zooca®
The Calanus® Company

Zooca® Calanus® Oil

White paper

Beyond the Established:
Exploring the Metabolic Impacts of Zooca® Calanus® Oil

By Alice Marie Pedersen, PhD

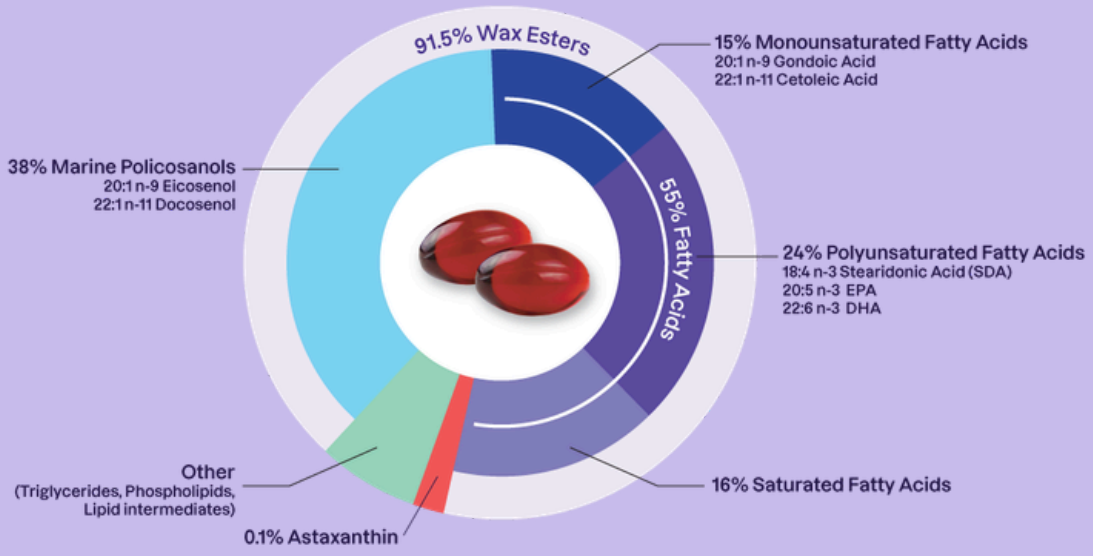


Figure 1 - graphical overview of the diverse composition of the natural lipid extract Zooca® Calanus® Oil

The relevance of Zooca® Calanus® Oil

In a world flooded with dietary supplements, it's a challenge to find natural, potent, and scientifically backed solutions that serve our intricate metabolic needs.

Introducing Zooca Calanus Oil ; a marine-derived oil like no other. Harvested from the abundant Calanus finmarchicus, this oil presents a combination of unique benefits anchored in its distinct composition and gentle extraction.

The uniqueness of Zooca Calanus Oil lies in its chemical structure, primarily composed of wax esters that contain bioactive compounds (fig 1).
This special composition distinguishes it from any other marine and plant oils.

The key components include omega-3 fatty acids such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and stearidonic acid (SDA). Additionally, it contains monounsaturated fatty acids (MUFAs) like cetoleic acid and gondoic acid. Astaxanthin, a potent antioxidant, and policosanols, a group of long-chain alcohols with potential health-promoting properties, further enhance its value.

Sourced from the pristine waters of the Norwegian Sea, Calanus finmarchicus plays an integral role in the marine food chain by transferring the energy from the plant kingdom to the higher trophic levels.

Impressively, the biomass of this resource is vast, estimated at up to 290 million metric tons annually, in this region alone.

The sustainable harvesting of *Calanus finmarchicus* not only offers a valuable source of nutrition but also supports the long-term health of the marine ecosystem and the fish populations that rely on it. This positions it as a sound alternative to traditional fisheries.

This white paper delves into the science behind Zooca® Calanus® oil, revealing why it stands out in the realm of metabolic health and flexibility

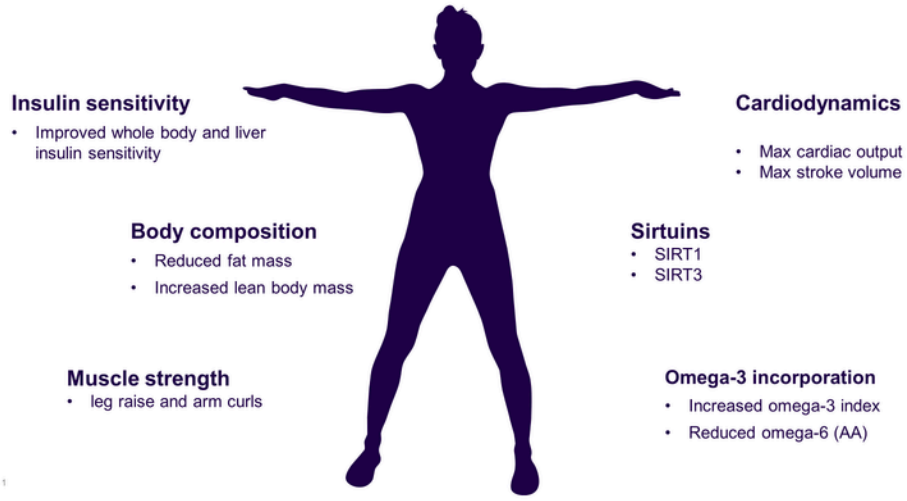


Figure 2 - graphical overview of the statistically significant findings from clinical trials with Zooca Calanus Oil

Zooca® Calanus® Oil impacts metabolic health

The body of scientific research, encompassing both preclinical studies and clinical trials on Zooca Calanus Oil, demonstrates that supplementation has a significant impact on metabolic health, as illustrated in Figure 2. The observed pronounced effects cannot be attributed solely to the content of EPA and DHA, suggesting we are witnessing the benefits of a naturally synergistic composition.

This moves us beyond the established understandings and invites further exploration.

Traditional dietary lipids such as triglycerides from generic fish oil and phospholipids found in krill oil consist of a glycerol backbone and esterified fatty acids, with either three fatty acids or two fatty acids and a phosphate group, respectively (Figure 3).
The uniqueness of *Calanus finmarchicus* -derived lipids is the chemical form of wax esters, and this lipid form may constitute as much as 90 % of the oil. Described chemically, they are fatty acids esterified to policosanols as monoesters. Wax esters are distinctly different from fat in any other marine (or terrestrial) oils in terms of chemistry, bioactivity, and health benefits.

