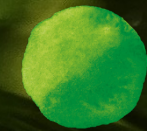


White Paper

By Dr John E. Bauer, Emma Tate, and Jeffrey Alix



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WHITE PAPER

Why algal ingredients with high concentrations of both EPA & DHA Omega-3 are the best alternatives to fish oil.



Executive Summary

EPA & DHA are among the most extensively studied dietary components in animal nutrition, with numerous studies in canines showing metabolic and health benefits specifically linking these fatty acids to skin health and coat condition; the immune response; healthy joints; and kidney and heart health. However, in vivo production of EPA & DHA is limited, therefore dietary supplementation with both of these fatty acids is required in order to observe the myriad of reported optimal health benefits.

Historically, high quality fish oils have been the primary source of Omega-3 fatty acids in pet food diets. This is changing because high quality fish oils, those providing sufficient levels of both EPA & DHA Omega-3 to achieve optimum health, are becoming less available to the animal feed and food industries.

High quality fish oils are sourced from wild caught forage fish, which has driven an increase in global demand and in turn has put increasing pressure on forage fish supplies. With these sustainability issues in mind, viable ingredients derived from marine microalgae have become available as a sustainable alternative source of EPA & DHA Omega 3. This is a logical approach to the issue because marine fish bioaccumulate both EPA & DHA in their tissues through the food chain in the ocean, originating from marine microalgae. It is important to note that while some algae ingredients like Veramaris Pets Natural Marine Algal Oil are rich in both EPA & DHA, other alternative ingredients contain only modest amounts of EPA & DHA. This paper investigates the suitability of fish oil alternatives that are frequently compared to fish oils, due to the established scientific evidence associated with EPA & DHA related dog and cat health benefits.

Some claim that a pet diet formulated with algae ingredients high in DHA and very low or no EPA would be sufficient to result in the production of significantly beneficial levels of both EPA & DHA in vivo (in the body), via retroconversion of DHA into EPA. The results of this analysis showed that a diet containing high DHA but only modest levels of EPA resulted in minimal increases of EPA in vivo, whereas Veramaris Pets Natural Marine Algal Oil and fish oil containing diets, which are rich in both EPA & DHA, showed markedly elevated plasma levels of both Omega-3 fatty acids. Therefore, it is clear that high DHA/low EPA algae diets are inadequate at delivering the quantities of fatty acids required and only the Veramaris Pets Natural Marine Algal Oil, which is rich in both EPA & DHA, is an effective and sustainable alternative to fish oil.



Benefits of EPA & DHA Omega-3 in dogs and cats



Long chain Omega-3 EPA & DHA not only support important physiological processes, such as cardiovascular function and inflammation, they are also vital for proper foetal development, and they maintain healthy cell membrane balance. Within cell membranes, they influence the activities of proteins such as hormone receptors and are the starting material for making substances involved in the control of the immune system.

The suitability of fish oils in supporting health benefits for dogs and cats, including recommendations for therapeutic veterinary clinical management, is well understood.¹ For this reason, a combination of EPA & DHA, sourced from marine fish, has primarily been used either as an ingredient in pet foods or as an additional dietary supplement.

Sustainability of Omega-3 fatty acid sources

Given the known health benefits of Omega-3 fatty acids, the supply of these nutrients to both humans and animals has driven an increase in global demand. As a result, questions regarding the environmental sustainability of using whole marine fish and marine fish-derived oils have been raised. Therefore, alternative sources of Omega-3 fatty acids are needed to help reduce any increasing dependence on marine fish harvests. The abundance of marine algae Omega-3 sources, which contain both EPA & DHA Omega-3, addresses this important environmental concern and provides a viable alternative to fish-based marine oils.

Only Veramaris Algal Oil is naturally rich in both EPA & DHA. Other alternative ingredients contain only small amounts of EPA. Optimal health benefits have been observed in studies where both fatty acids are present at significant levels in the diet. As it is not yet clear whether EPA or DHA is the more biologically active Omega-3, it is likely that an algae source containing sufficient pre-formed amounts of both EPA & DHA is required.²

Retroconversion of long chain Omega-3 DHA into EPA in humans

Previous studies looking at the in vivo conversion of dietary DHA into EPA in humans, via the process of retroconversion, have found only a modest resultant accumulation of EPA in the subjects' plasma³⁻⁵. Further studies even dispute if retroconversion is even involved, suggesting that DHA dietary supplementation only slightly increases EPA, primarily by slowing its metabolism.⁶ Whatever the mechanism involved, it is clear that EPA is not formed in sufficient quantities for optimal health benefits to be observed. Therefore EPA, as well as DHA, need to be supplemented in the diet.

