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Assessment of the Relative Absorbability of Orally Dosed Whole Marine Oils and A Standard, Processed 18/12 Omega-3 Oil: Does Nature Know Best?

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ABSTRACT

The typical western diet falls significantly short of the level of omega-3s needed to help support good health and wellbeing. Fish oil supplementation has become a popular way of addressing this shortfall with the majority of supplementation consumed in the form of 18/12 processed omega-3 oil, i.e., oil with 18% EPA and 12% DHA. However, the omega-3 in these processed oils is mostly in the form of ethyl ester (EE) rather than the natural triglyceride (TG) and phospholipid (PL) form. EE fats are harder for the gut to absorb which could significantly impact their bioavailability and their overall health benefits. A C57BL/6 diet-induced obesity (DIO) mouse model was used to assess the absorption of two marine oils, OmeGo, a whole fish oil gently released from fresh Norwegian salmon offcuts and krill oil, a processed, 18/12 omega-3 oil and a control group that received no treatment. From baseline (day 0) to end of study (day 7) the marine oils significantly increased serum DHA and EPA levels. This increase was two to four times greater than with processed 18/12 omega-3 oil whilst control animals showed a small decline in serum omega-3 levels. This suggests that natural marine oils are significantly more bioavailable than processed oils and therefore more likely to deliver health benefits akin to eating fresh fish. A follow-on study is planned to assess dose-response in terms of serum omega-3 levels and associated health benefits attained with natural marine oils compared to processed 18/12 concentrated oils.

Abbreviations: PUFAs: Polyunsaturated Fatty Acids; AHA: American Heart Association; EPA: Eicosapentaenoic Acid; DHA: Docosahexaenoic Acid; EEs: Ethanol to form Ethyl Esters; FFA: Free Fatty Acid; DIO: Diet-Induced Obesity; PL: Phospholipid; TG: Triglyceride; SPMs: Specialist Pro-Resolving Mediators

Introduction

The health benefits of eating the polyunsaturated fatty acids (PUFAs) contained in fresh, fatty fish are well recognized, including a reduction in cardiovascular disease, a reduced risk of allergic diseases and overall, aiding the body to resolve inflammation [1-3]. As such expert medical bodies, including the American Heart Association (AHA), have recommended minimal levels of weekly fish intake [4]. However, the typical western diet falls short by a significant extent and fish oil supplementation has become a popular method of addressing this deficit [5]. The majority of these supplements are consumed in the form of concentrated 18/12 omega-3, i.e., typically containing 18% eicosapentaenoic acid (EPA) and 12% docosahexaenoic acid (DHA). As EPA and DHA naturally occur in the triglyceride form, they must be broken down into their constituent parts (de-esterified) and distilled from whole fish oil to be concentrated. In brief, this requires significant processing and the most cost-effective approach is to reconstitute the free fatty acids with ethanol to form ethyl esters (EEs) rather than with glycerol, which would reform them as TGs. Ethyl esters are harder for the body to absorb, requiring further digestion in the gut compared to natural TGs [6]. To overcome this limitation of processed fish oil the supplement can be consumed with a higher fat meal to stimulate increased bile acid production and digestive enzymes.

OmeGo is a whole fish oil from the side streams of fresh Norwegian Atlantic salmon processing. The oil is gently liberated using only moderate heat and natural, non-GMO protease enzymes.

OmeGo therefore has all the PUFAs contained in whole fish, 99.5% in their natural TG form and minimal free fatty acid (FFA) levels, rather than only EPA and DHA, 94% in a modified EE form, the rest as pro-inflammatory FFAs. Another natural form of marine oil is derived from the crustacean, krill. However, in contrast to fish oil, the omega-3 fraction in krill has a significant proportion in the phospholipid form as well as in the TG form [7]. There is an increasing recognition of the benefit of minimal processing of foods and supplements to optimise health benefits. In this study we assessed the impact of processing oil on the absorption of omega-3s, as a proxy for bioavailability, and compared a typical processed 18/12 omega-3 concentrate, a whole fish oil, OmeGo, and krill oil, in an oral mouse model.