Whereas other lipid-based supplements claim their benefits due to rapid absorption, Zooca Calanus Oil explains it the other way around; The unique chemistry of these lipids allows them to withstand the first line of digestive enzymes, letting the lipids reach the distal part of the digestive tract without compromising the bioavailability of the fatty acids.

This property is particularly advantageous for activating the GPR120 receptor, a nutrient sensor involved in regulating metabolic and inflammatory processes . GPR120 is expressed in various tissues throughout the body, including the distal intestine, colon, adipose tissue, and macrophages. It is a receptor for medium- and long-chain unsaturated fatty acids, such as omega-3 fatty acids, and studies have demonstrated that its activation can play a central role in regulating gut hormone secretion, insulin sensitivity, and body weight (1). The potent fatty acids released by Zooca Calanus Oil during digestion can activate the GPR120 receptor and exert their beneficial effects, making it an exciting new option for supporting metabolic and inflammatory health.

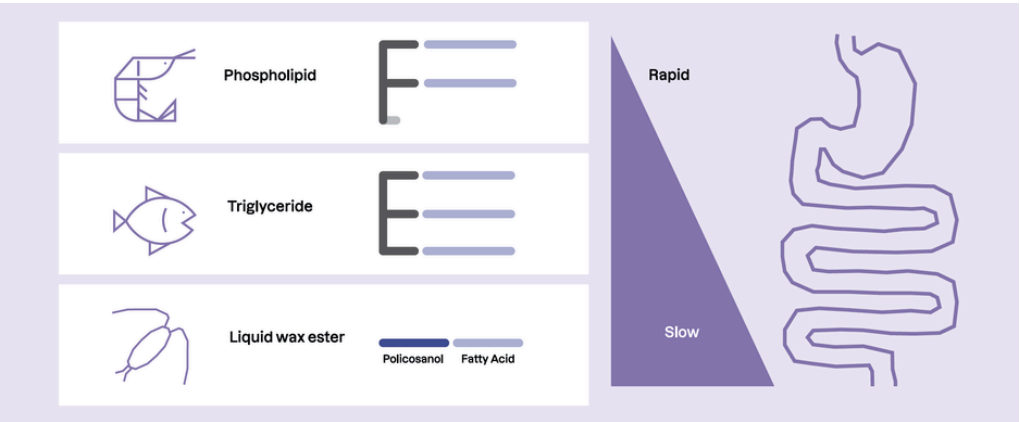
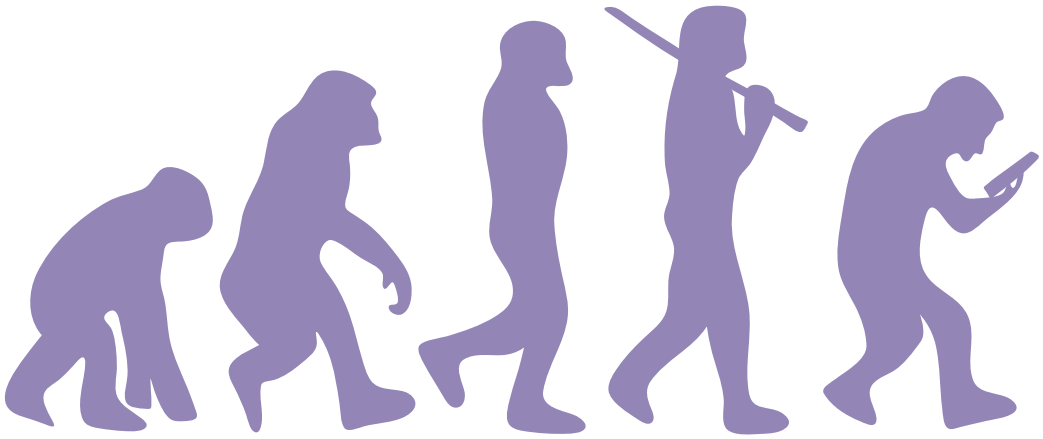


Figure 3 - Schematic chemical structures of relevant lipid classes. Phospholipid consisting of a glycerol backbone, two fatty acids and a phosphate group. Triglyceride consisting of a glycerol backbone and three fatty acids. Wax ester consisting of one fatty alcohol and one fatty acid.



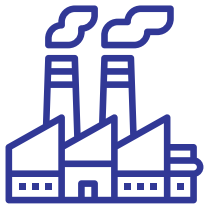
The growing concern of metabolic health in today's world

How did we end up here?

Human evolution has been a long journey of adaptation, where our metabolism, food consumption, and energy expenditure have been intricately tied to the environments we've navigated through millennia. This evolutionary path has equipped us with a metabolism that is highly flexible, capable of optimizing energy usage from various sources, whether in times of abundance or scarcity. However, the modern lifestyle, characterized by constant food availability and significantly reduced physical activity, represents a stark departure from the conditions that shaped our evolutionary adaptations.

The beginning of agriculture, followed by industrialization and now the digital revolution, has fundamentally changed how we interact with food and exercise. Food scarcity has been largely eliminated in many parts of the world, replaced by constant access to high-calorie, high-processed, nutrient-poor foods.

This shift has led to a dietary pattern that is drastically different from our ancestors', who consumed a varied diet rich in fibrous plants, lean proteins, and healthy fats, which supported optimal metabolic health



Our modern sedentary lifestyle further worsens this divergence. Many people now engage in little to no regular physical activity, a far cry from the daily rigorous physical exertion that was a hallmark of ancestral life. This has significant implications for our metabolic health, contributing to the rise in metabolic diseases such as obesity, type 2 diabetes, and cardiovascular diseases. Our bodies, adept at storing energy for future use, are ill-equipped to handle the constant influx of energy with minimal expenditure, leading to an energy imbalance and the subsequent health issues.

Our metabolic systems, designed for flexibility and efficiency, are now overwhelmed by the constant supply of food and lack of physical challenge.

This mismatch between our evolutionary heritage and current lifestyle is at the core of many modern health issues, underscoring the need for a return to practices that more closely mimic the conditions under which our metabolism evolved.

