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Omega - 3 Acid and Their impact in Health, review of Existing Knowledge

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Abstract

Introduction and objective

Omega-3 fatty acids are associated with a range of beneficial physiological properties, such as anti-inflammatory, lipid-lowering, antiarrhythmic, and antithrombotic effects. The potential health benefits have been the subject of ongoing research. Particularly concerning cardiovascular health, inflammation, diabetes, and obesity. This summary synthesizes the current state of knowledge regarding these effects.

Review methods

A literature review was performed using the PubMed database to assess the effects of omega-3 fatty acids. The primary search term used was "omega-3 fatty acids," and the review focused on the most recent scientific studies examining their impact on the body.

Description of the state of knowledge

Omega-3 fatty acids are essential nutrients crucial for various bodily functions, particularly in cardiovascular and neurological health. The three main types of omega-3s relevant to human health are alpha-linolenic acid (ALA), eicosapentaenoic acid(EPA), and docosahexaenoic acid (DHA). While ALA is primarily found in plant sources, EPA and DHA are predominantly sourced from marine life.

Conclusions

The analysis of the review article demonstrates that omega-3 fatty acids present promising benefits. Omega-3s significantly reduce triglyceride levels, they help lower blood pressure by promoting vasodilation and reducing vascular resistance, they are essential for maintaining eye health and may help prevent age-related macular degeneration.

KEYWORDS

Omega-3 fatty acids, obesity, diabetes, dietary suplements, Cardiovascular disease, bowel disease

Introduction and purpose

With the advent of the Industrial Revolution, dietary habits underwent significant changes, leading to an imbalance in the intake ratios of omega-6 and omega-3 fatty acids. This shift resulted in a decreased consumption of omega-3 fatty acids, which became less prevalent in the diet. Blasbalg et al. [1] provide a detailed analysis of this change in the intake of polyunsaturated fatty acids from 1909 to 1999. During this period, the proportion of omega-6 polyunsaturated fatty acids increased significantly, from 2.79% to 7.21% ($p < 0.000001$), while omega-3 polyunsaturated fatty acids rose modestly from 0.39% to 0.72% . Additionally, a notable decline in the omega-3 index (a direct measure of EPA + DHA in erythrocytes as a percentage of total fatty acids) was observed, dropping from 8.28% in 1909 to 3.84% in 1999. This trend highlights the long-term reduction in omega-3 intake.The imbalance created by this shift—where omega-6 fatty acids are consumed in much higher ratios compared to omega-3s—has been linked to various health issues. The typical modern diet may have an omega-6 to omega-3 ratio as high as 20:1 or even 30:1, compared to a historical ratio closer to 1:1 [2]. This imbalance is associated with increased risks for cardiovascular diseases, inflammatory disorders, and other chronic health issues
Recent publications highlight the importance of consuming omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), their are essential components of human diet. Over the years, studies have demonstrated their role in modulating immune and inflammatory responses, they are characterized by antiarrhythmic, antithrombotic, and anti-atherosclerotic effects.

This review aims to present the latest evidence regarding the impact of omega-3 fatty acids on diseases such as inflammatory bowel diseases [3], cardiovascular conditions[4], depression[5], and diabetes[3]. Additionally, it seeks to provide up-to-date information on the supplementation of these fatty acids, including their use in vegetarian and vegan diets.

Description of the State of knowledge

Polyunsaturated fatty acids, including omega-3 fatty acids, exert a significant influence on cellular processes at the molecular level. Specifically, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) incorporate into cellular membranes, replacing saturated fatty acids and omega-6 polyunsaturated fatty acids, thereby altering membrane properties [6]. An increased ratio of omega-3 to omega-6 fatty acids contributes to a reduction in pro-inflammatory factors within the cell, as omega-6 fatty acids serve as precursors for these mediators. Additionally, the presence of omega-3 fatty acids in cell membranes enhances membrane fluidity, which is critical for the proper functioning of cells, particularly in the nervous system. Studies on platelets [7] have demonstrated that pro-inflammatory factors exhibit proaggregatory and prothrombotic properties. However, omega-3 fatty acids, through mechanisms that inhibit the development of inflammatory responses, reduce excessive blood clotting. These effects may be mediated by a reduction in fibrinogen levels, highlighting the potential therapeutic role of omega-3 fatty acids in modulating coagulation and inflammation.

