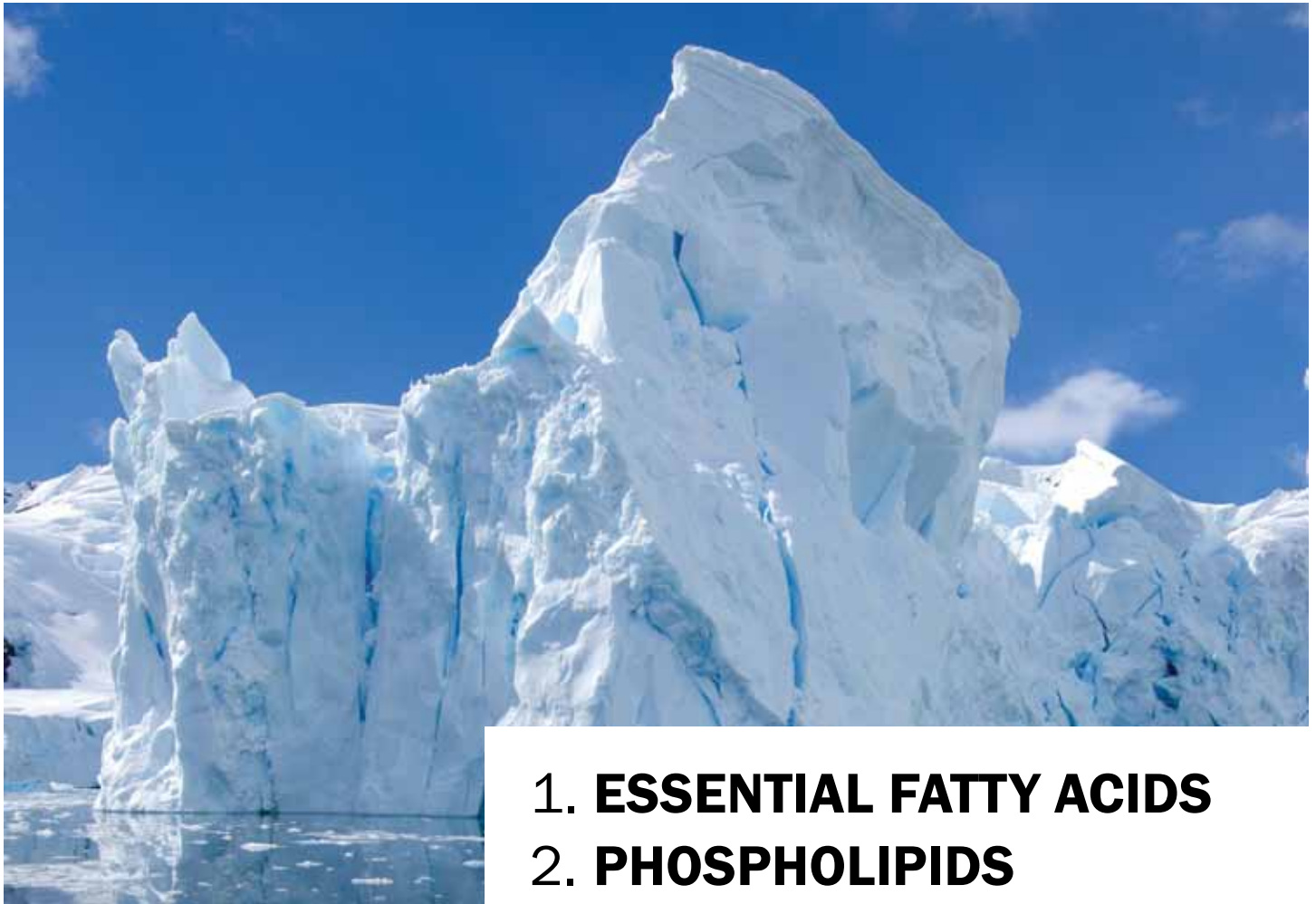


EDUCATIONAL SERIES:

KRILL OIL: BACKGROUND AND BENEFITS

by K. Maresz, PhD; K.Meus; B. Porwolik



- 1. ESSENTIAL FATTY ACIDS**
- 2. PHOSPHOLIPIDS**
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INTERNATIONAL
SCIENCE AND HEALTH
FOUNDATION

Phospholipid EPA & DHA

Essential Building Blocks for Life

Overview

Until recently, cognitive disorders, heart disease and memory problems were assumed to be non-related. Now, we know there is one factor that they may have in common: a deficiency in essential fatty acids (EFAs), particularly, EPA and DHA - two forms of omega-3 fatty acids, which are important for developing and maintaining cellular health.

Krill oil supplementation is a highly beneficial way to acquire these vital nutrients. Not only is it a rich source of EFA components, but it's also purer and more tolerable than marine alternatives.