Pure resource and gentle extraction

Calanus finmarchicus

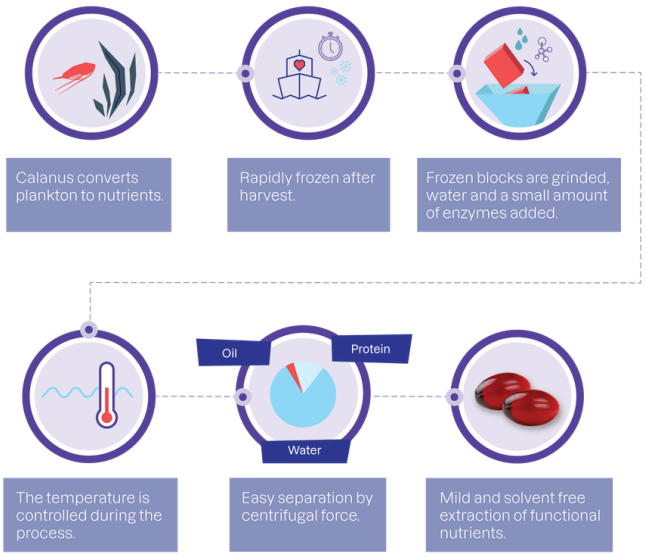
In the vast, cold waters of the North Atlantic, a tiny yet incredibly significant organism thrives— *Calanus finmarchicus*. This small copepod, not much larger than a grain of rice, plays a crucial role in the marine ecosystem. Its significance has not only been recognized by marine biologists but also harnessed by an innovative company, Zooca, (Calanus AS) which has ventured into pioneering a biomarine industry centred around this microscopic creature.

Calanus finmarchicus is a species of zooplankton, predominantly found in the North Atlantic Ocean. It forms one of the largest animal biomasses on Earth, making it a critical resource in the marine food web. This copepod serves as a primary food source for various fish species, whales, and seabirds.

The biomass of *Calanus finmarchicus* in the Norwegian Sea, estimated at around 290 million tonnes annually (3), highlights its ecological importance. As a primary consumer, it plays a key role in transferring energy from the plant levels and further up the marine food chain.

Adhering to the 10% rule of ecological energy transfer - that approximately 90% of the energy is lost between each trophic level - harvesting organisms like Calanus finmarchicus becomes a model of efficiency and sustainability.

Positioned lower on the food chain, they utilize the energy directly from the primary producers, making them a more sustainable choice compared to species at higher trophic levels, where the energy has been substantially diminished through the chain of consumption.



In a world where many foodstuffs lose their natural essence through refinement, Zooca Calanus oil remains true to its origins. This return to unrefined lipid sources offers an array of benefits, echoing the profound advantages of whole foods in our diets.

These copepods have adapted to the harsh seasonal changes of the North Atlantic Ocean, hibernating on the sea floor during winter and resurfacing in spring to feed on the abundant blooming phytoplankton. This synchronization with the phytoplankton bloom, facilitated by their efficient energy storage in compact lipids, is crucial for their survival and reproduction.

Seizing the opportunity presented by this abundant resource, Zooca has established a model for sustainable harvesting of *Calanus finmarchicus* in the pure waters of Northern Norway. Their approach ensures minimal impact on the marine ecosystem while extracting valuable nutrients. The company innovates in processing *Calanus finmarchicus* into high-value products such as nutritional supplements, and aquaculture feed ingredients.

In a society increasingly aware of the implications of processing in our food and supplements, Zooca Calanus Oil presents a novel approach. Its extraction, favouring minimal intervention, stands in quiet contrast to more common methods that often involve solvents and multiple processing stages.

Due to the very short life span of the resource and its inherent purity, only enzymes and water are necessary to extract the finished oil.

The inherent potency of Zooca Calanus Oil is thus maintained, reflecting the shift towards valuing natural integrity and the reclaiming of less processed, purer forms of nutrition.

The science behind Zooca® Calanus® Oil

Through a series of preclinical and clinical trials it has become evident that Calanus Oil influences metabolic health through a complex interplay of mechanisms, which collectively enhance the body's metabolic state.

This action is not limited to a singular effector causing a single effect; rather, it involves various elements working synergistically across different areas.

Such comprehensive engagement not only boosts overall functionality but also has the potential to extend longevity, underscoring the interconnected nature of metabolic health and the multifaceted impact of Zooca Calanus Oil.

Studies with Calanus Oil and moderate exercise have shown that the body composition shifts to a more favourable distribution with a reduction in abdominal fat and an increase in lean body mass (4-7).

Fat oxidation

When the body has an improved ability to oxidize fat, several positive outcomes can occur, impacting health, energy levels, and physical performance. Here's an overview of what happens:

Reduced inflammation: An improved ability to oxidize fat can lead to reduced pressure on adipose cells (fat cells), which may in turn improve inflammation status in the body. Adipose tissue, particularly when excessive for obese and overweight, can become inflamed and contribute to the production of pro-inflammatory cytokines. By decreasing the size and number of adipose (fat) cells, the body can experience reduced adiposity, which is directly linked to lower inflammation levels.

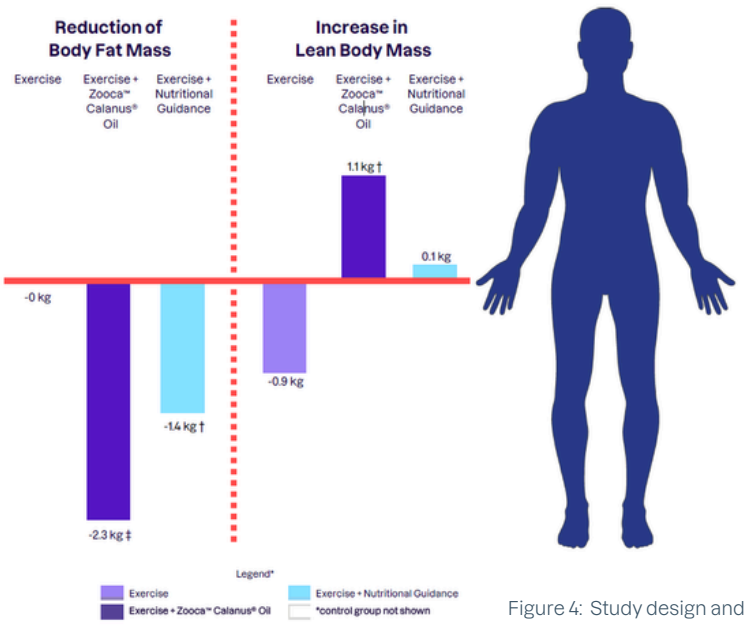


Figure 4: Study design and main findings reported by Wassertfurth et al 2020 (7-8)

This enhanced ability to oxidize fat plays a crucial role in weight management by effectively utilizing fat as an energy source, which can lead to a reduction in fat stores and support efforts towards weight loss or maintenance, assuming a balanced caloric intake. Moreover, improved fat oxidation is associated with a reduced risk of chronic diseases such as obesity, type 2 diabetes, and cardiovascular conditions. By promoting a healthier body composition and potentially improving metabolic markers like blood sugar levels and lipid profiles, it contributes to better overall health.