Materials and Methods

A C57BL/6 diet-induced obesity (DIO) mouse model was used to compare the absorption of OmeGo fish oil, krill oil, a standard, processed omega-3 oil versus control (no oil). The study was conducted as per GLP guidelines and the laws and regulations of India where the study was performed. Prior to the start of the study approval was sought from and granted by the Institutional Animal Ethics Committee. A veterinarian assessed health status on receipt of the animals. All the animals were in good health and were acclimated to laboratory conditions. Veterinary examination was also performed prior to the first day of treatment and confirmed that all animals remained in good condition. Randomisation was performed the day before the first day of treatment and 4 mice were allocated to each group. Each test diet was formulated to deliver a 6mg dose of EPA per day and the dosage of test items consumed was confirmed by the calculated average weight measurement of feed consumed by each group of mice. Standardizing the EPA dose resulted in the oils supplying different doses of DHA: 9.4mg, 9mg and 3mg for OmeGo, 18/12 omega-3 oil and krill oil, respectively. Therefore, a correction was carried out on the DHA absorption results to adjust for these differing baseline DHA dosing levels. The mice were fasted for approximately 6 hours prior to the blood draw. Blood was collected in vials without anticoagulant, by retro-orbital sinus procedure at Day 0 and Day 7. Animals were anesthetized with isoflurane prior to blood collection. Serum samples were prepared using the instructions in the EPA and DHA ELISA analysis kits. Basically, a serum separator tube was used after allowing the blood samples to clot for two hours at room temperature followed by centrifuge for 20 minutes at 1,000xg. Serum DHA was assayed using the Abbexa LLC, (TX, USA) Docosahexaenoic acid (DHA) ELISA Kit Catalog No. abx258057 while serum EPA was assayed using the Cloud-Clone Corp (TX, USA) Eicosapentaenoic Acid (EPA) ELISA Kit Product No: CEO122Ge.

Statistical Analysis

A statistical analysis was conducted with the data analysed using ANOVA. Data showing significance in their variances were subjected to t-test analysis. P values ≤ 0.05 were deemed statistically significant.

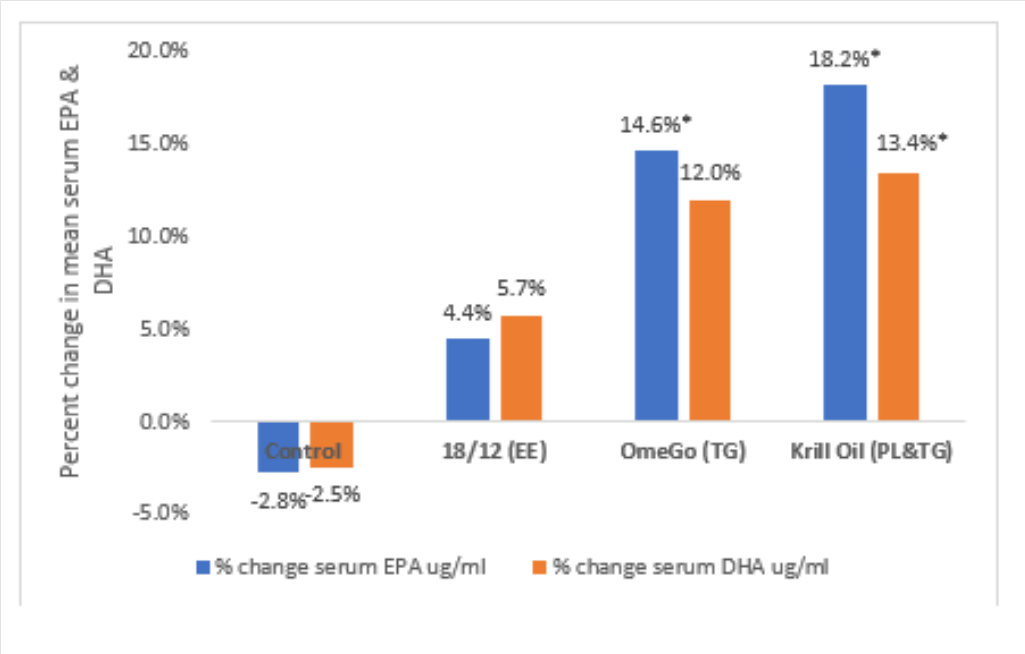

Figure 1: Percent change in mean serum EPA and DHA from day zero to day seven. 6mg/d equivalent doses of EPA were provided daily. DHA results have been normalized to correct for differing dosing levels in each oil format. EE = ethyl ester; TG = triglyceride; PL = phospholipid. *denotes p<0.05.