EPA & DHA in canines

EPA & DHA are among the most extensively studied dietary components in animal nutrition. Numerous investigations in dogs have shown metabolic and health benefits specifically linking both these fatty acids to skin health and coat condition; the immune response; healthy joints; and kidney and heart health. In addition, vision and brain health, puppy development, trainability, and cognitive function are also supported.^{7,17, 19-21}

More recently, twenty canine studies were reviewed where diets were supplemented with EPA & DHA. A therapeutic benefit was found in canine allergic dermatitis, haircoat disorder, keratoconjunctivitis sicca, valvular disease, and canine osteoarthritis. Dogs diagnosed with chronic heart failure and lymphoma also appeared to benefit from supplementation with both EPA & DHA.²² Both EPA & DHA are needed because forward conversion of short chain Omega-3 precursors derived from terrestrial plant sources (i.e. flaxseed), was found to be metabolically limited.²³ Although small amounts of EPA Omega-3 synthesised from such precursors in dogs may be sufficient for health maintenance²³ in some cases, it certainly does not provide for optimal function. The problem is that the degree of synthesis varies from breed to breed, as do their requirements. Therefore, dietary supplementation with EPA is recommended for all canines to ensure the animal's nutritional baseline requirements are being met. For DHA, conversion of precursors is even more limited and therefore dietary supplementation with DHA is also needed.

Additional insights on the above topic came from a study where the diets of adult Alaskan Huskies were supplemented with either marine-sourced high EPA/high DHA or flaxseed oil containing ALA (a short chain Omega-3 fatty acid). They assessed the effects of the two diets by measuring the Omega-3 Index, which is a test that measures the amount of EPA & DHA in red blood cell membranes, expressed as a percentage of all fatty acids. The results showed that supplementation of the marine-sourced high EPA/high DHA led to a significant increase in the Omega-3 Index in comparison to the flaxseed oil in the dogs. The authors concluded that not only was the flaxseed oil the inferior supplement, but in addition preformed EPA & DHA both need to be supplemented in significant levels in order to meet the dog's dietary requirements.²³

Retroconversion in the canine model

There are very few published studies assessing retroconversion in canines. Consequently, it is unknown whether the small amounts of EPA that accumulate in the plasma of subjects fed only dietary DHA, are sufficient to elicit the same health benefits seen in those where both fatty acids are included in the diet. One report found that an algae-based Omega-3 diet enriched in DHA but containing very little EPA supported cognition in older animals.⁷ Although a modest enrichment of EPA was seen in this study, it could not be determined whether this was due to retroconversion of DHA or just slowed metabolism, as noted for humans above. Furthermore, published clinical research has found that diets supplying both EPA & DHA support overall health benefits for all life stages. A convincing argument for this is that a metabolic relationship exists between EPA & DHA, with these two fatty acids working together in order to provide their anti-oxidative, anti-inflammatory and neurotrophic effects.⁸

Data review and analysis of available canine studies

In addition to the mechanism involved, a practical question for pet nutrition and health is whether dietary algae-based DHA alone results in sufficient enrichment of both EPA & DHA to support the many overall health benefits observed in dogs whose diets are supplemented with both EPA & DHA fatty acids.

In order to address this question, average plasma EPA & DHA concentrations were analysed from studies where three different Omega-3 sources were fed. These data were then depicted graphically showing plasma EPA & DHA enrichment among the various groups. The three groups were:

- Fish oil studies showing clinical benefits,⁹⁻¹⁵
- Dried whole cell algae Omega-3 containing nearly exclusively DHA (High DHA/Low EPA),⁷ and
- A newly developed algae-based Omega-3 oil containing both EPA & DHA (Veramaris Pets Algal Oil or VPAO).¹⁶