Another significant benefit is metabolic flexibility, which refers to the body's capacity to seamlessly switch between carbohydrates and fats as fuel sources depending on availability and demand. Improved fat oxidation enhances this flexibility, associated with better health outcomes, including lower risks of metabolic syndrome and type 2 diabetes.

Improved physical performance. The reason lies in the body's increased reliance on fat as a fuel source during long-lasting activities, which conserves glycogen stores and may boost endurance and overall performance. Additionally, the process of fat oxidation promotes a more efficient energy production mechanism. Since fat is a denser source of energy than carbohydrate, this may result in sustained energy levels over extended periods.

Study design	Randomized, controlled intervention with moderate exercise
Intervention	• Resting control group • Exercise twice a week, resistance and aerobic • Exercise + Nutrition Guidance • Exercise + 2 g Zooca Calanus Oil
Duration	12 weeks
Population	134 healthy, untrained 50-70 years

Table 1: key information clinical study, exercise and health

Adipose tissue and skeletal muscles: metabolically active organs

A greater reliance on fat for energy can help reduce fatigue and facilitate quicker recovery after physical activities. By conserving glycogen stores for when they are most needed, such as during high-intensity efforts, athletes may perceive less exertion during prolonged activities and recover more efficiently, as the body can better manage its energy reserves.

In summary, the ability to better oxidize fat leads to numerous benefits that encompass enhanced endurance, energy efficiency, effective weight management, reduced chronic disease risk, greater metabolic flexibility, and improved fatigue management and recovery, showcasing the comprehensive impact of this metabolic improvement on overall health and physical performance.

Skeletal muscles

The studies combining exercise and Zooca Calanus Oil supplementation (tables 1 and 3) further revealed enhancements in both skeletal muscle mass and strength (fig 5), underscoring the profound metabolic benefits of stronger and healthier muscles for overall health and well-being.

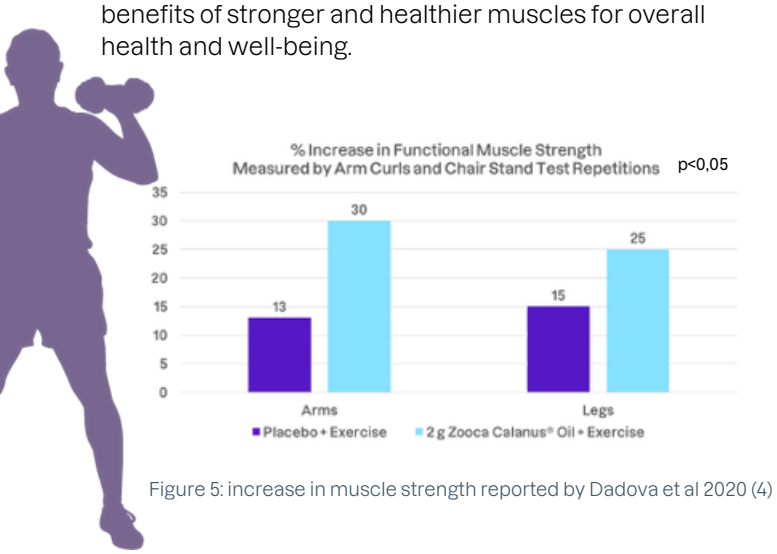


Figure 5: increase in muscle strength reported by Dadova et al 2020 (4)

These benefits extend across various facets of physical and metabolic health: Stronger muscles can better utilize glucose from the bloodstream, which in turn helps improve insulin sensitivity. This reduction in insulin resistance is crucial for preventing type 2 diabetes and managing blood sugar levels.

Muscles act as a reservoir for glucose in the form of glycogen. With more muscle mass, the body is able to store more glucose, again - underpinning the skeletal muscle's role of regulating blood sugar levels

Muscle tissue is a highly metabolically active organ, meaning it burns energy even when at rest.
By increasing muscle mass, the body oxidize more energy throughout the day, which can aid in weight management and reduce fat accumulation.

Stronger muscles improve the body's ability to burn fat for as fuel before using the glycogen - increasing the fat oxidation and consequently improving the metabolic flexibility

Longevity and Aging: Stronger muscles and regular physical activity are associated with longer life expectancy and a lower risk of dying from cardiovascular disease and cancer. Muscular strength is also crucial for maintaining quality of life and independence in older age.

Insulin sensitivity

The impacts of Zooca Calanus Oil on metabolic health have been rigorously assessed through intervention studies employing gold-standard methodologies. Specifically, insulin sensitivity and resistance improvements were quantified using the euglycemic clamp technique (figure 6, ref 9) , alongside the widely recognized Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and the Hepatic Insulin Resistance Index (HIRI) Figure 7, ref 10 . These measures collectively point to the multifaceted enhancements in insulin-mediated glucose regulation at both systemic and organ-specific levels.

