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Review

A Novel Marine Oil from the Copepod *Calanus finmarchicus*: Source, Harvesting, Chemistry and Potential Application in Human Health

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Abstract: In the first part of this paper, we introduce the marine copepod *Calanus finmarchicus*, its lifecycle and ecology, and describe the technologies developed for harvesting and extracting oil from this copepod. Calanus oil has a unique composition, with its fatty acids—including a high concentration of long-chain omega-3 polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs)—bound to long chain fatty alcohols in the form of wax esters. In the second part of this paper, we review pre-clinical and clinical studies conducted over the last two decades, which demonstrate the potential health benefits of Calanus oil. These studies highlight its role in preventing obesity-related metabolic distortions, such as inflammation and reduced insulin sensitivity.

Keywords: *Calanus finmarchicus*; harvesting; oil extraction technology; omega-3 polyunsaturated fatty acids; potential health effects

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1. Introduction

Modern society faces an unprecedented health crisis due to the obesity pandemic and the subsequent rise of diabetes and cardiovascular diseases. These conditions are largely driven by unhealthy dietary habits and sedentary lifestyle, leading to significant public health challenges globally. Exacerbating these issues is the rapidly increasing global population, which highlights the demand for sustainable, nutritious food sources. Unfortunately, many current food systems fail to provide essential nutrients, contributing to the deterioration of health and increase in chronic diseases. Thus, preventive strategies that focus on enhancing nutrition through natural, healthy nutrients are needed.

Oceans, which cover approximately 71% of the Earth's surface, represent a vast and largely untapped reservoir of potential food sources with essential nutrients and bioactive compounds. These marine resources could play a crucial role in addressing current health challenges. Among these marine resources, oils rich in long-chain omega-3 polyunsaturated fatty acids (LC-PUFAs) and their precursor molecules have gained significant scientific attention due to their numerous physiological benefits, including cardiovascular protection and anti-inflammatory properties.

In recent years, the demand for marine oils has increased significantly, driven by advancements in the aquaculture and health food industries. This growing demand,

combined with fluctuation in fish stock and enhanced resource management practices, has led to the exploration of alternative sources, such as Antarctic krill. According to the Food and Agriculture Organization's (FAO) State of World Fisheries and Aquaculture (SOFIA) report, approximately one third of global fish stocks are overexploited, with more than 60% being exploited at maximum yields. Consequently, there has been a heightened focus on identifying alternative sources of LC-PUFA, with an emphasis on more sustainable options within the marine ecosystem. The sustainable use of marine resources aligns closely with several United Nations Sustainable Development Goals (SDGs), particularly SDG 2 (Zero Hunger), SDG 3 (Good Health and Well-being) and SDG 14 (Life Below Water). It may also play a crucial role in ensuring sufficient intake of natural ingredients that support health maintenance and prevention of chronic diseases.

Despite the promising potential of marine resource utilization, translating scientific discoveries into market-ready products requires navigating a complex landscape of regulatory and technological challenges. These may include establishing sustainable harvesting and processing practices, meeting stringent food safety and quality standards, and securing regulatory approval for novel nutrient or food substances entering the market. Additionally, significant interdisciplinary collaborations are essential to develop the necessary technologies and validate the quality and potential health benefits of such innovations.

The objective of this paper is to elucidate the multidisciplinary research efforts that have culminated in the isolation of a novel oil derived from *Calanus finmarchicus*, known as Calanus oil. This work integrates ecological insights, innovative harvesting methods and advanced processing technologies with rigorous biochemical and biomedical research.

2. *Calanus finmarchicus*—An Unexploited and Sustainable Source of Omega-3 Fatty Acids

A promising avenue of research has been the exploration of marine resources lower in the food chain, such as zooplankton. This approach not only provides a sustainable strategy with potentially higher yields, but also minimizes ecological impact and promotes the health of marine ecosystems. Among these resources, the copepod species *Calanus finmarchicus* sensu latu has emerged as a particularly noteworthy candidate due to its abundance and critical role in the marine food web of the Northern Hemisphere. The availability of *Calanus finmarchicus* as food for other species is secured through cautious and timely adapted harvesting. Since the 1970s, this copepod species has been the subject of extensive studies conducted by biological oceanographers and marine ecologists as part of international multidisciplinary research programs. Building on this solid knowledge base, Norwegian scientists initiated efforts around the turn of the millennium to enable the commercial utilization of this highly abundant species.