Krill (*Euphausia Superba*) are small crustaceans that resemble shrimp, and are the most abundant biomass in the sea. Krill are found in all oceans of the world and in abundance in the Antarctic Ocean. They are a key species in the Antarctic ecosystem and feed directly on the phytoplankton (algae), which is a source of oil and protein.

Antarctic krill is a rich source of long-chain polyunsaturated fatty acids (LC-PUFAs); particularly in two forms of omega-3 that are necessary for all known life: the aforementioned eicosapentaenoic acid (EPA) and docosahexaenoic (DHA). With krill oil supplements these are delivered to the body in the desirable phospholipid form. Phospholipids are key components in cell membranes that are responsible for cellular transport and cell recognition.

Krill oil has been proven to be a superior source of omega-3 EPA &

DHA for several reasons. Because of the very low levels of contaminants in the Antarctic Ocean, krill is virtually free of heavy metals and mercury. Moreover, it is a renewable, abundant, and sustainable source. Krill oil may be considered as an essential part of a healthy daily lifestyle.

Numerous studies have identified the antithrombotic, antiarrhythmic, antiatherosclerotic, and anti-inflammatory mechanisms associated with an increase in krill oil omega-3 fatty acid consumption.

Furthermore, Antarctic Krill oil contains a powerful antioxidant ca-

rotenoid known as astaxanthin that helps prevent oxidation of the omega-3 fatty acids.

The omega-3 in krill oil has been shown to relieve the emotional and physical problems associated with post menstrual syndrome.¹

Krill oil has been shown to regulate blood lipids to healthy levels; to increase good cholesterol (HDL) while decreasing bad cholesterol (LDL),² and to reduce fat content in the heart and liver.^{3,4} Omega-3 found in krill oil has also been shown to improve chronic inflammation.⁵

Krill Oil* composition

KRILL OIL INGREDIENTS	QUALITIES AND EFFECTS
Omega-3 & Omega-6	<ul style="list-style-type: none">• Phospholipid - Bound Omega-3• Recognized health benefits
Phospholipids	<ul style="list-style-type: none">• Safe, effective and stable marine phospholipids• The best source of EPA, DHA• Phospholipids are the building blocks of cell membranes• Are readily absorbed• No aftertaste or repeating
Antioxidants	<ul style="list-style-type: none">• Contains astaxanthin• Natural, no additives
General	<ul style="list-style-type: none">• Phospholipids are more bioefficient than triglycerides• Rich in antioxidants/fights free radicals• Free from heavy metal contamination• Benefits the heart, joints and brain• Does not contain preservatives• Safe and pure

* Tests carried out on Superba™ Krill Oil

1. Essential fatty acids

Fat is necessary for life and good health. The human body actually needs fat to function properly: fat provides energy, insulation from the cold and the heat, absorbs vitamins (A,D,E,K), gives food flavor and texture, protects organs and bones from shock, helps transmit nerve impulses, and transports nutrients and metabolites across cell membranes. It is also used to synthesize a

way to obtain them is through the diet.

There are two types of essential fatty acids: omega-3 and omega-6. What distinguishes these two acid forms from each other is the location of the double bonds (Fig 1).

Consumption of essential fatty acids is fundamental for the healthy



Fig 1. Essential fatty acids. In the omega-3 fatty acids, the first double bond is located in the 3-position, whereas in the omega-6 fatty acids, the first double bond is located in the 6-position from the methyl end. Blue = oxygen; red = carbon; gray = hydrogen.

variety of building blocks and signal molecules needed by every cell and every process, from DNA and hormones to immune defense.

growth, proper functioning and long lifespan of each single cell within the body. In fact, research suggests that EFAs play an important role in the prevention and treatment of coronary artery disease, hypertension, diabetes, arthritis, and other inflammatory and autoimmune disorders.⁶

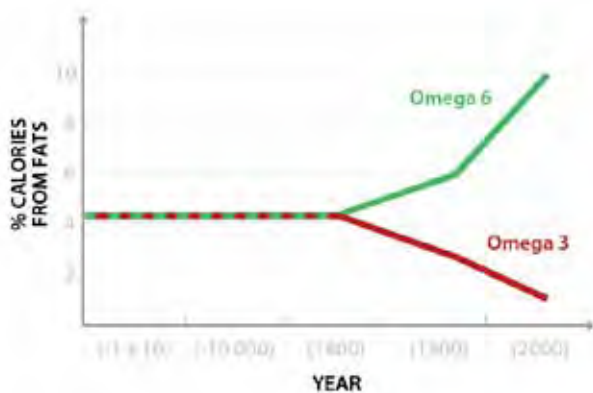


Fig 2. Changes in the omega-3 to omega-6 ratio.

Fat is required for all vital processes occurring within the body.

But there is one type of fat that our body can't produce by itself: **essential fatty acids (EFAs)**.