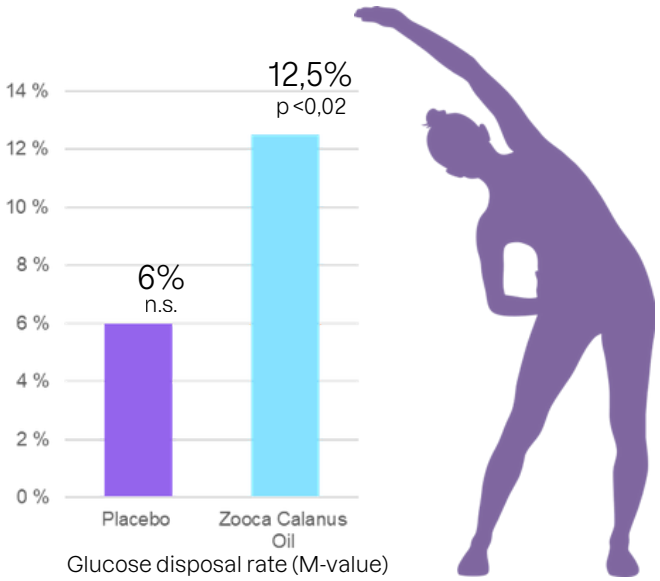


Figure 6: increase in insulin sensitivity reported by Brezinova et al 2019 (9)

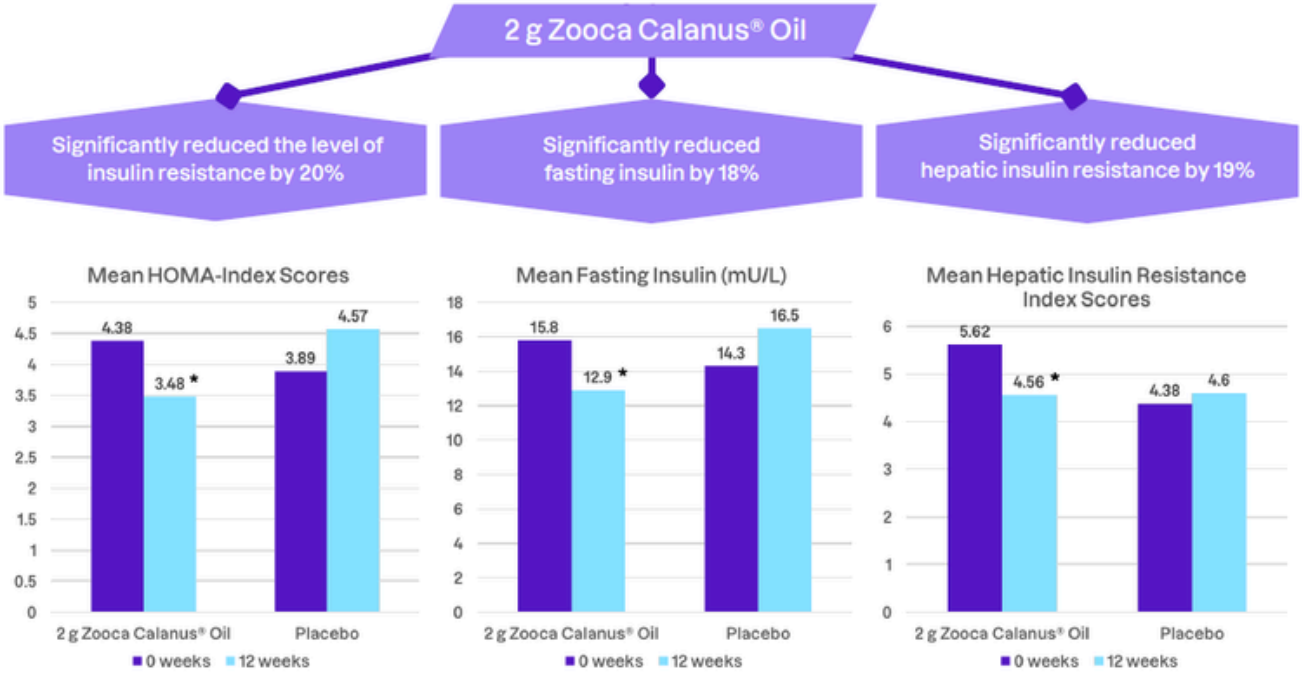


Figure 7: improved HOMA-index, fasting insulin and HIRI reported by Burhop et al 2022 (10)

Improved insulin sensitivity means that the body's cells are more responsive to insulin, the hormone critical for regulating blood sugar levels. This responsiveness enables the body to use insulin more efficiently, facilitating the uptake of glucose by cells for energy production.

This efficiency in glucose management has several beneficial metabolic effects. It may to better control of blood glucose levels. After eating, insulin help move glucose from the bloodstream into cells, particularly muscle and fat cells, to be used for energy or stored for future use. Improved insulin sensitivity makes this process more efficient, reducing the risk of high blood sugar levels that can damage blood vessels and organs over time.

In addition, improved insulin sensitivity is associated with a healthier lipid profile. These changes can reduce the risk of atherosclerosis, a condition characterized by the hardening and narrowing of the arteries, thereby lowering the risk of heart disease and stroke .

Table 2: key information clinical study, prevention of prediabetes

Study design	Double-blinded, placebo-controlled
Intervention	• Zooca Calanus Oil, 2g • Placebo, 2g
Duration	12-16 weeks
Population	64 healthy prediabetic participants

Individuals with improved insulin sensitivity typically have a lower risk of developing type 2 diabetes. Insulin resistance, where cells in the body do not respond well to insulin, leads to elevated blood sugar levels and is a key feature of type 2 diabetes. By enhancing the efficiency of insulin action, the likelihood of glucose accumulation in the blood is decreased, thus mitigating the risk of this condition.

Enhanced cellular response to insulin can help in regulating appetite and reducing excessive fat storage, making it easier for individuals to maintain a healthy weight or lose excess weight if necessary.

Overall, improved insulin sensitivity has profound effects on metabolic health, including better glucose and lipid regulation, reduced risk of type 2 diabetes, and support for healthy weight management.

These benefits collectively contribute to a lower risk of metabolic syndrome and cardiovascular diseases, highlighting the importance of lifestyle choices that promote insulin sensitivity.