2.1. Lifecycle and Role in Marine Food Webs

The marine crustacean *Calanus finmarchicus* (Figure 1) is an herbivorous species with a one-year lifespan, consisting of twelve growth stages: six naupliar stages, followed by five copepodite stages and the final reproductive adult stage [1,2]. Reproduction and spawning occur during the spring phytoplankton bloom in March and April. A very intensive growth period in the surface layers of the sea follows for the next two months, during which the lipid stores gradually increase. This growth phase ceases in the fifth copepodite stage in May and June in Subarctic and Arctic waters. This advanced life stage carries the oil deposits, forming the basis for harvesting and industrial extraction. Harvesting is conducted while the stock is still in surface waters. By late summer and early autumn, the stock descends to deeper waters where the life cycle is completed by a diapause phase

lasting up to six months, typically taking place in cold, deep oceanic waters. At the end of the overwintering period in January, the copepodites molt into adults [2].

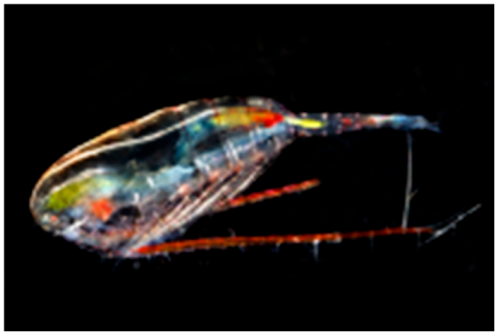

Figure 1. The marine copepod *Calanus finmarchicus*, which is found in enormous amounts in the North Atlantic Ocean. The adult size ranges from of 3–4 mm. (Photo: Kurt S. Tande).

The species plays a key role in the marine food web throughout the North Atlantic and Arctic Oceans [3], where it is the most important zooplankter by biomass. Its annual production of 200–400 million tons [2] is several tens of times more than the accumulated biomass production of all the fish species in the same waters. *Calanus finmarchicus* serves as a major food source at one or more life stages of all commercially harvested fish species in the North Atlantic, including cod, saithe, herring, capelin, mackerel and salmonids [2]. It is generally recognized that only between 10–15% of its energy is being incorporated as biomass moving upwards from one trophic level to the next in the marine ecosystem. Since the highest biomass is found concentrated at the base of the food pyramid, utilizing resources such as zooplankton are both ecologically feasible and recommended.

2.2. Developing Harvesting Technology and Management Policy

Harvesting technology has been developed stepwise for some 20 years and is today conducted using gentle scooping nets, which are hauled through the water at a speed of approximately 1 knot. This method allows adult and juvenile fish to escape, thereby avoiding capture. Due to surface currents and topography, this zooplankter becomes trapped and aggregated in specific areas during its swarming period. Consequently, some geographical regions are more suitable for commercial harvesting than others. By-catch of fish larvae is generally very low or nonexistent due to the carefully designed harvesting technique. While by-catch of gelatinous organisms may occur, these are removed by coarse filters before freezing and storage onboard. The raw material remains consistent in composition, as harvesting is conducted within a narrow time window during spring and early summer.This technology development has been instrumental for the Norwegian government to establish the knowledgebase for the proposal of a management plan released in 2016 (https://www.fiskeridir.no/rapporter/Forvaltningsplan-for-raudaate, accessed on 21 May 2025) for commercial harvesting of *Calanus finmarchicus*. The quantitative impact of this harvesting activity is very modest, where the recommended, precautionary annual quota of this resource is 0.5% of the standing stock in the Norwegian Sea. The authority in Norway responsible for the management of the Calanus fishery is the Directorate of Fisheries, while the Ministry of Trade, Industry and Fisheries is responsible for the fishing fleet and the aquaculture industry. The major legal instrument, under which the authorities, enterprises and fisheries operate, is the Marine Resources Act (MRA). This legislative framework has an explicit precautionary approach based on sustainability principles. The harvesting activity complies with the allocated quotas and precautionary principles in the MRA. Furthermore, to secure the health of the ocean, sustainable fishing practices are

carried out with full transparency by the harvesting companies, under the guidelines from the Norwegian Directorate of Fisheries.

2.3. Developing Extraction Technology

The development of extraction technology for Calanus oil is a critical process in transforming this marine biomass into a consumer-ready product. Due to the unique properties of the biomass, especially its high content of hydrophobic wax esters and antioxidants such astaxanthin [4], the focus has been on designing processes that preserve these compounds while ensuring sustainability and efficiency. Over time, researchers have refined the extraction methods, changing from basic techniques to more advanced enzyme-assisted and cold-press processes that maximize oil yield and quality. A significant breakthrough came with the application of proteolytic enzymes, as highlighted by Vang et al. (2013) [5]. This approach improved oil recovery and preserved the bioactive components during extraction. By breaking down cellular structures more effectively than mechanical methods alone, this enzymatic process offered an efficient process tailored to *Calanus*'s unique lipid profile, while avoiding exposure of the lipids to high temperatures [4].