In the study by Ścińska et al. [8], key findings regarding the effects of omega-3 fatty acids on human health were presented, including their roles in gene expression regulation, anti-inflammatory, antithrombotic, antiarrhythmic, and anti-atherosclerotic actions, as well as in reducing triglyceride levels, improving blood lipid profiles, and decreasing the production of pro-inflammatory mediators. Furthermore, several publications [9][10], have demonstrated the antidepressant effects of omega-3 fatty acids, as they are involved in the synthesis of dopamine and serotonin. Omega-3s have also been found to be beneficial in the treatment of acne and even in the management of dry eye syndrome [10][11].

Material and methods

A comprehensive literature review was conducted utilizing the PubMed database to evaluate the effects of omega-3 fatty acids on human health. The primary search term employed was "omega-3 fatty acids," and the review specifically targeted the most recent peer-reviewed studies. The aim was to analyze current scientific evidence regarding the physiological impacts of omega-3 fatty acids, with a particular focus on their role in various health outcomes, including cardiovascular, metabolic, eyes and inflammatory diseases.

Results

Fatty acids consist of a hydrocarbon chain with a methyl group at one end and a carboxyl group at the other. Fatty acids are classified into three categories: saturated, unsaturated, and polyunsaturated, based on the number of bonds between carbon atoms. Saturated fatty acids contain only single bonds, whereas unsaturated fatty acids have one or more double bonds.

In dietary recommendations, essential fatty acids (EFAs) play a critical role. These include omega-3 and omega-6 fatty acids, which are polyunsaturated. Although omega-3 and omega-6 fatty acids share similar structural characteristics, they differ in the position of the first double bond relative to the methyl group. Omega-3 fatty acids have this double bond at the third carbon atom, while omega-6 fatty acids have it at the sixth carbon atom [12].

Omega-3 Fatty Acids

- Alpha-linolenic acid (ALA)

- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA)

Omega-6 Fatty Acids

- Linoleic acid (LA)
- Arachidonic acid (AA)

Due to the lack of an appropriate enzymatic system, the human body is unable to synthesize essential fatty acids (EFAs) de novo, which is why these fatty acids must be obtained from external sources (exogenously). However, the human body is capable of modifying these fatty acids using specific enzymes, such as desaturases and elongases. Desaturases are responsible for introducing double bonds into the carbon chains, while elongases extend these chains by two carbon atoms [13].

Among omega-3 fatty acids, alpha-linolenic acid (ALA) is the only one that is considered fully essential in the human diet. The human body can convert ALA into eicosapentaenoic acid (EPA) and, to a lesser extent, into docosahexaenoic acid (DHA). However, this conversion process is limited, and the body's ability to synthesize sufficient EPA and DHA from ALA is insufficient to meet all physiological needs. Therefore, direct dietary intake of EPA and DHA is crucial for optimal health, as these omega-3 fatty acids are essential for the proper functioning of various biological systems.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the most well-known and biologically significant omega-3 fatty acids. These essential fatty acids (EFAs) are primarily derived from marine sources[13], particularly fatty fish such as salmon, mackerel, and sardines, which are rich in EPA and DHA. In contrast, alpha-linolenic acid (ALA), the shortest-chain omega-3 fatty acid, is predominantly found in plant-based sources, with the richest dietary sources being walnuts, flaxseeds, and chia seeds.

Vegetarians and vegans are particularly at risk for deficiencies in essential omega-3 fatty acids, specifically EPA and DHA. In marine ecosystems, these fatty acids are primarily sourced from algae and phytoplankton, which has spurred the development of plant-based supplements in recent years. Although marine plants contain only minimal amounts of fat and are insufficient to fully meet the human body's omega-3 requirements, they have become the foundation for supplements that provide concentrated sources of DHA and EPA.

It is important to note that there are various types of vegan omega-3 supplements, which differ in their content of DHA and EPA. In their study, Gordan MM et al. [14] compared 12 omega-3 supplements, seven derived from land-based plants and five from algae, analyzing their fatty acid profiles. EPA and DHA were abundantly present in the algae-based supplements ((23.1 + 36.3)%; (3.3 + 72.2)%; 45.6% and 46.1% DHA in the microalgae *Schizochytrium* sp.), but were absent in the land-based plant supplements. Conversely, alpha-linolenic acid (ALA) was found exclusively in the plant-based supplements. The study demonstrated that, given the limited ability of the human body to convert ALA into EPA and DHA, algae-based supplements are a superior choice for vegans and vegetarians.

