Is There a Difference Between Re-esterified Triglyceride and Ethyl Ester Fish Oil?

A scientific and economic assessment.

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THE QUESTION

The health benefits of supplemental fish oil are associated with the long-chain omega-3 fatty acids known to have a positive impact on the inflammatory system. The American Heart Association recognizes the benefits of omega-3 fatty acids. It recommends that (1) all adults eat fish (particularly fatty fish) at least two times a week and (2) patients with documented coronary heart disease consume 1 g of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (combined) per day. [1] The American Heart Association also states that an EPA/DHA supplement may be useful in patients with hypertriglyceridemia.

Fish oil comes in many forms. Is there really any difference in the two primary forms, ethyl ester and triglyceride backbone fish oil? These omega-3 fatty acids must be consumed, as humans cannot synthesize them,[2,3] and it is logical that any manner to improve the delivery to the human system would be beneficial. The cleanliness of and the oxidation potential of the supplemental fish oil are also major issues. A number of concerns surrounding this supplement includes the potential contamination of the fish by pollutants in the environment. To reduce the potential of contamination, all fish oil is cleansed. What, then, is the most effective method by which to render fish oil safe, effective, and efficient to the human system? A simplification of the distillation process is

- Crude fish oil is altered with ethanol
- This mix is then heat distilled (molecular distillation) under a vacuum to remove contaminants
- The result is concentrated (50%-70%[4]) omega-3 molecules in an ethyl ester package
- The ethyl ester package is then sold or restructured (re-esterified triglyceride) in an attempt to more closely simulate the original long-chain omega-3s

In the formulation process of ethyl ester and triglyceride backbone fish oil production, several issues must be considered: safety and tolerability, delivery of high concentrations of EPA with minimal side effects, delivery of high concentrations of DHA with minimal side effects, maximum bioavailability, stability, and economical concerns to the consumer.

Which of the variations, ethyl ester or triglyceride backbone (the natural form in fish), better satisfies the aforementioned criteria?

THE ANSWER

To generate an answer, one must deduce which form of fish oil offers the maximal bioavailability. The concurrent question is, what is the cost for that differential?

Numerous studies have assessed the absorption and bioavailability of ethyl ester fish oils. Luley et al (1990) compared the absorption of EPA and DHA with natural fish oil triglyceride and ethyl ester and found no differences.[5] Norday et al (1991) found that there was similar absorption of EPA and DHA between ethyl ester and triglyceride in an experiment with 40-g fat test meals given with supplements.[6] Krokan et al (1993) discovered that EPA and DHA from ethyl ester were comparable to that from natural triglyceride, but the triglyceride variants delivered more bioavailability with a lower concentration of fatty acids.[7] Hansen et al (1993) concluded that EPA and DHA were equally incorporated into plas-

TABLE 1. COSTS OF OBTAINING 1,000 MG OF EPA UTILIZING THE BIOAVAILABILITY FACTOR OF 1.7

	Ethyl Ester Product	rTG Product
Products 1 and 2	$1.67/day to achieve 1,700 mg	$0.96/day to achieve 1,000 mg
Products 3 and 4	$1.89/day to achieve 1,700 mg	$1.69/day to achieve 1,000 mg

ma phospholipids, but the incorporation of EPA into plasma cholesterylesters from ethyl ester was significantly lower. [8] Beckermann et al (1990) presented conflicting data in a randomized triple crossover trial. Maximal plasma levels were 50% higher with free fatty acids and 50% lower with ethyl ester as compared with triglyceride. This equates to a 2.0 times multiple advantage for the triglyceride form over the ethyl ester form.[9] El Boustani et al (1987) found that natural triglyceride fish oil results in 50% more plasma EPA and DHA after absorption compared with ethyl ester oils. Triglyceride forms of EPA and DHA were shown to be 48% and 36% better absorbed than ethyl ester forms, respectively.[10] Lawson et al (1988) found nearly 100% absorption of EPA and DHA as free fatty acid, whereas only 68% and 20% of EPA as natural triglyceride (3.4 X) or ethyl ester were absorbed.[11]

In a major human double-masked, randomized, placebo controlled study, Dyerberg et al (1995) assessed the bioavailability of the five most common fish oil concentrates. The study showed the bioavailability of EPA plus DHA from the re-esterified triglyceride was far superior (134%) compared with the synthetic ethyl ester form (76%) by a factor of 1.763.[12] Dyerberg et al (2010) further stated that the bioavailability of EPA plus DHA from re-esterified triglycerides was superior (124%) compared with natural fish oil, whereas the bioavailability from ethyl esters was inferior (73%). This represents a multiple of 1.698.[13]

The argument can then be posited that the triglycerides backbone product should cost the consumer about 1.7 times as much. In an online survey of ethyl ester products and triglyceride products, the following comparison was generated looking at the bioavailability factor of 1.7. Table 1 illustrates the results.