Results

In the control group, a small, non-significant decrease was observed in DHA and EPA serum levels of just under 3% between day zero and day seven. The omega-3 (18/12) processed oil provided a small, non-significant increase in DHA and EPA of 4.4% and 5.7% respectively on day seven. In contrast, the marine oils drove significantly greater increases: more than two to four times the levels achieved with 18/12 omega-3 oil. For OmeGo the increase in DHA of 12% did not quite reach significance but the 14.6% increase in EPA was significant ($P<0.05$). For krill oil the 13.4% increase of DHA ($p<0.05$) and 18.2% increase of EPA ($p<0.05$) were both significant (Figure 1). All animals remained healthy throughout the duration of the study with no adverse events noted.

Conclusion

In this study we assessed the relative absorbability of two natural marine oils and one processed 18/12 omega-3 concentrate compared to non-treated control in a mouse oral gavage model (C57BL/6 diet-induced obesity model). The marine oils, OmeGo and krill, showed greater absorbability in terms of change in mean serum DHA and EPA with DHA absorption over two times greater and EPA over 3 times greater. This suggests that in a human, to try and match the absorption of omega 3 in 1g of OmeGo, around 1g of a standard 18/12 omega-3 concentrate would be needed and that 1g of OmeGo would provide the same amount of bioavailable omega 3 as 500mg of krill oil. The differential absorbability seen in our study is consistent with published research. This has shown the natural phospholipid (PL) and triglyceride (TG) forms of marine oils to be easier for the gastrointestinal tract to digest and absorb than the processed ethyl ester form [6-8]. The slightly enhanced absorption of krill oil in our study is also consistent with the known better absorbability of PLs than TGs [8]. Of note, we conducted this study in an animal model with a high background fat intake, reflecting the profile of a commonly consumed western diet. Prior studies have suggested that such a diet aids the absorption of ethyl ester-based DHA and EPA via an increased stimulation of pancreatic enzymes and bile acid. One such study showed that a high fat diet reduced the differential absorption between free fatty acids and EE formulations from four-fold to only 1.3-fold [9]. Nevertheless, in our study, a markedly >3-fold absorption of the natural marine oils was observed despite employing an animal model (C57BL/6 diet-induced obesity mouse model) that should help to improve the uptake of the processed ethyl ester fish oil.

A significant proportion of the health benefits of eating fish is derived from the array of polyunsaturated fatty acids which are metabolized into specialist pro-resolving mediators (SPMs) of inflammation: resolvins, maresins and protectins [10]. Whilst there are some overlapping effects, each individual PUFA provides differing effects on inflammation resolution, including increased neutrophil clearance, reducing IgE production and eosinophil activation [11,12]. To garner the anticipated health benefits of fish oil / omega-3 supplementation it would seem more logical to supplement the diet with whole marine oils rather than highly processed ones. Indeed, for optimal health benefits, ease of absorption is clearly a prerequisite, followed by PUFA structural integrity, and low oxidation and free fatty acid levels which can be negatively impacted by significant levels of processing [13]. In a healthy human study, OmeGo significantly reduced oxLDL levels, a highly inflammatory form of LDL-cholesterol which is now recognised as an initiator of atherosclerosis [14-16]. In contrast, omega-3 processed fish oil and algae oil both failed to meaningfully change oxLDL levels. OmeGo contains all the elements that are in the fat fraction of whole fish including the omega-3 DPA and a lipopeptide (microcolin), the latter not seen in other oils, processed, cold pressed or krill oil [17]. An in vitro study showed that this lipopeptide significantly moderates allergic inflammatory activity and other work has shown promising resolution of type 1 inflammation by OmeGo [17,18]. Importantly, these results are all consistent with the known health benefits of regularly eating fish. Weaknesses of our study include a lack of assessment of the health benefits of differential absorption or a dose-response. The former would have helped frame the relevance of greater bioavailability with enhanced health and the latter would have shed further insights into the way these oils are handled by the body and whether a higher dose could compensate for the apparent lower bioavailability of processed oils. A larger follow-on study is planned in an obesity animal model to assess bioavailability, inflammation-resolution and microbiome effects of both natural marine oil and processed omega-3 oil.

Conflicts of Interest

The authors are employees or consultants of Hofseth BioCare, the sponsor of the study.

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