Obesity

Obesity is a chronic condition characterized by the excessive accumulation of body fat resulting from a prolonged imbalance between energy intake and expenditure. Multiple factors contribute to the development of obesity, some of which are modifiable, such as physical inactivity and excessive caloric consumption, while others, including genetic predisposition, are non-modifiable [15]. The primary diagnostic tool for obesity is the body mass index (BMI), with a BMI greater than 30 kg/m^2 being indicative of obesity.

Over the past three decades, the proportion of total fat and saturated fat intake relative to total caloric intake has steadily declined in Western diets, while omega-6 fatty acid consumption has risen and omega-3 fatty acid intake has decreased. This dietary shift has led to a substantial increase in the omega-6/omega-3 ratio, which has risen from 1:1 in evolutionary times to 20:1 or higher in contemporary diets. This alteration in fatty acid composition coincides with a significant rise in the prevalence of overweight and obesity. [16] Numerous studies have suggested that omega-6 and omega-3 fatty acids exert opposing effects on body fat accumulation through various mechanisms, including adipogenesis, browning of adipose tissue, lipid homeostasis, the brain-gut-adipose tissue axis, and, crucially, systemic inflammation. Prospective studies have consistently shown that as the levels of omega-6 fatty acids and the omega-6/omega-3 ratio in red blood cell (RBC) membrane phospholipids increase, the risk of obesity also rises. In contrast, higher omega-3 content in RBC membrane phospholipids is associated with a reduced risk of obesity. [17]

Y.Y. Zhang et al. [18] conducted the first meta-analysis on omega-3 supplementation in overweight and obesity. The analysis demonstrated, among other findings, that omega-3 fatty acids can effectively reduce waist circumference and triglyceride level in obese adults. This meta-analysis included 11 randomized controlled trials (RCTs) with a total of 617 participants. The analysis of nine studies revealed no statistically significant difference in weight loss between omega-3 polyunsaturated fatty acids (n-3 PUFA) and placebo ($p = 0.99$; weighted mean difference [WMD] = 0.00; 95% confidence interval [CI] −0.42 to 0.43). However, n-3 PUFA demonstrated superior efficacy compared to placebo in reducing serum triglyceride levels ($p = 0.0007$; standardized mean difference [Std MD] = −0.59; 95% CI −0.93 to −0.25). A separate analysis of seven studies showed a significant reduction in waist circumference ($p = 0.005$; WMD = −0.53; 95% CI −0.90 to −0.16). No significant differences were observed in body mass index (BMI), total serum cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, or fasting glucose levels.

T. Burrows et al. [19] investigated the correlation between omega-3 fatty acid levels in erythrocytes, body weight, and insulin resistance in children. Their found out that obese children had altered erythrocyte fatty acid profiles, which were not associated with reported dietary intake. A higher proportion of obese children (BMI z-score ≥ 2.25) (33%) had an omega-3 index < 4.0 (indicating high risk) compared to their non-obese counterparts (BMI z-score ≤ 2.25) (17%). Conversely, fewer obese children (13%) had a higher omega-3 index (6.0–8.0, indicating lower risk) compared to non-obese children (25%). Additionally, a moderate, yet statistically significant, correlation was observed between the omega-3 index (O3I) and fasting insulin levels ($r = -0.3$, $P = 0.03$), as well as with homeostatic model assessment (HOMA) scores ($r = -0.3$, $P = 0.04$), suggesting a potential link between omega-3 levels and insulin resistance in children.

