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# OMEGA-3 FATTY ACIDS: CAPSULES OR OIL? COMPARISON OF STABILITY, BIOAVAILABILITY AND EFFECTIVENESS OF EPA AND DHA SUPPLEMENTATION

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**ABSTRACT**

Omega-3 fatty acids, primarily eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play a key role in human health, including protection of the cardiovascular system, support for neurological functions, and influence on anti-inflammatory processes. Despite the known importance of their consumption, the quality and form of supplementation (oil vs. capsules) are raising increasing doubts. One important aspect is the stability of these polyunsaturated fatty acids, as their susceptibility to oxidation may reduce their effectiveness or even lead to the formation of adverse products. In this context, the total oxidation index (TOTOX) is a commonly used marker for assessing the degree of oxidation of fish oils and omega-3 supplements. This article provides a comprehensive review of the scientific literature comparing oil and capsule forms of omega-3 supplements, taking into account criteria such as oxidative parameters (TOTOX, peroxide value, anisidine value), bioavailability, and user preferences. The results indicate that capsules often offer better protection against oxidation during storage (lower TOTOX values) compared to liquid forms. For example, syrup products achieved TOTOX values of ~97 meq/kg at the end of the study, while capsules achieved ~30 meq/kg under similar conditions. In addition, the bioavailability of EPA/DHA depended on the chemical form (triglycerides > ethyl esters) and the delivery system — emulsions or liquid forms showed faster absorption than traditional gel capsules.
Based on the data collected, it can be concluded that the choice of omega-3 supplement form should take into account not only the EPA/DHA content, but also the oxidative quality, chemical form, and storage method. For dietary practice, products with a low TOTOX index, adequately protected from light and oxygen, and taken with a meal containing fat to increase absorption are recommended.

**KEYWORDS**

Omega-3, EPA, DHA, TOTOX, Lipid Stability, Bioavailability, Supplementation

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## 1. Introduction

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play an important role in maintaining human health. With regard to the cardiovascular system, a recent meta-analysis involving 149,051 participants showed that omega-3 supplementation was associated with a reduction in cardiovascular mortality (RR 0.93 [0.88-0.98]) and the incidence of myocardial infarction (RR 0.87 [0.81-0.93]) and coronary heart disease (RR 0.91 [0.87-0.96]).

In addition, omega-3s are important for neurological function—DHA is a major component of brain phospholipids and affects cell membrane fluidity and neuronal signaling.

In terms of immunology and anti-inflammation: polyunsaturated fatty acids (PUFAs) participate in the modulation of inflammatory pathways, including by influencing cytokine production and converting into eicosanoids with lower pro-inflammatory activity.

## 2. Dietary deficiencies

### 2.1 The extent of EPA and DHA deficiencies in populations

Despite the widely known health benefits of EPA and DHA, many populations do not achieve the recommended intake of these long-chain omega-3 fatty acids. Epidemiological data show a significant deficit, especially in countries where consumption of fatty fish is low or irregular.

#### 2.1.1. Low consumption of fish and EPA/DHA

A report on dietary recommendations for fish found that fish consumption in the US is very low—an average of about 9 g/day per person, only some of which comes from species rich in EPA and DHA.

A study conducted in the European population shows that in many European countries, the average EPA + DHA intake is less than 100 mg per day in young adults, which is well below the recommendations.

In a 2025 paper, the authors emphasize that despite guidelines (WHO, AHA), many people do not consume adequate amounts of EPA and DHA.

In addition, a survey of the adult population (Poland) shows that the frequency of sea fish consumption is low: the study Stoś, K et al. (2024) "Fish Consumption Frequency..." found that many people do not consume two servings of sea fish per week, which corresponds to approximately 250 mg of EPA + DHA per day.

According to data from the National Institutes of Health (NIH), epidemiological studies link low EPA and DHA intake to an increased risk of cardiovascular disease and metabolic disorders.

#### 2.1.2. Recommended intake vs. reality

Many experts recommend a daily intake of EPA + DHA in the range of 250–500 mg/day to maintain cardiovascular health.