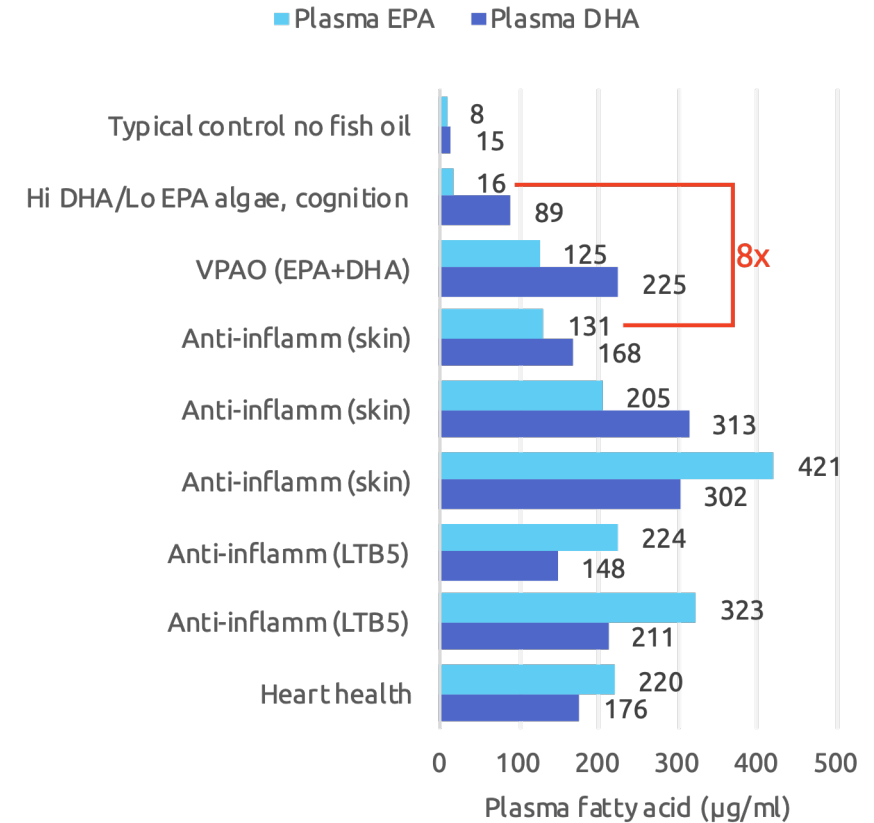
Group 1 was further divided into studies looking at the inflammatory response and skin and heart health (Figure 1),⁹⁻¹² osteoarthritis and joint health (Figure 2),¹³⁻¹⁵ and healthy reproduction (Figure 3),^{17, 18} and then compared with average plasma EPA & DHA levels from the other two groups. A control group of dogs fed low Omega-3 was also included for comparison in order to demonstrate typical plasma Omega-3 levels when dietary EPA & DHA are absent.^{10, 11}