Havva Banu Salman et al. [20] conducted a study aimed at investigating the effect of omega-3 polyunsaturated fatty acid (PUFA) supplementation on weight loss and cognitive function in overweight or obese adults undergoing a weight loss diet. The study involved 40 adult volunteers aged 30-60 years, with a body mass index (BMI) ranging from 27.0 to 35.0 kg/m². Participants were randomly assigned to one of two groups. All subjects followed a weight loss diet program. The omega-3 supplementation group ($n = 20$) received a daily dose of 1020 mg of omega-3 PUFAs (580 mg eicosapentaenoic acid [EPA], 390 mg docosahexaenoic acid [DHA], and 50 mg of other omega-3 PUFAs) for 12 weeks. Anthropometric measurements and body composition analyses were conducted at baseline, and again at weeks 4, 8, and 12. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) at baseline and after 12 weeks. Significant reductions in weight, waist circumference, and BMI were observed in both groups. Abdominal fat mass and percentage decreased more significantly in the omega-3 group compared to the control group ($p \leq 0.05$). Although MoCA scores increased in both groups over time, there was no significant difference between the groups. The conclusion of the studies was that Omega-3 PUFA supplementation enhanced the reduction in abdominal fat mass and percentage in overweight or obese individuals following a weight loss diet.

Diabetes

Diabetes mellitus is a long-term disorder marked by elevated blood glucose (hyperglycemia) and increased glycated hemoglobin (HbA1c) levels. The primary goals of diabetes management are to maintain blood glucose within a healthy range and to reduce HbA1c levels. Inadequate control of diabetes can result in numerous complications, including cardiovascular disease, neuropathy, retinopathy, and nephropathy.

One of the primary advantages of omega-3 fatty acids (v-3 FAs) in individuals with type 2 diabetes mellitus is their ability to improve the highly atherogenic lipid profile typically observed in this population [21]. Omega-3 fatty acids have been shown to reduce levels of triglycerides and increase high-density lipoprotein (HDL) cholesterol, both of which contribute to a lower cardiovascular risk. In addition to their beneficial effects on lipid metabolism, omega-3s may also enhance insulin sensitivity [22]. However, the evidence on their role in reducing insulin resistance remains mixed. While some studies have failed to demonstrate significant improvements in insulin resistance following omega-3 supplementation, other research has reported positive effects in treatment groups, suggesting that the clinical outcomes may depend on factors such as dosage, duration of treatment, and patient characteristics.

In a comprehensive analysis by Trace J. Brown et al. [23], several randomized controlled trials (RCTs) with a minimum duration of 24 weeks were conducted to assess the effects of increasing intake of α-linolenic acid, long-chain omega-3 fatty acids, omega-6 fatty acids, or total polyunsaturated fatty acids (PUFAs) in individuals at risk for or diagnosed with type 2 diabetes mellitus. These studies evaluated key metabolic parameters, including diabetes diagnosis, fasting glucose, insulin levels, glycated hemoglobin (HbA1c), and the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). The findings from these trials suggest that increasing the consumption of omega-3s, omega-6s, or total PUFAs has little to no significant impact on the prevention or management of type 2 diabetes. While some studies have indicated minor improvements in certain metabolic markers, the overall evidence does not support substantial therapeutic benefits of these fatty acids in altering disease outcomes or improving insulin resistance in patients with type 2 diabetes.

The ASCEND Study Collaborative Group et al. [24] reached similar conclussion. They conducted a large-scale, randomized trial to assess the effects of omega-3 fatty acid supplementation on vascular outcomes in patients with diabetes but without evidence of established atherosclerotic cardiovascular disease. A total of 15,480 participants were randomly assigned to receive either 1-gram capsules of omega-3 fatty acids (fatty acid group) or a matching placebo (olive oil) daily. Over a median follow-up period of 7.4 years, with an adherence rate of 76%, the study found no significant difference in the incidence of serious vascular events between the two groups. Specifically, 689 patients (8.9%) in the omega-3 group experienced a serious vascular event, compared to 712 patients (9.2%) in the placebo group (rate ratio 0.97; 95% confidence interval [CI], 0.87 to 1.08; P = 0.55). Furthermore, the composite outcome of serious vascular events or revascularization was similar between the two groups, with 882 (11.4%) of patients in the omega-3 group and 887 (11.5%) in the placebo group experiencing this outcome (rate ratio 1.00; 95% CI, 0.91 to 1.09). Mortality from any cause also did not differ significantly, with 752 (9.7%) deaths in the omega-3 group and 788 (10.2%) deaths in the placebo group (rate ratio 0.95; 95% CI, 0.86 to 1.05). Additionally, there were no significant between-group differences in the rates of nonfatal serious adverse events. The findings of this large, well-conducted trial suggest that omega-3 fatty acid supplementation does not significantly reduce the risk of serious vascular events in patients with diabetes who do not have pre-existing cardiovascular disease. Despite the potential cardiovascular benefits of omega-3s observed in other populations, this study provides important evidence that their role in primary prevention of cardiovascular events in diabetes patients without established atherosclerotic disease may be limited.