EFAs or “good fats,” are long-chain polyunsaturated fatty acids. They are crucial for health and the only

patterns, resulting in a higher intake of omega-6 and a dropped consumption of omega-3 fatty acids (Fig 2). Scientific estimates in Western cultures suggest that a ratio of omega-6 to omega-3 fatty acids switched from 1-4:1 to 10-30:1. The frequent consumption of highly processed food is the biggest reason for this change.

FACTS ABOUT KRILL

Krill, also known as *Euphausia Superba*, is a miniature, shrimp-like marine crustacean, commonly found in cold-water oceans. Its name comes from the Norwegian word meaning “young fry of fish”. Antarctic krill is also termed as the power house of the Antarctic ecosystem.

There are as many as 85 types of krill in the world's oceans and they live anywhere from right near the surface to miles below it. The approximate 750



million tons of krill is the largest biomass on the earth.

Antarctic krill lives only in a pure environment – unlike fish, which may be contaminated with mercury and heavy metals. And it can glow, emitting light produced by bioluminescent krill organs.

It may be said that Antarctic Krill is eco friendly – its waste, containing significant amounts of carbon derived from atmospheric carbon dioxide, sinks to the bottom of the sea, some 2,000–4,000m down. This process exports large quantities of carbon from the biosphere and sequesters it for about 1,000 years - helping to limit the extent of global warming.

Krill oil is recognized as a healthy ingredient not only on earth - it has also conquered the outer space market, becoming a novel space food. The beneficial activity of krill caught NASA Food Technology Commercial Space Center's interest and krill oil became a standard element of an astronaut's diet. Now NASA spaceship crews enjoy health benefits from this extremely rich source of omega-3 fatty acids.

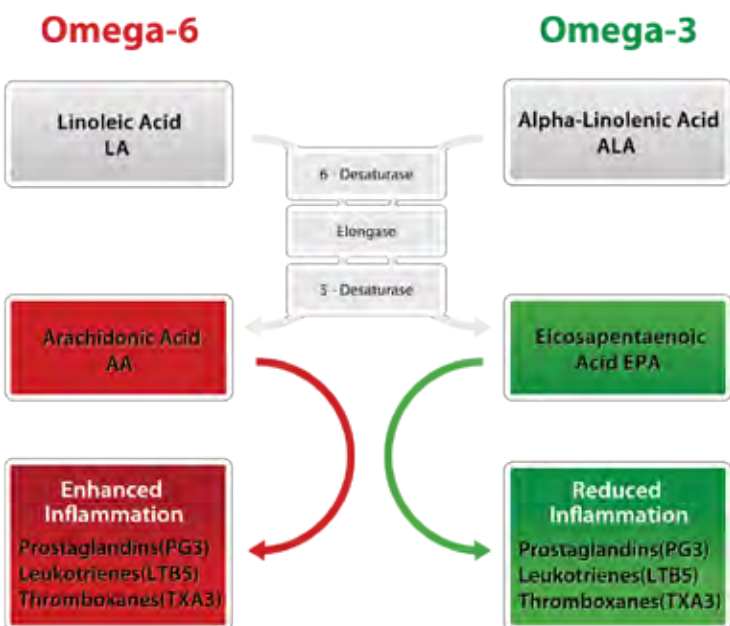


Fig. 3 Conversion of omega-3 and omega-6 fatty acids in the human body. Omega-6 fatty acids are a source of inflammatory eicosanoids, whereas omega-3 fatty acids are a source of reduced-inflammatory eicosanoids.

The average American diet provides more than 7 times the proper amount of omega-6. Moreover, obtaining enough omega-3 fatty acids has become very difficult for Western societies, primarily due to a growing consumption of processed food. Omega-6 is found in the primary oils added to most processed foods.

For optimal health, the proper ratio of omega-6 to omega-3 should be 4:1, respectively.²¹

When too much omega-6 is consumed, the balance between essential fatty acids is disturbed, the body produces too great of a number of pro-inflammatory molecules called eicosanoids. These molecules can have positive influences on health when derived from omega-3. But when they originate from omega-6, they cause serious troubles, such as increased blood clotting, impaired immune response, and systemic inflammation (Fig 3).

2. Phospholipids – the optimal form of essential fatty acids

Omega-3 fatty acids exist mainly in two different forms – triglycerides or phospholipids. Both have a backbone built of glycerol, and long 'tails' made of fatty acid chains. But here the structural similarities end.