Results

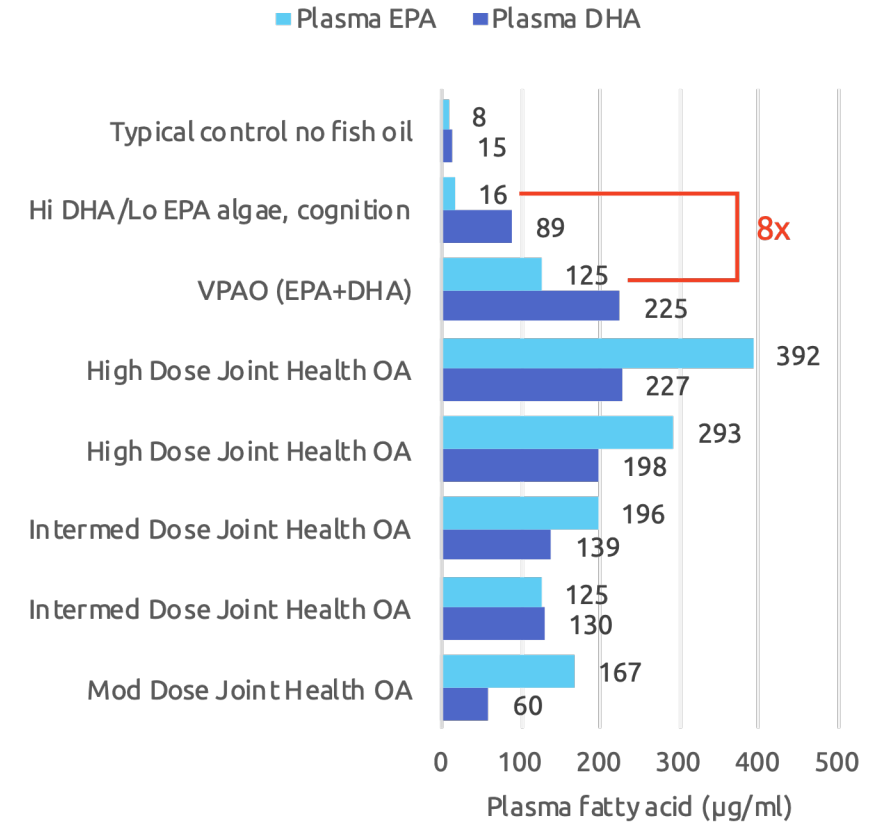
Results – Figure 1

When plasma is enriched in both EPA & DHA, benefits can be seen in heart and skin health, in the anti-inflammatory response, and in the response to osteoarthritis (Figures 1 and 2). EPA competes with the Omega-6 fatty acid, arachidonic acid, helping to balance immune system functions, and both EPA & DHA are involved in the production of the anti-inflammatory mediators resolvins and protectins, which help “turn off” inflammation as required. In the anti-inflammation/heart/skin category, the High DHA/Low EPA algae diet resulted in EPA levels lower than those seen with either the fish oil or the Veramaris Pets Algal Oil (VPAO). The High DHA/Low EPA algae diet resulted in plasma EPA levels 8-times lower than the nearest enrichment seen in studies where sufficient preformed EPA was fed (16 vs 131 µg/ml) and benefits observed. By contrast, the algae-based VPAO containing both EPA & DHA resulted in similar plasma levels of both fatty acids as observed in the clinical studies (Figure 1).



Results – Figure 2

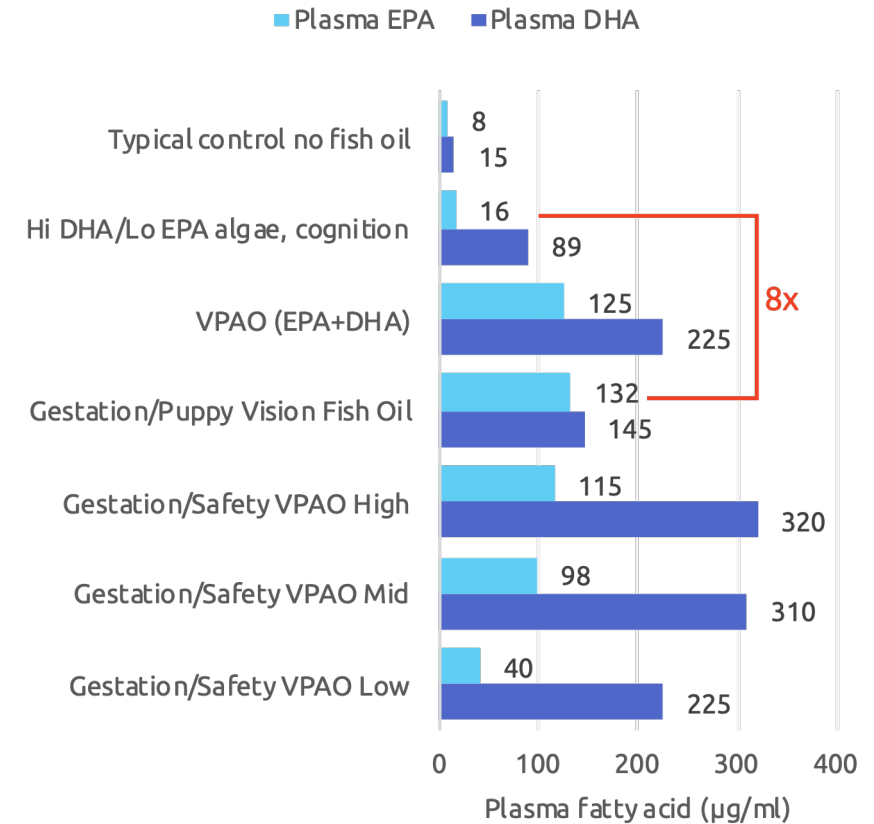
In the joint health category, plasma levels of both EPA & DHA were again lower with the High DHA/Low EPA diet for all but one comparison. In this latter case, the High DHA/Low EPA diet resulted in a plasma DHA level of 89 vs 60 µg/ml. However, it did not account for nearly enough plasma EPA compared to the nearest level from the clinical studies (16 vs 125 µg/ml), again an 8-fold difference (Figure 2). This amount of plasma EPA would therefore not be expected to provide the same amount of support for joint health as either fish oil or algae-based VPAO.