In a study conducted by Rehab H. Werida et al. [25], the effects of coadministration of omega-3 fatty acids with glimepiride on glycemic control, lipid profile, irisin, and sirtuin-1 were investigated in patients with type 2 diabetes mellitus. The study found that, compared to the control group, supplementation with omega-3 fatty acids led to significant improvements across several metabolic markers. Specifically, after three months of intervention, omega-3 supplementation resulted in a marked reduction in serum fasting blood glucose (FBG) levels ($p < 0.001$), glycated hemoglobin (HbA1c) percentage ($p < 0.001$), total cholesterol (TC) ($p < 0.001$), triglycerides (TGs) ($p = 0.006$), low-density lipoprotein (LDL) cholesterol ($p = 0.089$), and the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) ($p = 0.021$). Additionally, significant increases were observed in serum levels of irisin ($p = 0.026$) and high-density lipoprotein (HDL) cholesterol ($p = 0.007$) in the omega-3 group compared to the control group. The atherogenic index of plasma (AIP), a key marker of cardiovascular risk, decreased significantly in the omega-3 group, whereas it increased in the control group, with the differences between the two groups reaching statistical significance ($p < 0.001$). These findings suggest that supplementation with omega-3 fatty acids, when used in conjunction with glimepiride, may offer substantial benefits for patients with type 2 diabetes mellitus. Not only does it enhance glycemic control and improve lipid profiles, but it also appears to increase serum irisin levels, which may have additional metabolic and cardiovascular benefits.

Cardiovascular disease

Cardiovascular diseases (CVDs) are responsible for approximately 80% of deaths in middle- and low-income countries, and the World Health Organization (WHO) forecasts a continued increase in the burden of these diseases [26]. Enhanced consumption of omega-3 fatty acids may play a role in counteracting this rising trend. Omega-3s are recognized for their antiarrhythmic, antithrombotic, and anti-atherogenic effects [27]. In addition, they improve endothelial function, lower triglyceride levels, and help reduce blood pressure. Multiple epidemiological studies, focused on both primary and secondary prevention, have demonstrated that diets rich in fatty fish, fish oils, or supplements with an optimal omega-6 to omega-3 ratio can effectively lower the incidence of coronary heart disease (CHD) and reduce cardiovascular mortality.

In 2017, Maki et al. [28] published a study evaluating the impact of supplemental long-chain omega-3 fatty acids (LC-OM3) on the risk of cardiac death. The analysis included data from 14 randomized controlled trials (RCTs) involving 71,899 participants. Among those receiving LC-OM3, 1,613 cardiac deaths were reported (4.48% of participants), compared to 1,746 cardiac deaths (4.87%) in the control groups. The pooled relative risk estimate indicated an 8.0% reduction in the risk of cardiac death in the LC-OM3 groups (95% CI: 1.6%, 13.9%, $P = 0.015$). Further subgroup analyses revealed a more pronounced reduction in risk (ranging from 12.9% to 29.1%) in specific groups, including those receiving higher doses of eicosapentaenoic acid and docosahexaenoic acid (>1 g/day), as well as in individuals at higher cardiovascular risk (secondary prevention, baseline triglycerides ≥150 mg/dL, LDL-C ≥130 mg/dL, and statin use in <40% of participants). The heterogeneity of the results was low ($I^2 \leq 15.5\%$, $P > 0.05$) in both the primary and subgroup analyses. Overall, LC-OM3 supplementation was associated with a modest but statistically significant reduction in the risk of cardiac death.