The development of these technologies has resulted in a streamlined, low-impact process that transforms *Calanus finmarchicus* biomass into a high-quality oil without the need for extensive refinement. The natural low levels of contaminants in the oil [6], combined with the stability of the wax esters provided by the antioxidant, astaxanthin, mean that it can move directly from extraction to the consumer market, eliminating the need for additional purification stages.

A life cycle assessment (LCA) evaluating the environmental impact associated with all stages of harvesting and production was recently conducted [7]. This will play a crucial role in future developments of the oil, helping to reduce environmental impacts and improve sustainability.

2.4. Regulatory Framework

Historically, sailors and seafarers reportedly consumed *Calanus* during long voyages or shipwrecks, recognizing its nutritional value. However, due to the lack of significant consumption within regulated markets, Calanus oil had to undergo stringent regulatory scrutiny before being approved for widespread commercial use.

In the United States, Calanus oil has been on the market for several years, initially as part of dietary supplements like Arctic Ruby Oil. In 2011, it achieved self-affirmed Generally Recognized as Safe (GRAS) status [8], enabling it to be marketed without formal Food and Drug Administration (FDA) approval. This status was supported by an independent review of safety data, demonstrating that Calanus oil could be safely incorporated into dietary supplements. In the European Union, Calanus oil was approved under the Regulation (EU) 2015/2283 on novel foods. The authorization was granted in 2017 following a comprehensive review by the European Food Safety Authority (EFSA), which focused on the oil's chemical composition, production process and safety profile, leading to its approval for use in food supplements with specified daily intake limits (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0966, accessed on 21 May 2025). In Canada, Calanus oil was approved as a Natural Health Product (NHP) by Health Canada in 2019. This approval was issued by the Natural and Non-prescription Health Products Directorate (NNHPD). In Australia, Calanus oil was approved by the Therapeutic Goods Administration (TGA) in 2022. The TGA's rigorous approval process set strict standards for the oil's purity, stability and safety, ensuring that it met all regulatory requirements for use in therapeutic products and dietary supplements.

As part of ongoing efforts to establish Calanus oil as a globally recognized marine resource, Norwegian authorities, led by the Norwegian Food Safety Authority, applied in 2020 to include Calanus oil in the Codex Alimentarius Standard for Fish Oils (CXS 329-2017). During the 28th session of the Codex Committee on Fats and Oils (CCFO28) in 2024, Calanus oil was included in the Codex Standard for Fish Oils which recognized the oil as a safe and high-quality marine oil (https://www.fao.org/fao-who-codexalimentarius/sh-proxy/es/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS+329-2017%252FCXS_329e.pdf, accessed on 21 May 2025).

3. The Chemistry of Calanus Oil

Herbivorous copepods, such as *Calanus finmarchicus* from colder waters, synthesize large lipid reserves to compensate for limited food availability during periods of food scarcity, reproductive activity and other seasonal and environmental stresses [9]. While the primary lipid class in fish oil is triglyceride (40–99% of total lipids) [10], phospholipids prevail in krill oil at a concentration from 39–80% [11]. The lipid component in Calanus oil consists mainly (80–90%) of wax esters [4], which are fatty acids esterified to long-chain fatty alcohols (marine-policosanols) as monoesters (Figure 2).

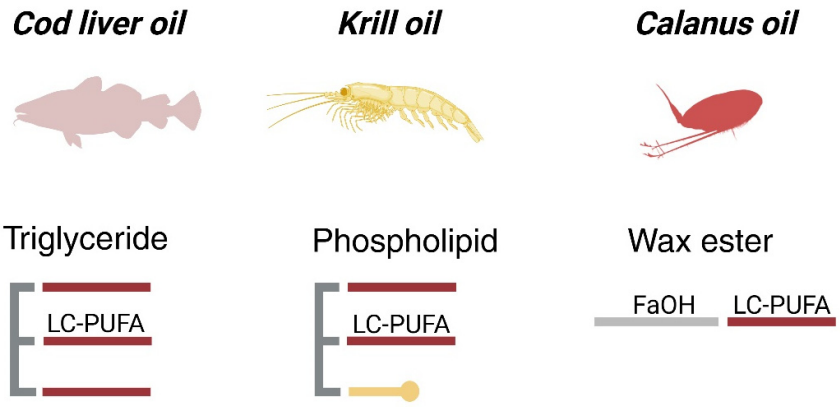

Figure 2. Different marine sources of long-chain polyunsaturated fatty acids (LC-PUFAs). In cod liver oil and krill oil, PUFAs are present in the form of triglycerides and phospholipids, respectively. The major lipid component of Calanus oil is wax ester, where PUFAs (and other fatty acids) are esterified to fatty alcohols. Dark grey: glycerol molecule; red: fatty acids; yellow: hydrophilic head group linked to a phosphate moiety; light grey: fatty alcohol (FaOH). Created in BioRender (2025).