Phospholipids are different in one important aspect. Instead of 3 elements in their tail, they have only 2 fatty acid chains, and an additional phosphate group which is negatively charged (Fig.4) and connected with glycerol by a "polar" covalent

DIETARY SOURCES OF ESSENTIAL FATTY ACIDS

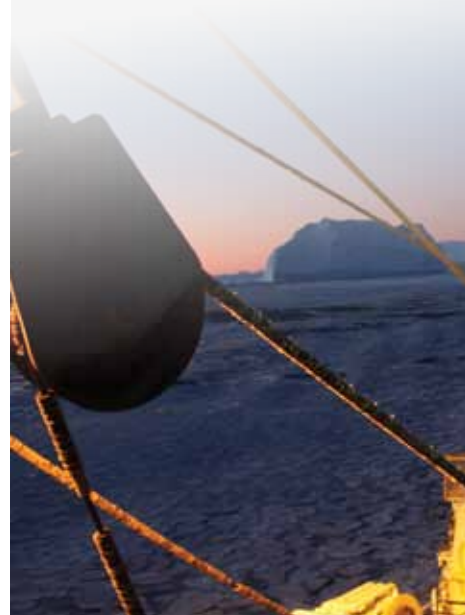
Omega-3 exists in different forms. First of them, ALA (alpha-linolenic acid) is found in vegetable sources such as:

- flaxseeds
- flaxseed oil
- canola (rapeseed) oil
- soybeans and soybean oil
- pumpkin seed oil
- perilla seed oil
- tofu
- walnuts, and walnut oil

Omega-3 is also found in two marine forms. They are EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) found primarily in cold-water fish, such as:

- salmon
- mackerel
- lake trout
- herring
- sardines
- albacore tuna

... and krill oil. Theoretically, our body is able to convert ALA into the more important forms – EPA and DHA. However, the conversion is not efficient enough to satisfy even the basic needs of all cells and tissues.



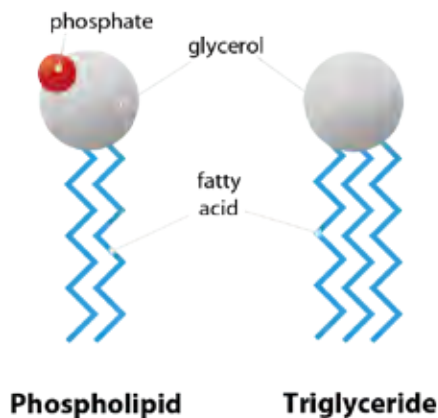


Fig. 4. Structural differences between phospholipids and triglycerides. A phospholipid molecule consists of a hydrophilic polar head group and a hydrophobic tail.

bond. This means that one end of the molecule is charged negatively, i.e. polar; and the other end, where fatty acids are present, is neutral, i.e. non-polar.

Due to this dual structure, phospholipids are able to mix with water (by forming micelles) unlike other fats.

The two forms differ in chemical structure and distribution routes within the body. Scientific data suggests that phospholipids present better bioavailability for cells and tissues in the human body.

Unlike triglycerides, phospholipids do not need bile salt in order to be digested. They are also better tolerated in the stomach. Phospholipids are water dispersible. They do not flow on the surface of stomach content, but mix in with stomach fluids, reducing the chance of a fish after-taste.

By contrast, triglycerides are water insoluble and require emulsification by bile salts via the formation of micelles.

Increased transport and utilization of omega-3 by various tissues has been scientifically proven, when delivered via phospholipids. Fatty acids from dietary phospholipids are absorbed by the brain twice as efficiently as fatty acids from triglycerides in infants.⁷

Phospholipids are superior in one more area. A look at the microscopic world of human cells solves this mystery. Phospholipids are tightly linked with physiological tasks performed within the body. Because of how they function, phospholipids are the preferred source of omega-3.

Simply put, each cell consists of a nucleus surrounded by fluid and protected by a membrane, which keeps the cell's content inside and foreign elements outside of the cell. The membrane is like a mosaic made up of many different molecules such as integral proteins, peripheral proteins, glycoproteins, phospholipids, glycolipids and cholesterol. The membrane is not impenetrable - otherwise the transport of nutrients and waste to and from the cell would not be possible.

Phospholipids are crucial for the proper functioning of the cell membrane. They create a double layer, interspersed with proteins, that is essential for cellular transport and cell recognition.

In other words, phospholipids function as cellular "gate-keepers." They are not only highly bioavailable and bioefficient, but are simply, essential for all life.

DEFICIENCY

Dietary imbalance between omega-6 and omega-3 fats may explain the rise of such diseases as asthma, coronary heart disease, many forms of cancer, autoimmunity and neurodegenerative diseases. All are believed to stem from inflammation in the body. The imbalance between omega-6 and omega-3 fatty acids may also contribute to arthritis, allergies, obesity, depression, dyslexia, diabetes, hyperactivity, inflammatory diseases, and even violent tendencies.

Both the omegas also affect the status and the general competence of the immune system and affect such things as resistance to infections. Therefore keeping balance between the two is crucial for health maintenance.