However, as a report by nutrition journalists points out, despite these recommendations, actual intake is significantly lower in many populations, which may lead to chronic deficiency.

An epidemiological study conducted in Denmark (cohort) confirmed that higher EPA and DHA intake was associated with a lower risk of atherosclerotic cardiovascular disease (ASCVD).

### 2.2. Consequences of EPA and DHA deficiency — chronic diseases

EPA and DHA deficiency is not just a nutritional issue — it has real clinical implications. The epidemiological and clinical data linking deficiency to chronic diseases, including lipid disorders, inflammation, cognitive function, and cardiovascular risk, are discussed below.

#### 2.2.1. Lipid profile and triglycerides

EPA and DHA have well-documented triglyceride-lowering effects. In a review in JACC (Journal of the American College of Cardiology), author Mozaffarian showed that EPA + DHA supplementation lowers TG by approximately –5.9 mg/dL for every gram of EPA + DHA per day.

In cohort studies, low EPA and DHA intake is associated with a higher risk of lipid disorders and cardiovascular disease. An example is the aforementioned Danish cohort, in which a diet rich in EPA/DHA was associated with a lower incidence of atherosclerotic disease.

Furthermore, recent studies indicate a link between lower levels of long-chain n-3 PUFAs (EPA + DHA) in the blood and a higher risk of premature death. A meta-analysis of 17 cohorts (FORCE Consortium) showed that individuals in the highest quintiles of LC n-3 PUFA (including EPA + DHA) had a 15–18% lower risk of all-cause mortality compared to the lowest quintiles.

**2.2.2. Inflammation and cardiovascular risk**

One of the key mechanisms by which EPA and DHA deficiency affects health is the modulation of inflammatory processes. Lower levels of these acids may result in weaker anti-inflammatory mechanisms (fewer pro-resolving mediators) and increased levels of pro-inflammatory cytokines, which in turn promote chronic inflammation, a risk factor for many chronic diseases.

Epidemiological data from meta-analyses and cohort studies show correlations between lower omega-3 status and an increased risk of cardiovascular disease, which can be interpreted in part as an inflammatory effect of deficiency.

**2.2.3. Cognitive functions and neurological diseases**

EPA and DHA deficiency may also have consequences for cognitive function. A study of patients with coronary artery disease showed that low serum EPA concentrations were associated with poorer scores on the Mini-Mental State Examination (MMSE), regardless of cardiac parameters.

In a population of very elderly people (80+ years old), in the KOCOA study in Japan, EPA (but not DHA) concentrations correlated positively with cognitive function (MMSE) and verbal fluency.

In the context of Alzheimer's disease, a prospective analysis showed that a low omega-3 index (EPA + DHA in erythrocytes) was associated with greater beta-amyloid deposition and long-term memory impairment.

In patients with Alzheimer's disease, lower baseline DHA (but not EPA) predicted faster cognitive decline over 2 years in a cohort study.

A prospective meta-analysis (48 studies, over 100,000 participants) confirmed that higher EPA and DHA intake and higher blood levels are associated with a ~20% lower risk of dementia or cognitive decline.

In young healthy women, a cross-sectional study found that a low Omega-3 Index (low EPA + DHA) was associated with poorer performance on attention tasks.

**2.3. Summary and implications**

Most of the population, especially in Western countries, does not meet the recommended intake of EPA + DHA (250–500 mg/day), mainly due to low consumption of fatty fish.

Deficiency of these fatty acids is associated with a poorer lipid profile (higher triglycerides), increased inflammation and cardiovascular risk, as well as cognitive impairment and a higher risk of dementia.

Data come from cohort studies, biochemical studies (measurement of EPA/DHA in serum or erythrocytes), and prospective meta-analyses.

Due to widespread deficiency, EPA/DHA supplementation or increased consumption of marine fish may be justified as a preventive strategy. At the same time, it is necessary to conduct nutritional education and health policies promoting regular consumption of fatty fish or alternative sources (e.g., algae) of omega-3.

**3. Popularity of supplementation**

With low fish consumption and growing health awareness, omega-3 supplementation has become commonplace. Available forms include liquid fish oils, emulsions, gel capsules, and algae oils (for those who prefer vegan sources).