The fatty acids in the Calanus oil wax esters are primarily derived from dietary sources [12], while the alcohol moieties, eicosenol and docosenol, are endogenously synthesized [13]. The content of LC-PUFA in the wax esters may account for approximately 20–30% of the fatty acids, with stearidonic acid (SDA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and α-linolenic acid as the dominating species (Table 1).

The monounsaturated fatty acids (MUFAs) consist primarily of palmitoleic, oleic, gondoic and cetoleic acid. It should also be noted that the fatty alcohols in the wax esters may be oxidized to their corresponding fatty acids after uptake [14], thus boosting the levels of MUFAs in the body. Saturated fatty acids, primarily myristic and palmitic acid, amount to 20–35% of the total fatty acids present in the wax esters. Calanus oil also contains high quantities of the carotenoid astaxanthin [15], which gives the oil an orange red color and has named *Calanus finmarchicus* as "red feed" in many countries. Astaxanthin is obtained from phytoplankton and is present in mono- and diester forms bound to fatty acids [16] and sometimes bound to proteins [17]. Due to its strong antioxidant properties, it prevents lipid oxidation in the oil.

Table 1. Major components of wax ester derived from Calanus oil.

Lipid Class	g/100 g	Individual Fatty Acids
SFA	16	Mysteric acid (14:0) Palmitic acid (16:0)
MUFA	15	Oleic acid (18:1 n-9) Gondoic acid (20:1 n-9) Cetoleic acid (22:1 n-11)
PUFA	24	α-Linolenic acid (18:3 n-3) Stearidonic acid (SDA, 18:4 n-3) Eicosapentaenoic acid (EPA, 20:5 n-3) Docosahexaenoic acid (DHA, 22:6 n-3)
FaOH	38	Eicosenol (20:1 n-9 Docosenol (22:1 n-11)
Sterols TAG, NEFA, PL Astaxanthin	0.5 6.3 0.2	

SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; FaOH, fatty alcohols; TAG, triacylglycerol, NEFA non-esterified fatty acids; PL, phospholipids.

4. Potential Health Effects of Calanus Oil

Interest in the health-promoting role of LC-PUFAs, particularly their protective effect on coronary artery disease, began in the early 1970s with the work of Bang et al. (1971) [18]. They reported a lower incidence of ischemic heart disease (IHD) in Greenland Eskimos compared with their Danish counterparts. This observation was attributed to a healthy plasma lipid profile, characterized by low plasma triglyceride and very low-density lipoprotein concentrations [19] due to the traditionally high intake LC-PUFAs from marine mammals and fish [18]. This view is, however, challenged [20], because there has been a decrease in mortality from ischemic heart disease in the adult Greenlandic population since the mid-1960ties, despite a westernization in diet and lifestyle (including a decline in the consumption of traditional marine food) and development of dyslipidemia in the same period and [21].

The beneficial effects of marine oils have traditionally been attributed to their content of the LC-PUFAs, EPA and DHA, as well as to the chemical structure of the complex lipids in which they occur (triacylglycerol, phospholipids, ethyl esters). The content of EPA and DHA is relatively low in Calanus oil, but unlike other marine oils, it has a high content of SDA, which is to some extent converted to EPA in humans [22]. In addition, and as noted earlier, LC-PUFAs in Calanus oil are present in a unique form—wax esters—where the fatty acids are bound to a fatty alcohol. The following sections focus on the preclinical and clinical literature where this oil has been used.

4.1. Explorative Preclinical Studies

In an early study, Eilertsen et al. [23] examined the effect of dietary supplementation with Calanus oil on atherosclerosis development in apoE-deficient mice, which were given a Western-type, high-fat diet (HFD) supplemented with Calanus oil (1% wt/wt). After a feeding period of 13 weeks, it was found that total aorta atherogenesis was reduced by 36.5% relative to mice given non-supplemented HFD. In addition, lower atherogenesis in mice fed Calanus oil was paralleled by reduced expression of proinflammatory genes in the liver, including chemokine ligand 2 (Ccl2), intercellular adhesion molecule 1 (Icam1), interleukin-1 beta (Il1b) and nuclear factor-kappa B (Nfkb).