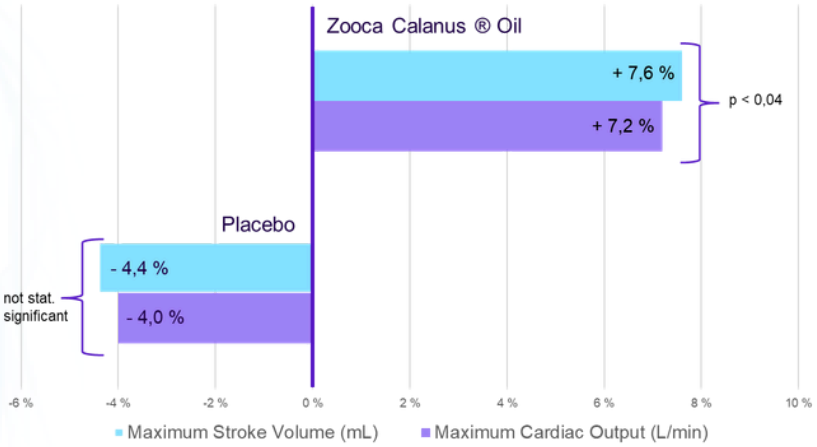


Figure 8: improved cardiodynamics reported by Stepan et al 2022 (6)

Improved cardiodynamics

The implications of improved cardiodynamics after 16 weeks of supplementation and exercise, as measured by a 7.6% increase in max stroke volume and 7,2% max cardiac output, can be significant in terms of cardiovascular health and overall physical performance (Fig 8, ref 6).

An increase in max stroke volume (the amount of blood the heart ejects with each beat) and cardiac output (the volume of blood the heart pumps per minute) indicates improved heart efficiency. This means the heart can pump more blood with each beat, supplying muscles and organs with more oxygen and nutrients without having to work harder. This is beneficial for overall cardiovascular health.

For individuals engaged in regular physical activity, improved cardiodynamics can lead to enhanced endurance and performance. A more efficient heart can sustain higher levels of activity for longer periods without fatigue, which is crucial for endurance sports and intense physical exercises.

Improved heart function can contribute to a lower risk of developing cardiovascular diseases. An efficient cardiovascular system can help in managing blood pressure, reducing the strain on the heart, and minimizing the risk of heart-related conditions such as heart failure, coronary artery disease, and stroke.

Improved cardiodynamics can also lead to better recovery after physical exertion. An efficient heart can more effectively remove metabolic waste products from muscles, reducing recovery time and enhancing the body's ability to adapt to physical stress.

An efficient cardiovascular system is crucial for longevity and a higher quality of life.

Study design	Double-blinded, placebo-controlled
Intervention	• Zooca Calanus Oil, 2,5 g + exercise 2x/week • Placebo, 2g + exercise 2x/week
Duration	16 weeks
Population	51 healthy women age 65-80 years BMI 35-30 kg/m2

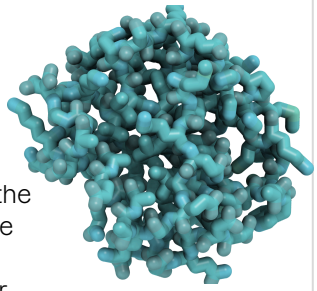
Table 3: key information clinical study, exercise and health elderly women

Sirtuins - regulators of metabolic pathways

Exercise-Induced Sirtuin Activation

The study described in Table 1 also measured the effect on the plasma sirtuin levels. All exercise groups showed a significant increase in the activities of SIRT1 and SIRT3 compared to the control group, which received no treatment (11) . This suggests that exercise alone can enhance the activity of these sirtuins, which are known to play roles in metabolic regulation and stress resistance.

The group that combined exercise with the intake of 2 g/day of oil from Zooca Calanus Oil not only showed increases in SIRT1 and SIRT3 activities but these increases were more pronounced than in the exercise-only group and the exercise plus nutritional guidance group. This indicates that Zooca Calanus Oil may have a synergistic effect with exercise on sirtuin activation



SIRT1 and SIRT3 are members of the sirtuin family of proteins, which are NAD+-dependent deacetylases involved in a wide range of cellular processes (12). These proteins are known for their role in regulating cellular health, metabolism, and longevity. Here are the main benefits associated with SIRT1 and SIRT3:

SIRT1

1. Metabolic Regulation: SIRT1 plays a crucial role in metabolic regulation, including glucose homeostasis and insulin sensitivity. It can help protect against metabolic syndrome, a cluster of conditions that increase the risk of heart disease, stroke, and type 2 diabetes.

2. Cellular Stress Response: SIRT1 promotes cellular survival by enhancing the response to oxidative and genotoxic stress, thereby contributing to cellular repair mechanisms and longevity.

3. Inflammation Reduction: It has been shown to suppress inflammatory pathways in the body, potentially protecting against various chronic diseases like cardiovascular disease, diabetes, and neurodegenerative diseases.

4. Neuroprotection: SIRT1 is involved in brain health, where it can protect against neurodegeneration by promoting neuronal survival and brain plasticity.

5. Longevity: By promoting DNA repair, reducing inflammation, and improving metabolic efficiency, SIRT1 activity is associated with increased lifespan in various organisms.

Sirtuins are a family of proteins that play critical roles in regulating cellular processes through deacetylation of proteins. They are known to be involved in various cellular functions, including aging, transcription, apoptosis (programmed cell death), inflammation, stress resistance, and energy efficiency.

Research on sirtuins has expanded greatly, suggesting their potential in treating age-related diseases, metabolic disorders, and even extending healthy lifespan. However, the exact mechanisms and effects of sirtuins are complex and still under intensive study.

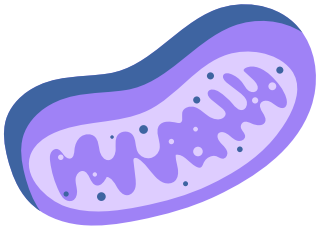
SIRT3

1. Mitochondrial Function: SIRT3 is primarily located in the mitochondria, where it regulates mitochondrial metabolism and energy production. It plays a key role in maintaining mitochondrial integrity and function.

2. Oxidative Stress Reduction: SIRT3 promotes antioxidant capacity by activating superoxide dismutase 2 (SOD2), which helps in reducing oxidative damage in cells.

3. Metabolic Regulation: Similar to SIRT1, SIRT3 has been implicated in the regulation of fatty acid oxidation, the tricarboxylic acid (TCA) cycle, and the urea cycle, contributing to overall metabolic efficiency and protection against metabolic diseases.

4. Aging and Longevity: SIRT3 has been linked to the aging process, where its activation is associated with increased lifespan and protection against age-related diseases, particularly those related to mitochondrial dysfunction.