In 2019, Yang Hu et al. [29] conducted an updated meta-analysis of 13 randomized controlled trials examining the effects of marine omega-3 supplementation on cardiovascular disease outcomes. The primary outcomes included myocardial infarction, coronary heart disease (CHD) death, total CHD events, total stroke, cardiovascular disease (CVD) death, total CVD events, and major vascular events. Rate ratios were calculated using a fixed-effect meta-analysis, and a meta-regression was performed to explore the dose-response relationship between marine omega-3 dosage and the risk of each outcome. Over a mean treatment duration of 5.0 years, the study documented 3,838 myocardial infarctions, 3,008 CHD-related deaths, 8,435 total CHD events, 2,683 strokes, 5,017 CVD-related deaths, 15,759 total CVD events, and 16,478 major vascular events. In an analysis excluding the REDUCE-IT trial (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial), marine omega-3 supplementation was associated with a significant reduction in the risk of myocardial infarction. When including REDUCE-IT in the analysis, inverse associations for all outcomes were strengthened, although this introduced statistically significant heterogeneity. A significant linear dose-response relationship was observed for total CVD and major vascular events in both the analyses with and without REDUCE-IT. In conclusion, marine omega-3 supplementation was found to reduce the risk of myocardial infarction, CHD death, total CHD, CVD death, and total CVD, even when excluding the REDUCE-IT trial. The risk reductions appeared to follow a linear relationship with the omega-3 dose.

In 2020, Asmaa S. Abdelhamid et al. [30] published a comprehensive systematic review assessing the effects of omega-3 fatty acids on cardiovascular health. This analysis included randomized controlled trials (RCTs) that lasted at least 12 months, comparing omega-3 supplementation or advice to increase omega-3 or ALA intake with usual or lower intake. Most trials focused on supplementation with long-chain omega-3 (LCn3) via capsules, although some utilized LCn3- or ALA-enriched foods or dietary advice. The doses of LCn3 ranged from 0.5 g/day to over 5 g/day, with 19 trials administering at least 3 g of LCn3 daily. Meta-analysis and sensitivity analyses revealed little to no effect of increasing LCn3 intake on various outcomes. For all-cause mortality, the risk ratio (RR) was 0.97 (95% CI: 0.93–1.01) based on data from 143,693 participants and 11,297 deaths across 45 RCTs (high-certainty evidence). Similarly, LCn3 had no significant effect on cardiovascular mortality (RR 0.92; 95% CI: 0.86–0.99; 117,837 participants; 5,658 deaths in 29 RCTs, moderate-certainty evidence), cardiovascular events (RR 0.96; 95% CI: 0.92–1.01; 140,482 participants; 17,619 events in 43 RCTs, high-certainty evidence), stroke (RR 1.02; 95% CI: 0.94–1.12; 138,888 participants; 2,850 strokes in 31 RCTs, moderate-certainty evidence), or arrhythmia (RR 0.99; 95% CI: 0.92–1.06; 77,990 participants; 4,586 events in 30 RCTs, low-certainty evidence). However, they found out that LCn3 supplementation may slightly reduce the risk of coronary heart disease (CHD) mortality (RR 0.90; 95% CI: 0.81–1.00; NNTB = 334) and CHD events (RR 0.91; 95% CI: 0.85–0.97; NNTB = 167), both with low-certainty evidence. No significant effects were found for serious adverse events, adiposity, lipids, or blood pressure. However, increasing LCn3 intake was associated with a 15% reduction in triglyceride levels in a dose-dependent manner (high-certainty evidence).

In 2024, Jie Yan et al. [31] published a comprehensive meta-analysis examining the efficacy and safety of omega-3 fatty acids in preventing cardiovascular disease. The analysis demonstrated that omega-3 supplementation was associated with a reduced incidence of major cardiovascular events (risk ratio [RR] 0.95; 95% CI: 0.91–0.99; P = 0.026), myocardial infarction (RR 0.90; 95% CI: 0.83–0.98; P = 0.021), and cardiovascular death (RR 0.94; 95% CI: 0.88–0.99; P = 0.028) compared to control groups. However, an increased risk of atrial fibrillation was noted in the omega-3 group (RR 1.25; 95% CI: 1.10–1.41; P < 0.001). No significant differences were observed between groups regarding heart failure, stroke, or all-cause mortality. Subgroup analysis revealed that the cardiovascular benefits of omega-3 fatty acids were primarily driven by the use of EPA ethyl ester. The authors concluded that omega-3 fatty acids may reduce the risk of major cardiovascular events in individuals with cardiovascular disease or risk factors and may lower the risk of myocardial infarction in those without cardiovascular disease. However, they may increase the risk of stroke in patients with a history of myocardial infarction. Additionally, prescription omega-3 acid ethyl esters were found to have a favorable safety profile, while EPA ethyl ester was associated with a higher risk of bleeding.

