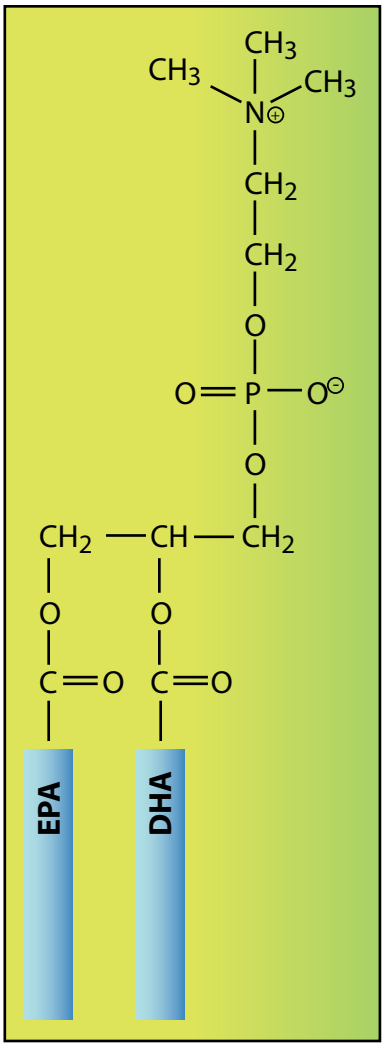
# Krill Oil Monograph




Phosphatidylcholine with EPA and DHA comprising the two fatty acid tails

## Introduction

Krill are small red-colored crustaceans, similar to shrimp, that flourish in the extremely cold waters of the Antarctic Ocean. Their survival in such a frigid environment is attributable to krill having a high content of long-chain polyunsaturated fatty acids (LCPFAs), including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), attached to their cell membranes via phospholipids (primarily phosphatidylcholine). This structure provides optimum membrane fluidity in cold temperatures and an ideal source of omega-3 fatty acids. Animal and human studies indicate LCPFAs bound to phospholipids (PLs), like those found in krill oil, have better absorption and delivery to the brain than their methyl ester or triglyceride-formed fish oil counterparts.[1-3] Unlike fish oil, krill oil contains a potent antioxidant carotenoid, astaxanthin, that helps prevent LCPFA oxidation.[4] Preliminary human studies indicate krill oil may be superior to fish oil in the reduction of premenstrual syndrome (PMS) complications[5] and biomarkers of dyslipidemia.[4] Krill oil consumption has also shown a positive effect on markers of inflammation.[6]

## Biochemistry

Krill oil is composed of 40-percent PLs (primarily phosphatidylcholine), 30-percent EPA and DHA, astaxanthin, vitamin A, vitamin E, various other fatty acids (FAs), and a novel flavonoid similar to 6,8-di-C-glucosyl luteolin.[4] The structure of the primary constituent in krill oil appears to contain choline, glycerophosphate, and the FAs EPA and DHA, esterified to astaxanthin and the 6,8-di-C-glucosyl luteolin-like flavonoid, respectively.[6]

## Pharmacokinetics

Comparison of animal and human studies demonstrates the absorption of phospholipid-bound LCPFAs is superior to non-phospholipid-bound fish oils. A primate study demonstrated that twice as many phospholipid-bound FAs accumulated in the brain compared to triglyceride-bound FAs.[1] Another animal study found phospholipid-bound LCPFAs elevated brain DHA levels more than fish oil.[2]

A human trial examining the response of both overweight and obese patients to LCPFA supplementation showed that daily doses of 216 mg EPA and 90 mg DHA from krill oil provided more profound FA elevations than daily doses of 212 mg EPA and 178 mg DHA derived from fish oil. At the end of the four-week trial, mean plasma EPA levels were 377 µmol/L in the krill oil group, compared to 293 µmol/L in the fish-oil group. Although the krill supplement provided half as much DHA as the fish oil, the plasma DHA was 476 µmol/L in the krill oil

group and 478 µmol/L in the fish oil group at the end of the month-long trial.[3]

## Mechanism of Action

Most of krill oil's health benefits are attributed to its high EPA and DHA content. Numerous studies have identified the antithrombotic, antiarrhythmic, antiatherosclerotic, and anti-inflammatory mechanisms associated with an increased consumption of these omega-3 fatty acids.[7-9] More studies are needed to determine whether phosphatidylcholine and astaxanthin provide an additive effect.