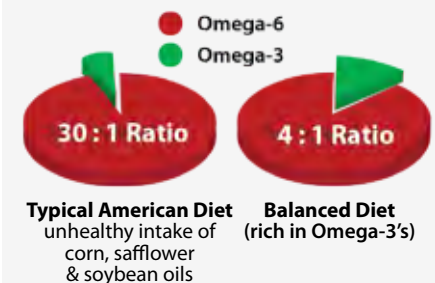


Fig. 5. Omega-3 and omega-6 content in food – comparison of typical American diet and healthy nutrition.

3. Scientifically proven benefits

Better heart protection

Cardiovascular diseases (CVD) may lead to heart failure and, eventually, death. It is a big threat because it develops slowly, over decades, usually with no visible signs of approaching danger. By the time the symptoms are detected, the underlying cause is already advanced and difficult to treat. Prevention is key: a healthy lifestyle and balanced diet helps avoid hyperlipidemia, whereas supplementation with omega-3 fatty



Fig. 6. Changes in blood lipids (LDL, HDL, TG) after Krill Oil supplementation (3,0 g/day)

acids supports ‘cleaning up’ the arteries.

Omega-3 fatty acids have been reported to reduce CVD risk through diverse mechanisms of balancing blood pressure and arrhythmia, soothing inflammation, reducing atherosclerotic plaque accumulation (as well as anti-thrombosis effect) promoting endothelial function,⁸ and lowering the lipid level in the blood stream.

High cholesterol is also a major risk factor of CVD development; too much cholesterol in the blood

stream can increase heart problems. High LDL cholesterol leads to a buildup of cholesterol in the arteries, and increases the risk of CVD. Human studies have revealed the ability of EPA and DHA to significantly reduce circulating levels of blood triglycerides and low-density lipoprotein (LDL), or “bad cholesterol.”

The effect of krill oil on hyperlipidemia was investigated in a recent clinical trial. The study was performed on a group of patients diagnosed with mild to high levels of cholesterol and triglycerides. During the trial, patients received supplements with krill oil or fish oil, and the control group received placebo. Krill oil reduced the level of circulating triglycerides significantly, compared to fish oil and placebo. Furthermore, krill oil appeared to have greater impact on total cholesterol levels. The results of this study demonstrated that krill oil is effective in managing hyperlipidemia by reducing total cholesterol, LDL, and triglycerides while increasing levels of HDL (good cholesterol).⁹

Healthier joints

Recent evidence has shown that omega-3 fatty acids have anti-inflammatory properties; and that krill oil may be effective for the management of arthritic symptoms.

Krill oil supplementation, in a mouse model of arthritis, has shown beneficial effects on inflammation processes in joint tissue as it suppressed the development of collagen-induced arthritis (CIA).

OMEGA-3 INDEX

The omega-3 index is a reliable diagnostic tool that presents the combined EPA and DHA concentration as a percentage of total fatty acids in red blood cells. The graph (Fig.7) shows that the participants in one study performed by Aker BioMarine started out with an average omega-3 index of 2.0, a relatively low value. After 8 weeks with daily intake of 2g Superba™ Krill Oil, the average index increased to 4.5, or by 125%. An increase of 45% in the omega-3 Index was seen already after 2 weeks. These observations verify that omega-3 from Superba™ Krill Oil is taken up from the gut to the blood stream and that it is incorporated into cells.

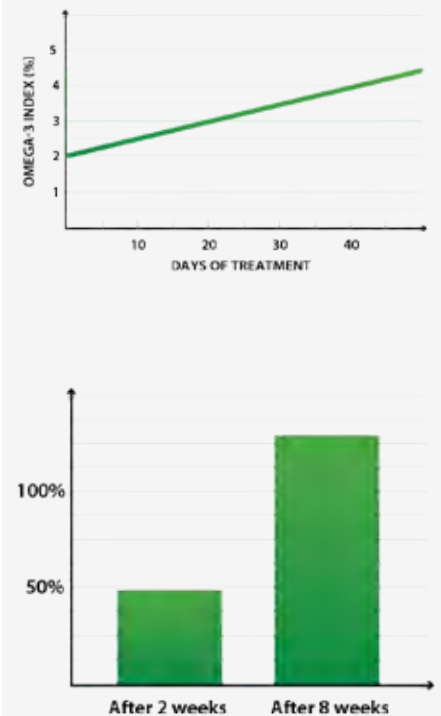


Fig. 7. Superba Krill more than doubles the omega-3 index (level of omega-3 in the red blood cells)

Krill oil was shown to reduce the arthritis scores and hind paw swelling when compared to a control diet not supplemented with EPA and DHA. Mice supplemented with krill oil presented lower infiltration of inflammatory cells into the joint compared to control animals. In conclusion, krill oil provided inhibition of arthritis scores and joint pathology in the CIA model.¹⁰

The effectiveness of krill oil was further investigated on arthritic symptoms in a human clinical trial. The study was performed on patients with confirmed cardiovascular disease and/or rheumatoid arthritis and/or osteoarthritis and with increased levels of C-reactive protein (CRP). The results clearly showed that krill oil significantly inhibited inflammation and reduces arthritic symptoms within a short treatment. Moreover, the group of patients treated with krill oil demonstrated a significantly lower consumption of classic non-steroidal anti-inflammatory drugs (NSAIDs).