Höper et al. [24], using HFD-induced obese mice as experimental model, reported that supplementing the diet with 1.5% Calanus oil over 26 weeks significantly reduced visceral fat accumulation and hepatic steatosis while improving glucose tolerance, suggesting increased insulin sensitivity. Additionally, the treatment markedly reduced macrophage infiltration and low-grade inflammation in adipose tissue, as reflected by significantly reduced expression of pro-inflammatory cytokines, including interleukin-6 (Il-6), monocyte-chemoattractant protein-1 (Mcp-1) and tumor necrosis factor-a (Tnfa), alongside increased expression of adiponectin. In a follow-up study [25], the authors also demonstrated that supplementing the diet with purified wax esters from Calanus oil (1%, *wt*/*wt*) had marked anti-obesity and anti-inflammatory effects similar to those observed previously with crude Calanus oil. This finding suggests that the active component(s) of Calanus oil are primarily confined to its main lipid constituent, wax esters. Notably, the treatment also increased aerobic capacity of the mice by approximately 10% during treadmill running. For comparative purposes, the metabolic effects of Calanus oil-derived wax esters were compared to those of ethyl esters of EPA and DHA, which are used clinically for treatment of hypertriglyceridemia. Thus, mice were given either wax ester supplemented HFD or HFD supplemented with EPA and DHA ethyl esters from fish oil, containing equivalent amounts of EPA and DHA as in the wax ester. The result showed that supplementation with EPA and DHA ethyl esters suppressed proinflammatory genes in adipose tissue to a similar extent as the wax ester, while they had less pronounced effect on obesity parameters, adiponectin expression and aerobic capacity.

Wax esters are hydrolyzed by pancreatic esterases in the small intestine [26]. According to the literature, wax esters are poorly digested in mammals [14], which may reduce the bioavailability of the esterified fatty acids. To investigate this, Pedersen et al. [27] examined the fate of the Calanus oil wax esters in mice given HFD supplemented with Calanus oil (2% wt/wt) over an 11-week period. The study documented that the wax esters were indeed hydrolyzed in the digestive tract and that the liberated fatty acids were absorbed and influenced the lipid profile of the animals, as demonstrated by enrichment of Calanus oil-derived fatty acids in adipose tissue and the liver. Additionally, they reported reduced amounts of arachidonic acid in visceral adipose tissues, which support previous observations of a reduced inflammatory status following Calanus oil intake. Interestingly, based on measurements of elevated levels of fatty acids and fatty alcohols in the feces, the authors suggested that the absorption process—rather than hydrolysis—could be a rate-limiting step in the utilization of the wax esters in Calanus oil.

In 2016, Salma et al. [28] investigated whether dietary supplementation with Calanus oil could antagonize angiotensin II (Ang II)-induced hypertension and ventricular remodeling in obese mice. The animals were initially subjected to 8 weeks of HFD with or without 2% Calanus oil and thereafter randomized for the administration of either Ang II (1 µg/kg/min) or saline for an additional two weeks. The results showed that angiotensin II-induced increase in blood pressure was attenuated in mice that had been pre-treated with Calanus oil. Furthermore, dietary Calanus oil antagonized the reduction in total body weight and weights of adipose tissue, liver, kidney and skeletal muscle caused by the metabolic stress associated with the angiotensin II infusion. Notably, dietary Calanus oil also led to a robust increase in cardiac protein O-GlcNAcylation—probably a protective adaptation. This effect, combined with the anti-inflammatory properties of Calanus oil, helped to alleviate the adverse cardiovascular system effects of Ang II. However, it was also observed that Ang II-induced cardiac hypertrophy and fibrosis were not significantly altered by dietary Calanus oil.

The potential effects of Calanus oil on cardiometabolic health were later examined by Jansen et al. [29]. The specific aim was to determine whether dietary supplementation with

Calanus oil could counteract obesity-induced alterations in myocardial metabolism and protect the heart from ischemia-reperfusion damage. Obesity was induced in female mice by 12 weeks HFD feeding, followed by another 8 weeks HFD feeding without or with Calanus oil (2% *wt*/*wt*) supplementation. A third group of HFD-fed mice were infused (via mini-osmotic pumps) with exenatide during the last 8 weeks (to compare its cardiometabolic effect vs. Calanus oil). Exenatide is a glucagon-like peptide 1 (GLP-1) receptor agonist (marketed as Byretta) which is used as an anti-diabetic medication. Interestingly, the study found that both Calanus oil supplementation and exenatide treatment counteracted the obesity-induced derangements of myocardial metabolism, i.e., elevated fatty acid oxidation at the expense of glucose. Furthermore, the restoration of cardiac metabolic flexibility in response to Calanus oil intake was also accompanied by cardioprotection from ischemia-reperfusion damage.

In summation, the results from these preclinical experiments on obese rodent models (Figure 3) demonstrate that Calanus oil, when used as a dietary supplement, exhibits significant anti-obesity and anti-inflammatory effects. These effects were associated with the attenuation of obesity-related dysfunction of metabolism, such as insulin resistance and liver steatosis, as well as preservation of cardiac metabolic flexibility and recovery of post-ischemic ventricular function. Notably, the concentrations of Calanus oil used in these studies (1–2%, *wt*/*wt*) were 2–10 times lower than those used in previous studies reporting reduced adiposity following intake of LC-PUFA [30]. Moreover, the findings from these preclinical studies provided valuable background and direction for the clinical studies discussed in the following section.