However, the quality of these products remains an issue. A study analyzing 44 fish supplements showed that the average TOTOX value was 23.8 meq/kg (range 17.4-30.3), meaning that a significant proportion of products exceeded the recommended limit of 26 meq/kg.

In addition, the study Ozyurt, G. et al. (2022) “Assessment of the safety of dietary fish oil supplements...” showed that the capsule group had a better content of declared EPA and DHA than the syrup group, and the PV values for syrups were significantly higher.

Globally, studies indicate that approximately 20% of the supplements analyzed exceeded the recommended PV and TOTOX levels.

**4. The issue of stability**

Lipid oxidation mechanisms involve the reaction of polyunsaturated fatty acids with oxygen, light, and high temperatures, leading to the formation of peroxides (PV – peroxide value), followed by aldehydes and ketones (AV – anisidine value).

In the context of omega-3 supplements, it is crucial to monitor the TOTOX (Total Oxidation Value) index, which is calculated as: TOTOX = 2 × PV + AV.

A low TOTOX level means better freshness, less oxidation, and higher product quality. A study analyzing 44 supplements found that 27.3% exceeded the recommended TOTOX level (<26).

The study Ozyurt, G. et al. (2022) "Assessment of the safety..." showed differences between forms: capsules had lower PV than syrups (1.97-2.89 meq/kg vs. 2.22-18.30 meq/kg), suggesting that the form of the preparation may affect stability.

The role of antioxidants (e.g., vitamin E, tocotrienols, plant extracts) in stabilizing omega-3 oils is also emphasized in the literature—they inhibit the chain of free radical reactions and help maintain the quality of fats.

**5. Purpose of the study**

The purpose of this article is to conduct a comprehensive comparison of the two main forms of omega-3 supplementation—liquid oil vs. capsules—in terms of their effectiveness, oxidative stability, and bioavailability.

The study aims to answer the following questions:

Does the form (capsule vs. oil) affect the degree of oxidation of the preparation and its quality?

What are the differences in EPA/DHA absorption between chemical forms (triglycerides vs. ethyl esters) and forms of administration?

What are the practical implications of these differences for supplement manufacturers, nutritionists, and consumers?

On this basis, the article presents practical conclusions regarding the selection of omega-3 supplements, including paying attention to the TOTOX index, the chemical form of fatty acids, and storage conditions.

**6. Results**

**6.1. Oxidative stability of omega-3 supplements**

**6.1.1. Comparison of TOTOX oils vs. capsules**

A review of 171 supplements from 49 brands found that approximately 50% exceeded at least one oxidation parameter (PV or p-AV) and 39% exceeded the TOTOX limit.

A market study from the UAE showed that of the 44 products analyzed: 40.9% exceeded PV (>5 meq $O_2$/kg), 6.8% exceeded p-AV (>20), and 27.3% exceeded TOTOX (>26) according to the standards of the Global Organization for EPA and DHA Omega 3s (GOED).

A study from New Zealand found that "most fish oil supplements available on the market exceeded the recommended oxidation levels."

Conclusions: Both capsules and liquid forms can have stability issues, but liquids (especially flavored ones) seem to exceed limits more often due to greater exposure to oxygen, light, and the possibility of faster degradation.

**6.1.2. Frequency of IFOS/GOED exceedances**

In a UAE study, compliance was generally good, but ~27% of products still exceeded TOTOX <26 meq/kg according to the GOED standard.

A US/Canadian study found significant variations in the quality of n-3 supplements, including their oxidative status.

Conclusions: Certification (e.g., International Fish Oil Standards – IFOS) may be an indicator of higher quality, but exceedances still occur.

**6.1.3. PV/p-AV differences between forms**

A New Zealand analysis found that higher p-AV and TOTOX were correlated with undeclared EPA+DHA content, suggesting that oxidation and acid loss affected the indicators in lower-quality products.

The analysis "Oxidative stability of fish oil dietary supplements..." by Suzan et al. (2022) states that TOTOX = 2×PV + AV.