Phosphatidylcholine by itself has shown promise as a dietary supplement to improve homocysteine status, liver disorders, and respiratory distress.[10]

Astaxanthin may have independent positive effects due to its antioxidant capabilities. When oxygen radical absorptive capacity (ORAC) values of various antioxidants were compared, astaxanthin was found to be 34-times more effective than CoQ10 and 48-times more effective than fish oil.[11]

## Clinical Indications

### Dyslipidemia

In the late 1990s several animal studies demonstrated that when LCPFAs are esterified to phospholipids, it changes how these FAs are distributed in lipoprotein fractions.[12,13] A recent study demonstrated that when animals fed a high-fat diet were supplemented with krill oil, they had a dose-dependent significant lowering of liver weight and total liver fat due to lower hepatic triglycerides and cholesterol. Both serum cholesterol and blood glucose were also reduced, while adiponectin was increased.[14]

Researchers in Quebec compared Neptune Krill Oil (NKO®) with high EPA and DHA fish oil (3:2 ratio) or placebo in a 12-week, prospective, randomized, double-blind clinical trial.[4] Subjects (n=120), ages 25-75, with moderate-to-high cholesterol (193.9-347.9 mg/dL) and triglycerides (203.8-354.4 mg/dL) for a minimum of six months, were divided into four groups. Group 1 received 2 or 3 g NKO daily, depending on body mass index (BMI). Group 2 received 1 or 1.5 g NKO daily (depending on BMI) during the 12 weeks of the study and an additional 500 mg NKO as a maintenance dose for a 90 day follow-up period. In both groups a BMI >30 justified the higher of the two doses. Group 3 received 3 g fish oil (180 mg EPA, 120 mg DHA per g) daily, while group 4 received a placebo. Parameters examined at baseline, 30, and 90 days (180 days for the follow-up in group 2) included HDL, LDL and total cholesterol, blood glucose, and triglycerides.

At the end of 90 days those taking krill oil at a daily dose of 1 g, 1.5 g, 2 g, or 3 g achieved significant reductions of LDL of 32-, 36-, 37-, and 39 percent, respectively, (p=0.000 for all). Reductions in total cholesterol were 13.4-, 13.7-, 18.1-, and 18 percent, respectively, (p=0.000 for all), while triglyceride reductions were 11.03- (p=0.114), 11.89- (p=0.113), 27.62- (p=0.025), and 26.51 percent (p=0.028), respectively. Blood glucose was reduced 6.3 percent (p=0.025) in the 1-g and 1.5-g krill group, and 5.6 percent (p=0.011) in those taking 2 or 3 g krill daily. In comparison, the fish oil group had an average 5.9-percent reduction in cholesterol (p=0.000) and the placebo group had a 9.1-percent increase (p=0.000). Subjects taking the fish oil also had a non-significant (p=0.141) 4.6-percent decrease in LDL cholesterol. Those receiving the placebo had a significant (p=0.000) 13-percent increase in LDL cholesterol. There was a non-significant decrease in glucose and triglycerides for both the 3 g fish oil (p=0.275 and p=0.239, respectively) and placebo groups (p=0.750 and p=0.215, respectively). The largest changes in serum lipids occurred for HDL cholesterol. After 90 days, the 1, 1.5, 2, and 3 g krill oil groups had significant (p=0.000) HDL increases of 44-, 43-, 55-, and 59 percent, while the fish oil group had only a 4.2-percent (p=0.002) increase; the placebo group had a non-significant (p=0.850) decrease of HDL.