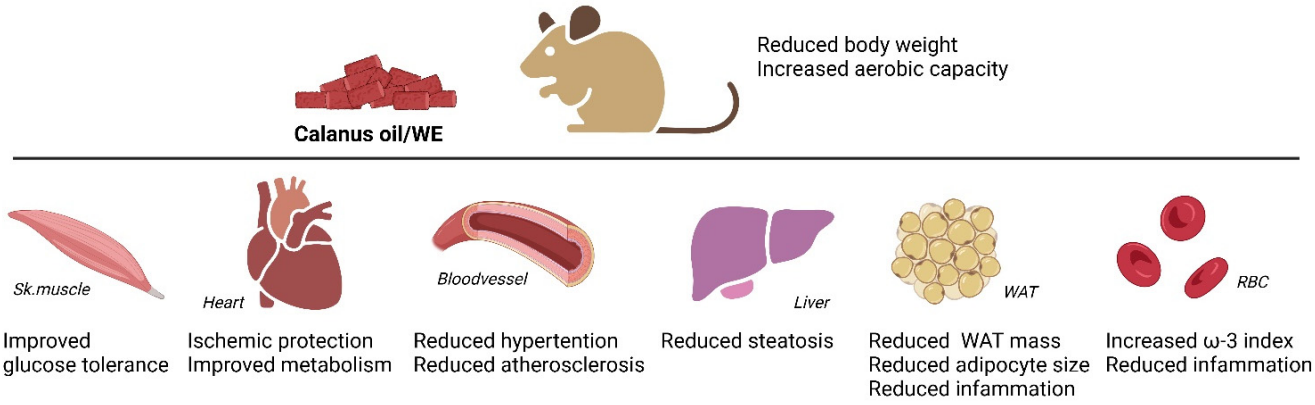

Figure 3. Physiological effects of dietary supplementation with low amounts of Calanus oil or purified wax ester (WE) in diet-induced obese mice. The feeding period in the various studies varied from 8 to 26 weeks. See the text above for details. Created in BioRender (2025).

4.2. Human Trials

Numerous clinical studies have demonstrated that LC-PUFAs are cardioprotective and reduce the risk for coronary heart disease (CHD) and sudden death. Relatively recent results from the REDUCE-IT trial [31] with high-dose EPA (4 g/day Icosapent Ethyl) strongly confirmed the cardioprotective role of EPA. More recent meta-analyses [32] also support the beneficial effect of LC-PUFAs. However, in contrast to these successful results, other trials with low-dose LC-PUFAs failed to show a beneficial effect on cardiovascular outcomes [33]. Several factors might explain these discrepancies such as dosage and composition of the marine preparations used, the initial LC-PUFA status of participants (e.g., the omega-3 Index, O3I) and choice of control and/or cohort selection.

Several clinical studies have been conducted to evaluate the safety, bioavailability and/or the biochemical and physiological effects of Calanus oil, as summarized in Table 2. These studies focus on bioavailability and changes in body fat, muscle mass and strength,

markers of glucose metabolism, as well as cardio-respiratory fitness. Their findings are discussed in the following sections.

Table 2. Overview of clinical impact of Calanus oil treatment.

Subjects	Dose/Duration	Samples/Measurements	Effect of Calanus oil	Reference
Healthy participants	Calanus vs. olive oil 2 g/day for 12 months	Clinical chemistry and hematology. Evaluation of vital signs/adverse effects.	No clinical or adverse effects.	[34]
Healthy participants	4 g Calanus oil vs. 1 g Lovaza for 72 h (crossover)	Analysis of plasma EPA and DHA.	Increase of plasma EPA in response to Calanus oil higher relative to Lovaza.	[35]
Healthy participants	Oil from Calanus, fish and krill. Equal dose of EPA+DHA/day for 12 weeks	Analysis of plasma fatty acids and O3I.	Similar increase in O3I.	[36]
Healthy elderly women (EXODYA)	Calanus oil vs. sunflower oil 2.5 g/day for 4 months Combined with exercise	Body composition. Analysis of plasma. Adipose tissue biopsies. Lipidomic. Functional fitness and muscle strength. Aerobic capacity. Cardiac function (impedance cardiography).	Reduced (visceral) fat mass. Reduced HOMA-IR. Increased muscle strength of lower body. Increased max cardiac output. No effect on VO_{2max} or changes in adipose tissue lipidome and inflammation.	[37–40]
Healthy participants	Calanus oil vs. olive oil. 2 g/day for 6 months	Body composition. Cardiopulmonary exercise test.	No change in body weight and composition or BMI. No effect on HRmax or VO_{2max}.	[41]
Healthy participants (BEGINN)	Calanus oil 2 g/day for 12–16 weeks Combined with exercise	Analysis of plasma. Body composition.	Reduced fat mass. Increased O3I. Bodyweight and BMI unchanged. No effect of fasting insulin, HOMA-IR and blood lipids.	[42,43]
Obese prediabetic patients	Calanus oil vs. paraffin 2 g/day for 12 weeks	Analysis of plasma. Body composition.	Increased O3I. Reduced fasting glucose, HOMA-IR and hepatic and muscle insulin resistance.	[44]