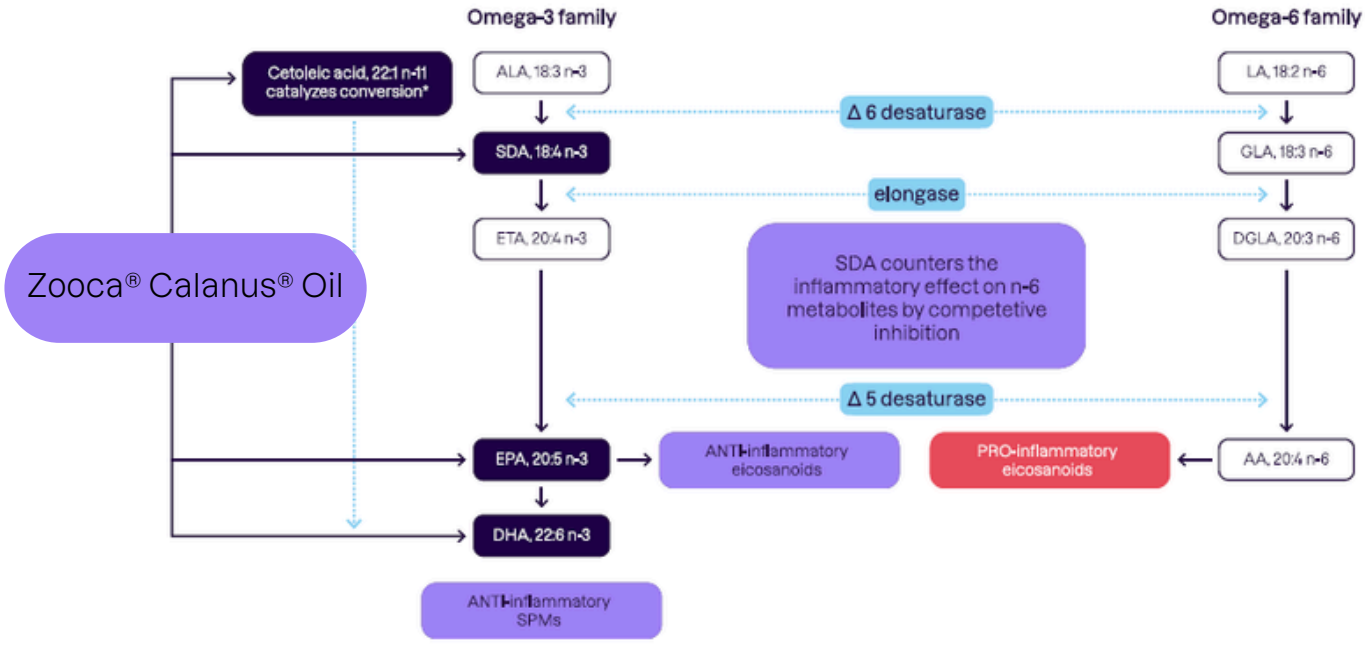


Figure 9: Metabolic pathways of omega-3 and 6-families and the fatty acids provided into the pathway from Zooca Calanus Oil

Omega-3 fatty acids

Bioavailability of the omega-3 fatty acids in Zooca Calanus Oil have been documented in several human studies (8,10,13-14). The bioavailability study showed that Zooca Calanus Oil gives a twofold uptake compared to ethyl esters, and is effective at increasing the omega-3 index compared to other omega-3 sources known to have superior absorption (figure 11, ref 13). The long-term evaluation of the incorporation of fatty acids in tissue by Zooca Calanus Oil supplementation has also shown a statistically significant decrease of the omega-6 fatty acid 20:4 n-6, arachidonic acid (AA)

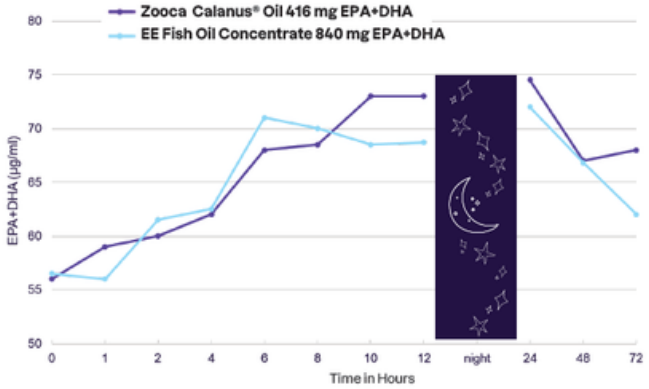


Figure 10 : Increase of plasma EPA +DHA from Zooca Calanus Oil and EE reported by Cook et al 2016 (12)

> *Wax Ester rich oil from the marine crustacean, Calanus finmarchicus, is highly absorbed and is a bioavailable source of EPA + DHA for human consumption*

Zooca Calanus Oil has the same anti-inflammatory benefits as other omega-3 sources, however offering additional potency by the reduction of low-grade inflammation through reduced body fat, as well as improvement of glucose tolerance. Stearidonic acid (SDA) also contributes to the anti-inflammatory potency by competing for the same enzymes, which is involved also in transformation of omega-6 fatty acids into proinflammatory arachidonic acid (Figure 9).

Very simplified; omega-6 derived metabolites are regarded as pro-inflammatory. In contrast, the omega-3 derivatives mostly promote anti-inflammatory effects. Furthermore, resolvins, protectins and maresins are families of highly potent mediators with inflammation-resolving properties, often referred to as Specialized Pro-Resolving mediators (SPMs), derived from omega-3 PUFA, adding to the insights of the important and diverse biological roles of these fatty acids (15).