Results – Figure 3

Regarding gestation (Figure 3) the High DHA/Low EPA diet showed a reasonable DHA enrichment which was only 1.6 times less than that reported for enhanced puppy vision development (89 vs 145 $\mu\text{g}/\text{ml}$) but again did not account for nearly enough EPA (again 8-times less at 16 vs 132 $\mu\text{g}/\text{ml}$).

Overall, these clinical comparisons demonstrate that a dietary algae source containing high levels of DHA but minimal EPA does not provide the full plasma complement of long chain Omega-3 fatty acids that resulted in the clinical health benefits seen in dogs, as did both the fish oil and the algae-based VPAO.





Conclusion

Conclusion

The results of this analysis clearly show that in each category studied, the diet containing High DHA/Low EPA (whole cell algae) resulted in minimal enrichment of EPA in the body. In contrast, the Veramaris Pets Algal Oil and fish oil diets, which are rich in both EPA & DHA, showed markedly elevated plasma levels of both Omega-3 fatty acids; these increased levels are sufficient to support a variety of health benefits in canines. By comparison, when High DHA/Low EPA diets are fed, only small amounts of EPA accrue that did not favourably compare with those seen with Veramaris Pets Algal Oil. Although plasma levels of EPA & DHA were not available from a feline study evaluating High DHA/Low EPA, felines fed diets containing VPAO had similar plasma levels of EPA & DHA compared to diets containing fish oil (See “The science supporting the health benefits of Veramaris® Pets by Dr. John Bauer”).

In conclusion, EPA & DHA Omega-3 fatty acids play a crucial role in all life stages of companion animal health, including foetal development, immune system function, heart and skin health, even down to cell structure. With only limited EPA & DHA production taking place in vivo, it is imperative that companion animal nutritional products are supplemented with enough of these fatty acids in order to reap the optimal health rewards. From the studies reviewed above, it is clear that High DHA/Low EPA algae diets are inadequate at delivering the quantities of fatty acids required and only the Veramaris Pets Natural Marine Algal Oil, which is rich in both EPA & DHA, is a suitable and sustainable alternative to fish oil.



About the authors

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Dr. Bauer received his B.S. in Chemistry with high distinction from the University of Kentucky. His DVM, MS, and Ph.D. in Nutritional Sciences are from the University of Illinois. He is a charter Diplomate of the American College of Veterinary Nutrition. Dr. Bauer is a past Chair of the Graduate Faculty of Nutrition, former Mark L. Morris Professor of Clinical Nutrition and Professor Emeritus at Texas A&M University. Currently an Affiliate Professor at Colorado State University, Bauer's areas of specialization are lipid biochemistry, disorders of lipid metabolism, and comparative biomedicine and nutrition. He has published extensively on the health benefits of the Omega-3 fatty acids for all life stages of both canine and feline companion animals. His studies on canine Omega-3 fatty acid metabolism have led to our current nutritional understanding of the dietary Omega fatty acids during puppy development. His investigations have also included lipoprotein and Omega-3 fatty acid metabolism of domestic and exotic animals, as well as animal models of hypercholesterolemia and atherogenesis of humans.

Dr. Bauer was appointed to the Committee on Nutrient Requirements of Dogs and Cats for the National Academy of Sciences, National Research Council which published "Nutrient Requirements of Dogs and Cats". He has served on numerous veterinary nutrition advisory boards and consultancies,

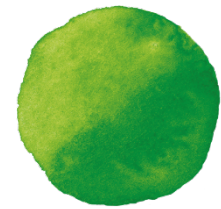
holds several patents with industry partners, and more than 190 peer reviewed publications, proceedings articles, and book chapters.

Emma Tate

Emma Tate is a freelance medical writer working with LionbridgePR. Emma received her BSC with honours from Bangor University in Zoology with Marine Zoology and is 18 months into a PhD in Comparative Physiology on 'The effect of diet on fish in aquaculture' at the University of Birmingham.

Jeffrey Alix

Jeffrey Alix is the Global Head of Business Development, Companion Animals for Veramaris. His career in the pet food industry spans 38 years. After receiving his BS in Chemistry from California State University, Northridge, Jeff has gained experience across a wide array of functional disciplines including ingredient and food science, flavour chemistry, animal nutrition, sales and marketing. He was a Research Scientist at Nestle Petcare for 10 years, Technical Support and Product Development Manager at Bioproducts (now AFB International) for 8 years, and more than 20 years as Sales, Business Development, and Marketing for DSM Nutritional Products and now Veramaris. Veramaris is a DSM and Evonik joint-venture company.



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