This analysis demonstrates that product 2, the triglyceride backbone product, is the economical choice in regard to bioavailability. There is more available EPA for less money.

The question of stability must also be addressed. According to one report, DHA in fish oils in the form of ethyl esters are much less stable than those in the natural triglyceride form. In the study, the ethyl esters fish oils are far less stable and more readily produce harmful oxidative products.[14] Another study analyzed the stability of DHA in phospholipid, triacylglycerol, and ethyl esters forms. Looking at a 10-week oxidation period, the ethyl esters DHA oil decayed 33% more rapidly.[15]

SUMMARY

Essential fatty acids are critical to the maintenance of health. They must be consumed to create EPA and DHA, which are employed in the balance of the immune system. Most diets are woefully low in the long-chain omega-3 fatty acids that are most efficient in the provision of EPA and DHA.

After a careful assessment of scientific fact, it appears that the delivery of high concentrations of both EPA and DHA occurs more efficiently with the triglyceride variations and even better with re-esterified triglyceride. There also appears to be more stability in the triglyceride form. When economy is considered, the triglyceride backbone product appears to offer the advantage.

While either form will help the patient, it is apparent that he or she must consume more of the ethyl ester form to achieve the same effect as a triglyceride form. ■

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1. Kris-Etherton PM, Harris WS, Appel LJ, for the AHA Nutrition Committee. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. *Arterioscler Thromb Vasc Biol*. 2003;23;151-152.
2. Ervin RWJ, Wang C, Kennedy-Stephenson J. Dietary intake of fats and fatty acids for the United States population: 1999-2000. Hyattsville, Maryland: Adv Data Vital Health Stat. 2004;348. US Department of Heart & Human Services.
3. Wang CM, Lichtenstein A, Balk E, et al. Evidence Reports/Technology Assessments, No. 94. Effects of omega-3 fatty acids on cardiovascular disease. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
4. Dyerberg J, Bang HO, Stoffersen E, et al. Eicosapentaenoic acid and prevention of thrombosis and atherosclerosis. *Lancet*. 1978;ii:117-119.
5. Luley C, Wieland H, Gruwald J. Bioavailability of omega-3 fatty acids: ethylester preparations are as suitable as triglyceride preparations. *Akt Ernaehr-Med*. 1990;15:122-125.
6. Norday A, Barstad L, Connor WE, et al. Absorption of the n-3 eicosapentaenoic and docosahexaenoic acids as ethyl esters and triglycerides by humans. *Am J Clin Nutr*. 1991;53:1185-1190.
7. Krokan HE, Bjerve KS, Moerk E. The enteral bioavailability of eicosapentaenoic acid and docosahexaenoic acid is as good from ethyl esters as from glycerol esters in spite of lowere hydrolytic rates by pancreatic lipase in vitro. *Biochem Biophys Acta*. 1993;1168:59-67.
8. Hansen JB, Olsen JO, Wilsgard L, et al. Comparative effects of prolonged intake of highly purified fish oils as ethyl ester or triglyceride on lipids, haemostasis and platelet function in normolipaemic men. *Eur J Clin Nutr*. 1993;47:497-507.
9. Beckermann B, Beneke M, Seitz I. Comparative bioavailability of eicosapentaenoic acid and docosahexaenoic acid from triglycerides, free fatty acids and ethyl esters in volunteers [Article in German]. *Arzneimittelforschung*. 1990;40(6):700-704.
10. El Boustani SE, Colette C, Nonnier L, et al. Enteral absorption in man of eicosapentaenoic acid in different chemical forms. *Lipids*. 1987;22:711-714.
11. Lawson LD, Hughes BG. Human absorption of fish oil fatty acids as triacylglycerols, free acids, or ethyl esters. *Biochem Biophys Res Commun*. 1988;52:328-335.
12. Dyerberg J, Madsen P, Moller J. Bioavailability of n-3 fatty acid formulations. In: *n-3 Fatty Acids: Prevention and Treatment in Vascular Disease*. London, UK: Bi & Gi Publishers, Verona-Springer Verlag; 1995.
13. Dyerberg J, Madsen P, Moller JM, et al. Bioavailability of marine n-3 fatty acid formulations. *Prostaglandins Leukot Essent Fatty Acids*. 2010;83:137-141.
14. Yoshii H, Furuta T, Siga H, , et al. Autoxidation kinetic analysis of docosahexaenoic acid ethyl ester and docosahexaenoic triglyceride with oxygen sensor. *Biosci Biotechnol Biochem*. 2002;66:749-753.
15. Song JH, Inoue Y, Miyazawa T. Oxidative stability of docosahexaenoic acid-containing oils in the form of phospholipids, triacylglycerols, and ethyl esters. *Biosci Biotechnol Biochem*. 1997;61:2085-2088.