Conclusions: form (capsule vs. bottle), presence of antioxidants, manufacturing and packaging processes may affect PV/p-AV — there is no clear data showing that capsules always have better values, but the trend is there.

**6.1.4. Impact of storage (time, temperature, light)**

The paper "Effect of packaging and encapsulation on the oxidative..." (Yenipazar 2023) shows that packaging, exposure to oxygen and light significantly affect PV/p-AV/TOTOX values.

The GOED guide "Oxidation in Omega-3 Oils: An Overview" (2015) states that prolonged storage in poor conditions (high temperature, light, metallic traces) accelerates oxidation.

Conclusions: even a high-quality supplement can degrade if stored improperly. A cool, dark place with minimal exposure to air is recommended.

**6.2. Impact of chemical form on bioavailability**

**6.2.1. TG (triglycerides) vs EE (ethyl esters) — comparison of bioavailability**

The review "Pharmacokinetics of Supplemental Omega-3 Fatty Acids" (Chevalier et al. 2021) states: "Single dose studies... reported that the most bioavailable form... is when provided in FFA > TG > EE."

The study "Steady-state bioavailability of prescription omega-3" (Offman et al. 2013) describes comparisons of TG vs EE forms in humans.

Conclusions: TG/rTG are more bioavailable than EE in many studies — with the same amount of EPA+DHA, a person can absorb more if the form is TG.

**6.2.2. Phospholipids (e.g., from krill) → higher bioavailability?**

Despite the currently limited number of available sources, one of them, the network meta-analysis "Comparison of Omega-3 PUFAs in fish oil and krill oil" (Hoang et al. 2024), suggests that krill (phospholipid form) may have higher bioavailability.

Conclusions: the phospholipid form may be beneficial, but there is less data available than for TG vs EE.

**6.2.3. Emulsions and liquid forms → faster absorption**

In a meta-analysis by Chevalier et al. (2021) states that emulsions and special forms improve absorption, although the specific quantitative data vary.

Conclusions: choosing an emulsion formula may be recommended if the goal is rapid and maximum absorption, but cost and stability must also be taken into account.

**6.3. The effect of meals and fat on absorption**

**6.3.1. The micellization effect**

A review by Alijani et al. (2025) entitled "Bioavailability of EPA and DHA in humans" indicates that the absorption of n-3 depends on the presence of fat in meals, which promotes the formation of micelles.

**6.3.2. The role of fat volume and type in meals**

A blog article ("Omega-3 forms explained...") NFO by Norwegian Fish Oil points out that with the EE form, fat intake in meals is crucial, as the hydrolysis process is less efficient if there is little fat.

Conclusions: taking an EPA/DHA supplement with a meal containing fat (e.g., ≥15 g of fat) increases absorption — especially important for EE forms.

**6.4. Effectiveness of supplementation in clinical trials**

**6.4.1. Effect on triglycerides**

Sources such as Wikipedia/EPA state that doses of 2–4 g/d of EPA+DHA lead to a reduction in TG of 20–35% or even more in cases of very high TG levels.

**6.4.2. Anti-inflammatory effects**

Chevalier et al. (2021) in a review of pharmacokinetics indicate that one of the effects after the inclusion of n-3 is the modulation of inflammation — although they note the heterogeneity of the results.

**6.4.3. Biomarkers (omega-3 index, EPA/DHA in erythrocytes)**

The article "Comparison of pharmacokinetics of omega-3 fatty acid..." (Chevalier et al., 2021) mentions that an omega-3 index ≥8% is associated with a lower cardiovascular risk than ≤4%.

**6.4.4. Differences between supplements and fish consumption**

In the same study, Chevalier et al. (2021) indicate that a diet rich in fatty fish and/or n-3 supplementation may be beneficial, but the conditions of intervention studies with supplements are more diverse than epidemiological data.

Conclusions: EPA/DHA supplementation has proven efficacy in lowering triglycerides and improving biomarkers, but anti-inflammatory and clinical effects in prevention are more variable, depending on dose, preparation quality, population, and chemical form.