This finding becomes even more significant due to the side effects of NSAIDs detectable among patients with chronic inflammatory diseases.

Omega-3 phospholipids might decrease the production of inflammatory mediators such as eicosanoids and cytokines. This clinical trial revealed that krill oil is safe and effective in reducing inflammation and may be used for example in joint inflammatory disorders.¹¹

Improvement in brain functions

Omega-3 has also been shown to improve brain function and memory due to its unique composition of phospholipids. Simply said, DHA is necessary for brain cells to communicate.¹² It is especially important for the proper development of the brain in the fetus and in young children.¹³

Moreover, DHA increases the production of two hormones, serotonin and dopamine. Increasing the level of the two hormones might improve the quality of life - in a natural way.

Increased memory abilities and more efficient learning were found linked with additional krill oil supplementation. Moreover, recently collected data from a clinical study presented an improvement in con-

THE OPTIMAL FORM OF OMEGA-3

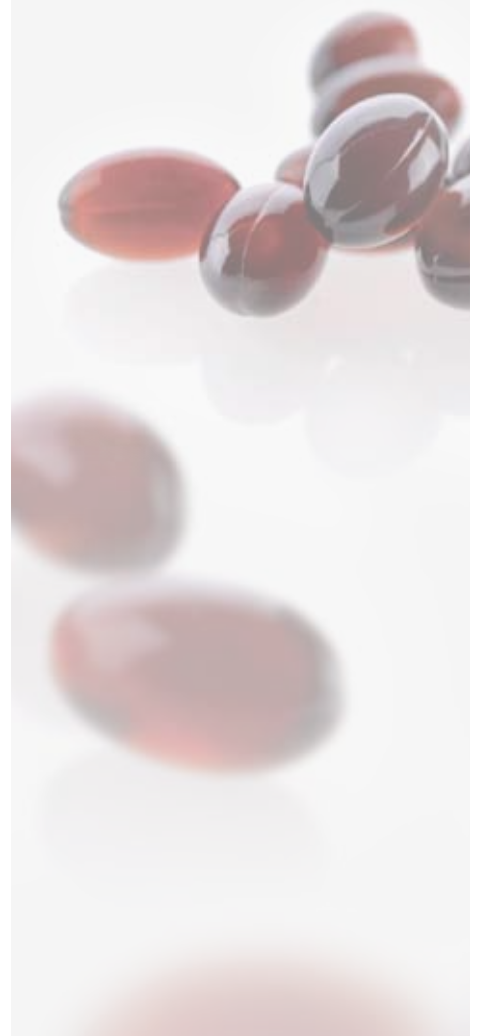
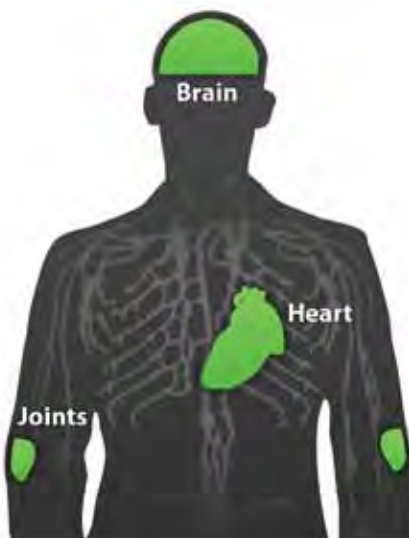
Phospholipids are a natural and integral part of cell function, as they are structural components of the cell surface membranes and the membranes within the cells.

Phospholipids are closely connected with liver function and nervous system function. Phosphatidylcholine is predominant within this important group of lipids. It has also become clear that phosphatidylcholine is needed to help avert high blood cholesterol levels, and also glucose uptake and glycogen synthesis.

Studies show that human cells **will readily absorb 95-98% of phospholipids.**

Omega-3 functions within the body

- Supporting central nervous system development
- Improvement of cognitive function
- Reducing the risk of cardiovascular diseases
- Lowering and balancing blood pressure levels
- Inhibition of inflammation
- Preventing certain cancers
- Improving skin health



centration and planning abilities after krill oil treatment.¹⁴

Krill oil is essential for brain health because it takes care of its appropriate structure and supports vital functions of the nervous system. Krill oil has been tested in many clinical trials that clearly confirmed its potency and contributory effect on human health. With no adverse events reported, it's safe for humans. And since the brain acts as a specific command center for other organs, krill oil is essential for the healthy functioning of the whole body.¹⁵

Fighting obesity

It appears that an increased intake of omega-3 krill oil can help support weight loss programs.