Eye disease

Recent evidence has highlighted the beneficial role of omega-3 fatty acids (FAs) in the prevention and management of several ocular conditions, particularly age-related macular degeneration (AMD) [32] [33], retinitis pigmentosa [34], and dry eye syndrome [35]. Omega-3 FAs, primarily derived from fish oil and certain plant sources, are known for their anti-inflammatory properties and potential to improve retinal health.

A meta-analysis of pooled data from nine studies [36] found a significant association between high dietary intake of omega-3 FAs and a 38% reduction in the risk of late-stage AMD. AMD is a leading cause of vision loss in older adults, and this finding underscores the potential of omega-3s as a preventive measure against its progression. Omega-3s, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are thought to exert their protective effects through their anti-inflammatory mechanisms, which may reduce the risk of macular degeneration by modulating the retinal immune response and reducing oxidative stress in the macula. Furthermore, fish consumption—which is a key source of omega-3 FAs—has been linked to a reduced risk of both early- and late-stage AMD. Studies have shown that individuals who consume fish at least twice a week have a lower likelihood of developing early AMD (pooled odds ratio [OR] 0.76) and a more pronounced reduction in the risk of late-stage AMD (pooled OR 0.67). This suggests that regular fish consumption can play an important role in maintaining retinal health and preventing the onset of vision-threatening AMD.

In addition to these conditions, dry eye syndrome, a common disorder characterized by discomfort, dryness, and inflammation of the eye, has also been linked to omega-3 FA intake. Omega-3 fatty acids may alleviate dry eye symptoms through several mechanism as reduction of inflamations, improvement of tea film quality - omega-3s enhance lubrication and reduce irritation, increased tear production. A systematic review and meta-analysis involving 17 randomized clinical trials the authorship of Giuseppe Giannaccare et. al. [37] found that omega-3 FA supplementation significantly improved dry eye symptoms and signs compared to placebo. The results showed a notable decrease in symptoms, an increase in tear break-up time and improved Schirmer test scores, indicating enhanced tear production.

Bowel Disease

In recent decades, there has been a noticeable rise in the prevalence of inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease. This increase has paralleled significant changes in dietary patterns, particularly a shift toward higher consumption of processed foods, refined carbohydrates, and vegetable oils rich in omega-6 fatty acids. As a result, there has been a notable imbalance in the intake of essential fatty acids, with a marked increase in omega-6 fatty acids relative to omega-3 fatty acids.

Omega-6 and omega-3 fatty acids are essential for maintaining cellular structure and function, but their roles in inflammation are different [38]. While omega-6 fatty acids, particularly arachidonic acid, can promote the production of pro-inflammatory mediators, omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are known for their anti-inflammatory properties. The shift toward a higher omega-6 to omega-3 ratio is thought to contribute to the development and exacerbation of inflammatory conditions like IBD.

The omega-3 to omega-6 ratio plays a crucial role in modulating immune responses. Inflammatory bowel diseases, including UC and Crohn's disease, are driven by an overactive immune response, leading to excessive production of pro-inflammatory cytokines and other inflammatory mediators. These imbalances, fueled by the overconsumption of omega-6 fatty acids, may exacerbate the inflammatory processes in the gastrointestinal tract. Increasing the intake of omega-3 fatty acids, particularly EPA and DHA, has been proposed as a therapeutic approach to correct this imbalance and reduce the inflammatory burden in IBD.Currently, the incidence of ulcerative colitis (UC) and Crohn's disease is on the rise, particularly in Western countries, where the dietary patterns have shifted dramatically over the past century. The prevalence of these diseases is now reaching concerning levels, with reports indicating an increasing trend in cases, particularly in industrialized nations.

The Industrial Revolution marked a significant change in global food systems, leading to a reduction in the intake of omega-3 fatty acids and an increase in omega-6-rich oils[39]. This dietary shift has been linked to an imbalance in the ratio of omega-6 to omega-3 fatty acids in the typical Western diet, which has contributed to rising rates of inflammatory conditions, including IBD. According to studies by Blasbalg et al. [40], the proportion of omega-6 polyunsaturated fatty acids in the diet rose significantly between 1909 and 1999, from 2.79% to 7.21%, while the intake of omega-3 fatty acids increased more modestly from 0.39% to 0.72%. This dramatic shift has had profound implications for immune function and inflammation, particularly in the context of chronic diseases like IBD. Furthermore, the omega-3 index, which measures the amount of EPA and DHA in erythrocytes as a percentage of total fatty acids, has decreased over the past century, dropping from 8.28% in 1909 to 3.84% in 1999. This decline is thought to reflect a decrease in the dietary intake of omega-3s, further contributing to the inflammatory milieu that characterizes many modern diseases, including IBD.