Bioavailabilty: Tande et al. [34] reported in 2016 that intake of Calanus oil is safe and can provide a source of EPA and DHA without causing adverse health effects. While demonstrated in animal studies, the scientific community has questioned to what extent a wax ester-based marine oil is digested so that its fatty acid moieties can be absorbed by humans [14]. To address this, Cook et al. [35] conducted a randomized two-period single-dose crossover study comparing the bioavailability of Calanus oil to that of Lovaza® (ethyl esters of fish oil-derived EPA and DHA). Eighteen healthy adults were given 4 g Calanus oil, providing a total of 260 mg EPA and 156 mg DHA or 1 g of Lovaza® providing 465 mg EPA and 375 mg DHA. The plasma concentrations of EPA and DHA were followed over the following 72 h period. Interestingly, despite the fact that the amount of EPA and DHA provided by Calanus oil was only half of that provided as Lovaza®, there was virtually no difference in the measured plasma concentration of EPA and DHA (individually or combined) between the two treatments.

Further evidence for the bioavailability of LC-PUFA from Calanus oil was reported by Wasserfurth et al. [42]. For the first time, the authors demonstrated that long-term intake of Calanus oil resulted in a significant increase in the O3I, which measures the content of EPA and DHA relative to the total erythrocyte fatty acids. After 12 weeks of Calanus oil supplementation (2 g/day), O3I increased by 21.4%. These findings were confirmed by Burhop et al. [44], who observed a similar increase in O3I with a comparable dose of Calanus oil. Additionally, Vosskötter et al. [36] compared the influence of 12 weeks

supplementation with Calanus oil, fish oil and krill oil on the long-term LC-PUFA status in healthy volunteers. They confirmed that Calanus oil can increase the LC-PUFA status comparable to fish and krill oil and concluded that it is an alternative marine source of bioavailable LC-PUFAs, particularly when considering its sustainability.

The increase in O3I following Calanus oil supplementation could probably be related to the high content of SDA. This fatty acid is formed directly from alpha-linolenic acid (ALA, 18:3 n-3) and further converted to EPA. For this reason, SDA has been referred to as a 'pro-EPA' fatty acid [45] and led to the suggestion that intake of SDA as such could be another strategy to increase tissue EPA levels. The presence of the marine long-chain MUFAs may have additional impact. Recent research has shown that cetoleic acid (22:1, n-11) enhances the biosynthesis of EPA and DHA by improving the efficiency of the omega-3 pathway [46]. MUFAs have also been associated with cardioprotective effects and reduction in risk factors for the development of metabolic syndrome [47,48]. In summary, these findings demonstrate that wax ester-bound LC-PUFAs from Calanus oil are highly bioavailable and suitable for human consumption.

Effect on fat loss, skeletal muscle mass and performance: In the EXODYA study, which was an interventional cross-sectional study, researchers investigated changes in selected fitness parameters following a 16-week moderate exercise program combined with dietary supplementation with Calanus oil or sunflower oil (placebo) in healthy elderly women [39,40]. Functional fitness was assessed using a battery of senior fitness tests. In addition, they evaluated hand muscle strength and exercise capacity (bicycle stress test). Most of the functional fitness parameters were improved following the exercise program, but there was no additional observed effect of Calanus oil intake, except for significantly higher improvement of functional strength of lower body (measured by chair stand test) [39]. Other results from the EXODYA study showed that Calanus oil supplementation resulted reduced fat mass in the trunk region, as measured by DXA technology [40]. Similar results were provided by the BEGINN study, where a decrease in body fat was observed when exercise was combined with Calanus oil intake [43]. Taken together, these results show that combining moderate exercise with Calanus oil intake might influence body composition. However, further studies are needed to determine the clinical relevance and broader health implications of these modest effects.