Research shows that polyunsaturated fatty acids improve the activity of fat burning enzymes and reduce the activity of lipid-synthesizing enzymes. A combination of weight loss and omega-3 supplementation helps reduce the risk of cardiovascular disease and diabetes risks by increasing adiponectin and reducing triglyceride concentrations.¹⁶

Moreover, a reduction in cholesterol and blood glucose has been observed in animal obesity models. Collected results demonstrated that dietary krill oil is effective in improving metabolic parameters in mice fed a high-fat diet, suggesting that it may be of therapeutic value in patients.⁴

A diet enriched with krill oil results in changes in membrane fatty acid composition. The reduction of substrates for inflammatory molecules and endocannabinoids may account for the inhibited inflammatory re-

sponse and the physiological re-equilibration of body fat deposition in obese rats.³

Tests proved that krill oil supplementation increased plasma EPA and DHA and was well tolerated, with no indication of adverse effects on safety parameters.¹⁷

PMS

PMS (Premenstrual Syndrome) is characterized by a set of hormonal changes that trigger disruptive symptoms in a significant number of women for up to two weeks prior to menstruation.

Tests were conducted with the use of krill oil supplementation in order to evaluate whether omega-3 is able to manage PMS.

Studies have shown that phospholipid molecules play an important role in membrane fluidity, which may be the most crucial activity in the management of emotional symptoms.

After a treatment period of 3 months, patients noticed significant improvement in the physical and emotional symptoms of PMS due to the consumption of krill oil.¹⁸

4. Bioavailability

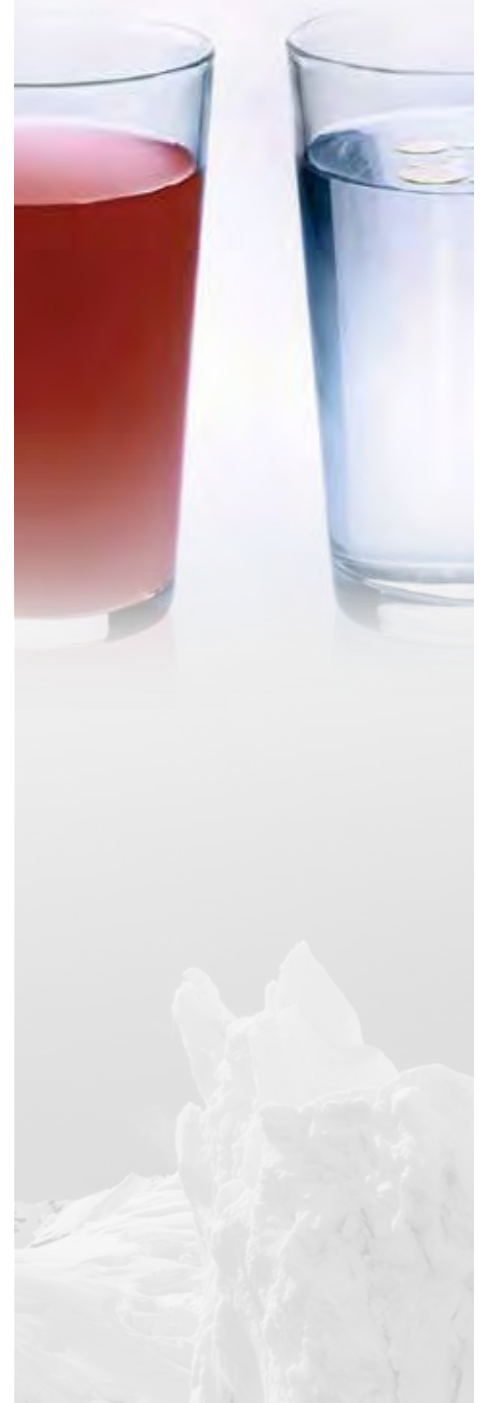
Bioavailability refers to the extent to and rate at which the active component enters systemic circulation.

Assessing bioavailability of a component is largely determined by the properties of the dosage form (which depend partly on its design and manufacture), rather than by the components' physicochemical properties, which determine ab-




PHOSPHOLIPIDS

Unlike triglycerides, phospholipids do not need bile salt in order to be digested. They are also better tolerated in the stomach. Phospholipids are water dispersible. They do not flow on the surface of stomach content, but mix in with stomach fluids, reducing the chance of a fish aftertaste.

By contrast, triglycerides are water insoluble and require emulsification by bile salts via the formation of micelles.