### 6.5. Sensory and practical aspects

#### 6.5.1. Taste, smell, user acceptance

In a market study from the UAE (Jairoun et al. 2020), forms (syrup, capsule) were considered as one of the factors influencing consumer choice, although taste/aftertaste was not examined in depth.

#### 6.5.2. Frequency of side effects (fishy aftertaste, burping)

The publication "Oxidation in Omega-3 Oils: An Overview" (GOED) mentioned that fishy aftertaste is one of the main problems with consumer acceptance.

#### 6.5.3. Ease of dosing and mg EPA/DHA to price ratio

Market analyses of omega-3 supplements (e.g., Albert et al. 2015) have noted that more expensive brands tended to have better EPA/DHA content compliance and lower oxidation exceedances — but price increases with quality and certification.

Conclusions: practical aspects (taste, form, dose size, cost) are important for regular use of a supplement — after all, even the best preparation will not work if the consument does not take it.

## 7. Discussion

### 7.1. Introduction

This discussion aims to provide an in-depth interpretation of the results presented in the study in the context of the current scientific literature on omega-3 fatty acid supplementation, with particular emphasis on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The analysis focuses on key issues determining the effectiveness of supplementation, such as the oxidative stability of preparations, bioavailability depending on the chemical and pharmaceutical form, the importance of the TOTOX index as a synthetic measure of quality, and practical implications for consumers, dietitians, and dietary supplement manufacturers. The limitations of available studies and potential directions for further research that may contribute to a better understanding of the actual effectiveness of omega-3 supplementation are also discussed.

### 7.2. Comparative analysis of supplementation forms: capsules vs. liquid oils

One of the most important conclusions from the analysis of the collected data is that the form of the omega-3 supplement significantly affects its oxidative stability. Gel capsules, thanks to the hermetic sealing of the oil in a gelatin matrix, limit the direct contact of lipids with atmospheric oxygen and reduce exposure to light. As a result, many studies have observed lower peroxide values (PV), anisidine values (p-AV), and TOTOX indices in encapsulated products compared to liquid forms, especially after prolonged storage.

This phenomenon is of practical importance because polyunsaturated fatty acids such as EPA and DHA are particularly susceptible to lipid peroxidation. Oxidation not only leads to a reduction in the content of biologically active fatty acids, but also to the formation of secondary oxidation products, which can negatively affect the sensory properties of the preparation (taste, smell) and potentially have adverse biological effects.

Although liquid oils are often preferred by consumers due to their precise and flexible dosing, they are more susceptible to oxidative degradation. Frequent opening of the bottle, greater surface area of contact between the oil and air, and inappropriate storage conditions (room temperature, exposure to light) contribute to accelerated increases in PV, p-AV, and consequently TOTOX. Literature data indicate that flavored oils or oils intended for children in particular can reach very high TOTOX values at the end of their shelf life.

On the other hand, it should be emphasized that liquid oils may be beneficial in clinical situations requiring high doses of EPA and DHA, for example in the treatment of severe hypertriglyceridemia. In such cases, the ease of dose adjustment and the possibility of using emulsion forms may outweigh the potential risk of oxidation, provided that the high quality of the product and appropriate storage conditions are maintained.

### 7.3. Bioavailability of EPA and DHA – the importance of chemical form and method of administration

The bioavailability of omega-3 fatty acids is a key factor determining the effectiveness of supplementation. Numerous pharmacokinetic and interventional studies have shown that the chemical form of EPA and DHA significantly affects their absorption in the gastrointestinal tract. Triglycerides (TG), re-esterified triglycerides (rTG), and ethyl esters (EE) are most commonly compared.

The data collected indicate that TG and rTG forms have higher bioavailability than EE. This mechanism is related to the physiology of lipid digestion—triglycerides are a natural substrate for pancreatic lipase, while ethyl esters require an additional hydrolysis step, which may be less efficient, especially with a low fat intake

in the diet. In clinical practice, this means that supplements containing EPA and DHA in EE form may require higher doses to achieve a comparable biological effect.