A critical review of the literature highlights several studies that have explored the relationship between the intake of polyunsaturated fatty acids and the risk of IBD. One notable study by bid in EPIC Study Investigators et al. [41] used dietary questionnaires to assess the dietary intake of over 200,000 participants in the EPIC cohort (European Prospective Investigation into Cancer and Nutrition). This large-scale prospective study tracked participants for the development of UC over a follow-up period of 4 years. The findings from this study revealed that a high intake of omega-6 fatty acids (specifically linoleic acid, or LA) was strongly associated with an increased risk of developing UC, with an odds ratio (OR) of 2.49 (95% CI: 1.23–5.07; $p = 0.01$). This suggests that excessive omega-6 consumption may contribute significantly to the development of UC. On the other hand, higher intake of omega-3 fatty acids (particularly DHA) was linked to a reduced risk of UC, with the highest quartile of omega-3 intake showing an OR of 0.23 (95% CI: 0.06–0.97), indicating a protective effect against the disease.

These findings underscore the potential of dietary intervention with omega-3 fatty acids as a means of modulating disease risk in individuals predisposed to UC. In addition to the EPIC study, a broader literature review by Hou et al. [42] assessed the relationship between diet and the risk of IBD. Among the 19 studies included in the review, high intake of total fat, omega-6 polyunsaturated fatty acids, and meat was consistently linked to an increased risk of ulcerative colitis (UC). Moreover, the consumption of omega-6 fatty acids, saturated fats, and meat was associated with an increased risk of Crohn's disease (CD), further supporting the idea that dietary fats play a significant role in the development of IBD. Interestingly, despite the potential benefits of omega-3 fatty acids in reducing inflammation, the review found no conclusive evidence supporting the protective effect of a diet high in omega-3 fatty acids against UC or CD.

Conclusions

The beneficial effects of omega-3s are attributed to several mechanisms: triglyceride reduction - omega-3s effectively lower triglyceride levels, which are a known risk factor for cardiovascular disease; anti-inflammatory properties: omega-3s exert anti-inflammatory effects that may help mitigate the progression of atherosclerosis; antithrombotic effects: they may also reduce platelet aggregation, thus lowering the risk of thrombosis. They modulate inflammatory pathways by altering eicosanoid production and reducing pro-inflammatory cytokines. This modulation can help alleviate conditions such as rheumatoid arthritis and inflammatory bowel disease. Research suggests that they can improve insulin sensitivity and lipid profiles in individuals with type 2 diabetes. Omega-3 supplementation has been associated with reductions in fasting blood glucose levels and improvements in glycemic control. In the context of obesity, omega-3 fatty acids may contribute to weight management and metabolic health. They have been shown to influence fat metabolism and reduce body fat accumulation. Moreover, omega-3s may aid in improving metabolic parameters such as insulin resistance and lipid profiles among obese individuals.They are essential for maintaining eye health and may help prevent age-related macular degeneration. However, while there is substantial evidence supporting their efficacy, inconsistencies in study outcomes warrant further investigation to clarify their roles and optimize their therapeutic use.

Author's contribution Statement

Conceptualization, Zuzanna Kukla, Maciej Gołębski; methodology, Wojciech Nowak; software, Jagoda Mikołajczyk; Stella Mieruszyńska; check, Paulina Krzemińska and Mirosław Sawicki; formal analysis Izabela Sadowska; investigation, Jakub Włosiański and Sebastian Musialik; resources, Zuzanna Kukla; data curation Sebastian Musialik, Stella Mieruszyńska and Maciej Gołębski; writing - rough preparation, Zuzanna Kukla; writing - review and editing, Zuzanna Kukla and Wojciech Nowak; visualization, Jagoda Mikołajczyk, Izabela Sadowska; supervision, Zuzanna Kukla; project administration Paulina Krzemińska

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