variability, adaptive metabolic mechanisms, and the clinical relevance of different n-3 PUFAs biomarkers, including whether increasing O3I values above current levels provides additional cardiometabolic or neurological benefits in plant-based populations.

14. Conclusions

Adequate intake of ALA-rich foods, together with potential physiological adaptations, may contribute to maintaining physiologically relevant n-3 PUFA status in vegetarian and vegan populations. Despite generally lower O3I values and lower intake of preformed long-chain n-3 PUFAs, vegetarian and vegan dietary patterns are consistently associated with favorable cardiovascular outcomes at the population level. An overall healthy dietary pattern and replacing concentrated sources of n-6 PUFAs with foods high in oleic acid, such as avocado, olive and canola oils, may improve the bioconversion pathway of ALA to EPA and DHA. When intake or conversion of ALA to EPA and DHA is insufficient, microalgae-derived EPA/DHA supplementation can optimize n–3 PUFA status. Future research should assess whether higher n–3 PUFA biomarker levels confer additional health benefits in populations following plant-based diets.

Human and animal rights and informed consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

CRediT authorship contribution statement

Ariel Kraselnik: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Miguel López-Moreno:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

ML-M reported receiving consulting fees from Danone and Foods for Tomorrow outside the submitted work. AK declares no competing interests.

Data availability

No datasets were generated or analyzed during the current study.

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