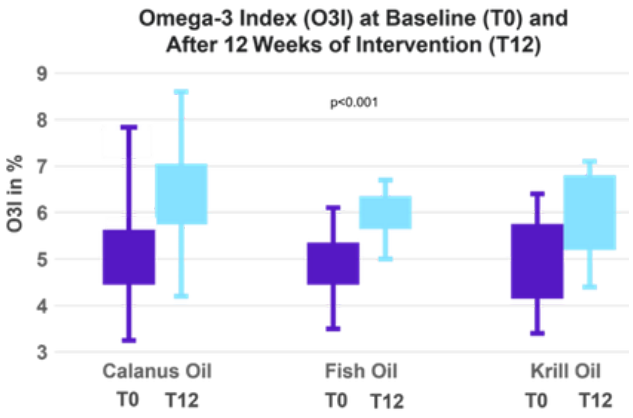
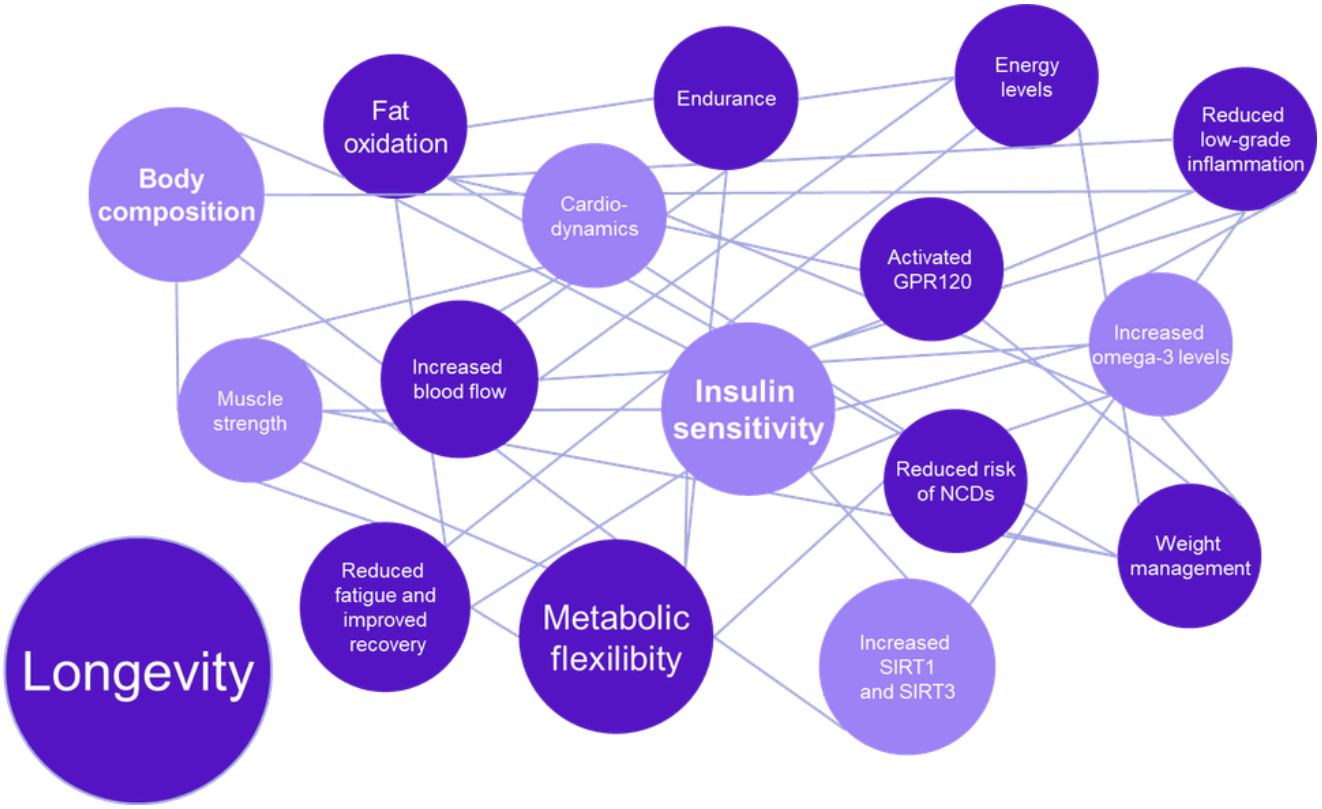
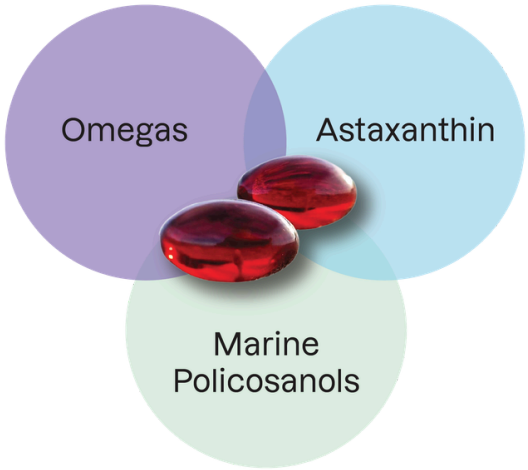


Figure 11 : Increase of omega-3 index by different lipid forms, reported by Vosskötter et al 2023 (13)



In conclusion, while the search for a "magic bullet" in nutrition may be a futile quest, the synergy found in Zooca Calanus Oil offers a compelling alternative, bridging together a unique composition of fatty acids, policosanols and astaxanthin.

It exemplifies how the intricate interplay of nutrients within whole foods can provide comprehensive health benefits, supporting the body in a way that isolated compounds cannot replicate. This synergy, rooted in the diversity and balance of nature, is where the true magic lies, offering a pathway to health that is both effective and in harmony with our biological heritage.



Pioneering the Biomarine Industry

Seizing the opportunity, the Norwegian company Zooca (Calanus AS) has developed a sustainable biomarine industry based on harvesting Calanus finmarchicus. Located in the Arctic region of Northern Norway, the company has established a model for sustainable harvesting and utilization of this resource. Their approach ensures minimal impact on the marine ecosystem while extracting valuable nutrients.

The range of products derived from Calanus finmarchicus extends from nutritional supplements for human consumption to key ingredients for aquaculture feeds. Demonstrating an unwavering commitment to sustainability, the company employs environmentally responsible harvesting and processing techniques, conducting comprehensive research across the entire value chain. This approach encompasses every stage, from the initial harvesting through to the production process, and culminates in rigorous documentation of the finished ingredients. By ensuring sustainability at each step, Zooca® not only protects marine ecosystems but also guarantees the highest quality and ecological integrity of their products.

Global Significance

The work of Zooca® is not just a business venture; it represents a shift in how marine resources are viewed and utilized. By focusing on a species such as Calanus finmarchicus, which has a high reproductive rate and significant biomass, the company is setting a precedent for sustainable marine resource management. This approach could pave the way for other biomarine industries to explore similar sustainable practices.

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