Effect on glucometabolic control in obese/pre-diabetic subjects: In the EXODYA study, it was observed that insulin sensitivity, measured by the hyperinsulinemic-euglycemic clamp method, was improved in the Calanus group after the 16-week intervention period, as demonstrated by a significant increase in the rate of glucose disposal related to fat-free mass [38]. The beneficial change in glucose disposal was interpreted as improved insulin sensitivity primarily to muscle, whereas parameters such as HOMA-IR and Adipo-IR were unchanged, indicating unaltered insulin sensitivity in liver and adipose tissue, respectively. Improved glucose homeostasis by Calanus oil was also observed in the CADIP study, where two groups of pre-diabetic subjects (average BMI of 31.7 kg/m^2), receiving either Calanus oil (2 g/day) or paraffin (2 g/day), without any exercise intervention [27]. After 12 weeks of supplementation, the Calanus oil group showed significant reductions in several markers of glucose metabolism, including fasting plasma insulin, HOMA-IR and hepatic insulin resistance index. These results indicate a potential effect of Calanus oil on glucose metabolism and insulin resistance in obese subjects.

Obesity is closely associated with a low-grade inflammatory state in adipose tissue, with release of pro-inflammatory adipokines which will impair insulin signaling in peripheral tissues [49]. The improvement in glucometabolic control following Calanus oil supplementation might therefore depend on the anti-inflammatory action of the oil, which was previously demonstrated in rodents [24]. In addition, LC-PUFAs released

from the digestion of wax esters may bind to and activate G protein-coupled receptor 120 (GPR120), which is highly expressed in the distal part of ileum and colon [50]. Improved glucometabolic control in response to LC-PUFAs may thus be linked to GPR120 activation and release in GLP-1, which in turn will stimulate insulin release from the pancreas. Finally, GPR120 is also expressed in macrophages and adipocytes [51], where its activation by LC-PUFAs mediates insulin sensitizing and anti-diabetic effects in vivo by repressing macrophage-induced tissue inflammation. Therefore, it is plausible that Calanus oil reduces the inflammatory state and, as a result, contributes to the improvement of insulin sensitivity, as reported in EXODYA and BEGINN.

Effect on aerobic capacity and cardiac muscle: A central question in the EXODYA study was whether combining exercise training with Calanus oil supplementation could potentiate maximum oxygen uptake (VO_{2max}) in elderly women. The study showed that VO_{2max} was increased by approximately 20% following 16 weeks exercise training, but the effect of exercise plus Calanus oil supplementation was not different from that of exercise combined with placebo [40]. Similarly, a study by Tauschek et al. [41] on healthy young volunteers failed to show any effect on VO_{2max} following 6 months intake of Calanus oil. Interestingly, however, in the study by Stephan et al. [40] the increase in VO_{2max} in the placebo group was due solely to peripheral mechanisms (i.e., increased arterio-venous oxygen extraction). In contrast, the increase VO_{2max} in the Calanus oil group was due not only to the peripheral mechanisms, but also to central mechanism in the form of increased maximum cardiac output (CO_{max}). It was calculated that CO_{max} increased by 8% in the Calanus group, which was explained primarily in terms of increased stroke volume (SV). Increased stroke volume SV (in the presence of unchanged ventricular filling) is indicative of enhanced cardiac contractility, i.e., force of contraction of the heart during ejection of blood into the vasculature. This potentially beneficial effect on the cardiac muscle aligns with the finding that Calanus oil may promote muscle growth/function in elderly or overweight individuals [39,43]. It is also in line with the results by Walser and Stebbins [52], who reported that supplementation with EPA and DHA for 6 weeks increased maximum stroke volume and cardiac output in response to a low or moderate exercise load in healthy adults. Nevertheless, further studies are needed to confirm these findings and to evaluate their relevant in appropriate study populations.

5. Conclusions

Over the years, a wide range of dietary lipids of both traditional and novel origins have been investigated for their potential health-related benefits. Among the marine-derived preparations, the introduction of marine oil from *Calanus finmarchicus* stands out due to its unique lipid composition, primarily wax esters, which contains a diverse array of fatty acids varying in chain length and saturation. Notably, Calanus oil is likely the richest source of stearidonic acid in the animal kingdom, which can improve the body's EPA status. The findings from preclinical and clinical research discussed suggest that Calanus oil has the potential to alleviate obesity-related metabolic disorders. However, further studies are needed to examine the role of Calanus oil as a dietary supplement, with respect to dosage and duration of the treatment, the interplay between the various components of the oil and targeted study population. Moreover, the biochemical and physiological mechanisms behind the observed effects of Calanus oil require further investigation.

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Abbreviations

The following abbreviations are used in this manuscript:

LC-PUFA	long-chain omega-3 polyunsaturated fatty acids
ALA	alpha-linolenic acid
SDA	stearidonic acid
EPA	eicosapentaenoic acid
DHA	docosahexaenoic acid
MUFA	monounsaturated fatty acid
FaOH	fatty alcohol
HFD	high-fat diet
O3I	omega-3 Index
VO_{2max}	maximum oxygen uptake
CO_{max}	maximum cardiac output
SV	stroke volume
GLP-1	glucagon-like peptide 1
GPR120	G protein-coupled receptor 120

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