During the 12-week follow-up, when subjects in the 1- and 1.5-g krill group were maintained on 500 mg krill oil daily, all markers maintained statistical significance (p=0.000) except glucose (p=0.20).[4]

### Inflammation

A double-blind, placebo-controlled, randomized, prospective study examined the effect of 300 mg NKO daily on C-reactive protein (CRP) and functional testing scores for arthritis.[6] Ninety participants had a diagnosis of cardiovascular disease and/or rheumatoid arthritis and/or osteoarthritis, and an elevated CRP (>1.0 mg/dL) for three consecutive weeks. Western Ontario and McMaster Universities (WOMAC) osteoarthritis score and CRP were measured at baseline and at days 7, 14, and 30.

After seven days of krill supplementation, CRP decreased by 19.3 percent in the experimental group, while it increased by 15.7 percent in the control group (p=0.049). By day 14 and day 30, CRP decreased by 29.7 and 30.9 percent, respectively, in the krill oil group, while the placebo group experienced an increase of 32.1 percent by day 14 and a lowering to a total increase of 25.1 percent by day 30. When comparing krill supplementation to placebo, differences at day 7 (p=0.049), day 14 (p=0.004), and day 30 (p=0.008) were all statistically significant. When compared to placebo, WOMAC results showed krill significantly reduced pain scores (p=0.05 day 7, p=0.049 day 14, and p=0.011 day 30), stiffness scores (p=0.001 day 7, p=0.018 day 14, p=0.023 day 30), and functional impairment scores (p=0.008 day 7, p=0.040 day 14, p=0.005 day 30).[6]

### Premenstrual Syndrome

In a 90-day study, Sampalis et al compared the effects of NKO to fish oil on multiple parameters of function in PMS (via an assessment questionnaire) and the total consumption of analgesics for pain and discomfort associated with PMS.[5] Seventy subjects of child-bearing age were assigned to ingest 2 g krill oil daily (800 mg phospholipids, 600 mg EPA and DHA) (n=36) or 2 g fish oil daily (600 mg EPA and DHA at an 3:2 ratio) (n=34) for the first 30 days of the trial. In the final 60 days both groups were instructed to take the assigned supplements eight days prior to and two days during menstruation. Questionnaires were completed and analgesic medication intakes were measured at baseline, 45, and 90 days.

After the first 45 days the krill oil group showed significant (p<0.001 for all parameters) improvements in breast tenderness, joint pain, weight gain, abdominal pain, swelling, and bloating, as well as feelings of being overwhelmed, stressed, irritable, and depressed. The fish oil group demonstrated significant improvements in weight gain and abdominal pain (both with p value of 0.04) at day 45, and improvements in weight gain (p<0.01), abdominal pain (p<0.001), and swelling (p<0.001) at day 90.

When consumption of analgesic medication during menstruation by the krill oil group was compared to the fish oil group, it was found that the average consumption of 1.2 g ibuprofen or 2.5 g acetaminophen taken at baseline changed in both groups. The krill oil group had reduced consumption to 0.9 g ibuprofen and 1.5 g acetaminophen at day 45, and 0.6 g ibuprofen and 1.0 g acetaminophen at day 9) – a total decrease in analgesics of 50 percent after 90 days. The fish oil group decreased intake to 0.9 g ibuprofen and 1.65 g acetaminophen by day 45, and 0.8 g ibuprofen and 1.48 g acetaminophen by day 90 – a total reduction of 33- and 41 percent, respectively. Interestingly, the authors noted, "Patients taking NKO did not experience any gastrointestinal difficulties such as regurgitation, while 64 percent of the women in the fish oil group complained of unpleasant reflux."[5]

## Side Effects and Toxicity

There are currently no known toxicity levels for krill oil. Side effects associated with the consumption of krill oil may include an increase in gastrointestinal complaints such as flatulence, gas, bloating, and/or diarrhea.[3]

## Dosage

Therapeutic doses range from 1-3 g krill oil per day, with maintenance dosing of 500 mg daily.

## References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