The method of intake also plays an important role in the absorption of omega-3 fatty acids. Consuming supplements with a meal containing fat significantly increases the bioavailability of EPA and DHA by increasing bile secretion and the formation of lipid micelles. The micellization effect is particularly important for ethyl esters, but it also remains significant for triglyceride forms. In this context, recommendations to take omega-3 supplements "with a meal" have a solid physiological basis and should be clearly communicated to consumers.

Phospholipid forms (e.g., krill oil) and emulsion preparations are also attracting increasing interest. Although some studies suggest their potentially higher bioavailability, the number of well-designed randomized clinical trials in this area remains limited, preventing clear conclusions.

### 7.4. The significance of the TOTOX index for biological efficacy

The TOTOX index, which takes into account both primary (PV) and secondary (p-AV) lipid oxidation products, is a widely accepted measure of the quality of fish oils and omega-3 supplements. High TOTOX values indicate an advanced degree of oxidation, which can significantly reduce the biological efficacy of EPA and DHA.

Oxidized fatty acids lose their anti-inflammatory and cardioprotective properties, and the resulting aldehydes and ketones can increase oxidative stress. Although direct clinical studies linking TOTOX levels to health effects are limited, indirect data and mechanistic studies suggest that supplements with high oxidation levels may not only fail to provide benefits but may also have adverse effects.

In this context, quality certifications such as IFOS or compliance with GOED standards, which set upper limits for PV, p-AV, and TOTOX, play an important role. However, it should be emphasized that certification does not always guarantee that product quality will be maintained throughout the storage period, which indicates the need for regular monitoring and appropriate logistical conditions.

### 7.5. Practical aspects and implications for consumers

From the perspective of consumers and dietary practice, it is crucial to make an informed choice when selecting an omega-3 supplement. In addition to the declared EPA and DHA content, attention should be paid to the chemical form, quality indicators, and packaging. Gel capsules and dark glass bottles provide better protection against light, and airtight closures limit oxygen exposure.

Storage conditions have a significant impact on the stability of preparations. It is recommended to store omega-3 supplements in a cool, dark place, and in the case of liquid oils, preferably in the refrigerator. It is equally important to observe the expiry date, as the risk of oxidation increases over time.

### 7.6. Limitations and future research directions

Despite the growing number of publications on omega-3 supplements, there are several significant limitations. First of all, there is a lack of long-term clinical studies comparing different forms of supplementation while controlling oxidative parameters. In addition, better standardization of methods for determining PV, p-AV, and TOTOX is necessary.

A promising direction for future research is also the evaluation of the synergy of omega-3 with antioxidants such as tocopherols, tocotrienols, and astaxanthin, which may improve the stability of preparations and the safety of their use.

## 8. Conclusions

Both gel capsules and liquid oils can be effective sources of omega-3 fatty acids, provided that they maintain high oxidative quality and are stored under appropriate conditions. Analysis of the available data indicates that capsules offer greater stability and convenience of use, while liquid oils provide greater dosing flexibility and potentially faster absorption.

The key factor determining the effectiveness of supplementation remains the quality and freshness of the product, best reflected by a low TOTOX index. In practice, this means choosing certified products that are properly packaged and used in accordance with the manufacturer's recommendations.

For supplement manufacturers, these results underscore the importance of controlling production processes, using antioxidants, and transparently reporting quality parameters. For consumers and dietitians, they provide a basis for more informed choices about omega-3 supplements, taking into account not only the EPA and DHA dosage, but also the chemical form, oxidative stability, and storage conditions.

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Authors do not report any disclosures

**Authors' contribution statement:**

Conceptualization, J.B., and D.G.; methodology, J.B., and D.G.; check, M.A., A.Z., J.B., R.S., and D.G.; formal analysis, M.C., R.S., A.Z., and M.A..; investigation, J.B.; resources, R.S., and A.Z.; writing – rough preparation, J.B., M.C., R.S. and M.A.; writing – review and editing, J.B., M.A., M.C., R.S., D.G., and A.Z.; visualization, M.A.; supervision, J.B.,R.S., M.C.,A.Z., D.G., and M.A.; project administration, R.S., M.A., and D.G.

All authors have read and agreed with the published version of the manuscript.

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