OMEGA-3

CARDIOVASCULAR HEALTH 	JOINT HEALTH 	BRAIN HEALTH 
<ul style="list-style-type: none"> • Balancing blood pressure and arrhythmia • Lowering levels of TG and "bad" cholesterol in the blood stream • Soothing inflammation • Reducing atherosclerotic plaque accumulation • Inhibition of thrombosis • Promotion of endothelial function 	<ul style="list-style-type: none"> • Soothing inflammation • Reduction of inflammatory markers such as CRP • Reduction of arthritic symptoms such as stiffness, pain and functional impairment • Lowering the consumption of NSAIDs in arthritic patients 	<ul style="list-style-type: none"> • Modulates brain development • DHA is necessary for proper brain cells communication • DHA increases the production of two hormones: serotonin (hormone of happiness) and dopamine (neurotransmitter) • Effective in the treatment of ADHD in adults • Improves concentration • Improves planning and social skills

sorption potential. Differences in bioavailability among formulations of a given component can have clinical significance; therefore, knowing whether component formulations are equivalent is essential.

Bioequivalence indicates that the component, when given to the same patient in the same dosage regimen, results in equivalent concentration in plasma and tissues.

Single dose absorption study in humans*

The goal of the study was the comparison of the 72 hour pharmacokinetic profiles of EPA, and DHA, after single doses of Superba™ Krill Oil (8g), omega-3 enriched fish oil (8g) and Superba™ Krill Powder (8g).

The study demonstrated better bioavailability and superiority of EPA in

Superba™ Krill Oil than in omega-3 enriched fish oil.

Multi dose absorption study in humans*

A randomized clinical trial assessed changes in EPA and DHA in phospholipid membranes after eight weeks of daily intake of 2g Superba™ Krill Oil or 2g omega-3 enriched fish oil in healthy male and female subjects.

The study demonstrated that a steady state in EPA levels, omega-3 index, and DHA levels were attained earlier after Superba™ Krill Oil compared to omega-3 enriched fish oil.

After Superba™ Krill Oil administration, the mean serum insulin level decreased, whereas the mean adiponectin level increased. The study products were proved to be safe and

well-tolerated.

* Data not published

5. Safety aspects

Currently there are no known toxicity levels for krill oil. Antarctic krill lives in a naturally clean environment, devoid of pollution, so there's significantly less risk of heavy metals contamination. Superba™ Krill Oil has undergone extensive in vitro, in vivo and human studies to determine its safety and lack of toxicity. In a recently published human study with 76 men and women, four weeks of krill oil supplementation increased plasma EPA and DHA and was well tolerated, with no indication of adverse effects on safety parameters.¹⁹ People with known allergies to crustaceans (shrimp, crab, lobster etc) should not use krill products.

6. Stability

The stability of omega-3 products and the susceptibility to oxidation of omega-3 fatty acids are well-known challenges to those working with marine omega-3 oils.

Krill Oil has a high content of omega-3 phospholipids and the naturally occurring antioxidant astaxanthin.²⁰

Scientific studies have shown that the omega-3 fatty acids bound to phospholipids from krill are far less prone to oxidation than omega-3 fatty acids in traditional triglyceride form. The powerful antioxidant astaxanthin gives additional protection to the omega-3 fatty acids and prolongs product shelf life. Astaxanthin helps inhibit fatty acid oxidation and thereby secures a more stable oil product.

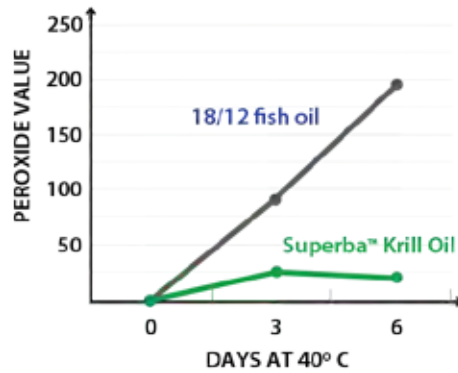


Fig. 8. In this study, Superba™ Krill Oil and 18/12 fish oil were kept at 40°C for 6 days. An increase in peroxide value is seen upon oxidation of fatty acids in the products under examination. The curves show that no oxidation occurred in the Superba Krill Oil test samples; 18/12 fish oil did not demonstrate this resistance to oxidation



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International Science and Health Foundation.

About Superba™ Krill

Superba™ Krill is a pure, natural source of the health-promoting EPA & DHA omega-3 essential fatty acids and the naturally occurring antioxidant astaxanthin. The uniqueness of Superba Krill is that the omega-3 fatty acids are provided in phospholipid form. In vitro, in vivo and human clinical research has demonstrated the safety and efficacy of Superba Krill. www.superbakrill.com

About Aker BioMarine

Aker BioMarine is an integrated biotechnology company dedicated to the sustainable harvesting of krill and development of krill-derived biotech products. The company supplies biomarine ingredients through an optimized value chain from raw materials to customers. Aker BioMarine's Superba™ Krill products are provided with 100-percent traceability from the Antarctic Ocean to the end user. Aker BioMarine is the only krill harvester that has been awarded Marine Stewardship Council (MSC) Certification. www.akerbiomarine.com