

Research on Omega-3s: Going ahead in leaps and bounds

Welcome to this second Special Edition of DHA Update. It's hard to miss the publicity around long chain Omega-3 fatty acids (Omega-3s) nowadays. Scientific researchers around the world are taking a very active interest in these exciting nutrients – in a huge diversity of areas.

This issue will focus on some recent research using Nu-Mega's HiDHA® tuna oil – a rich source of long chain Omega-3 DHA. Nu-Mega Ingredients assists many researchers to help uncover the effects of long chain Omega-3s on health through supply of HiDHA® tuna oil and control oils in capsules. We will bring you further updates as results of research currently underway are available.

If you missed our first Special Edition which focused on safety and ecological issues related to fish and fish oils or you would like back copies of any of our DHA Updates please contact Natasha Duck at natashad@nu-mega.com.

I hope you enjoy this Special Edition.

Wendy Morgan
Registered Nutritionist



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Facts about HiDHA®

Rich in long chain Omega-3 DHA

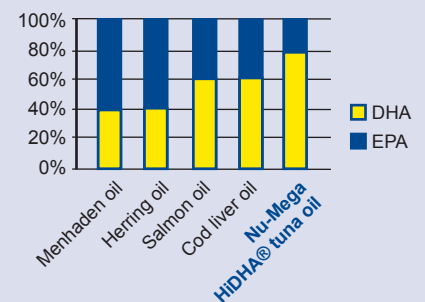
The two long chain Omega-3s which have been the subject of most scientific research are EPA and DHA found mainly in the oil of fish. Both DHA and EPA have important but different roles:

DHA (docosahexaenoic acid) has a more complex structure (22 carbon units and 6 unsaturated bonds) and is the most difficult Omega-3 to include in the diet. In the body it is found in the retina, brain, heart and other tissues and has a role in gene expression, the nervous system and production of hormones-like substances.

EPA (eicosapentaenoic acid) has 20 carbon units and 5 unsaturated bonds. It also produces hormone-like substances with roles in blood flow and inflammation.

HiDHA® tuna oil contains approximately 25% DHA and 6% EPA. Compared to many other fish oils it is much higher in DHA.

Chart 1: Proportions of DHA and EPA in different types of fish oils



References:

- Nu-Mega Ingredients HiDHA® tuna oil, Product Information (2006).
- USDA National Nutrient Database for Standard Reference, Release 20 (2007).

Let me know if there are any specific issues you would like our next issue to cover. Your feedback is always welcome! My email is: wmorgan@innovationsandsolutions.com

HiDHA® and exercise – a great partnership for weight loss and cardiovascular benefits

Dr Alison Hill and colleagues at the University of South Australia received a huge amount of publicity when their research was published – not surprisingly as overweight is a major health problem today.

Her study compared the effects of HiDHA® tuna oil either with or without an exercise regime. Overweight volunteers were placed on one of 4 treatments as described in Table 1.

The researchers wanted to look at not only whether regular exercise and consuming long-chain Omega-3s could independently improve cardiovascular and metabolic health, but whether combining these lifestyle modifications would be more effective than either alone.

The exercise consisted of walking 3 times a week for 45 min at 75% age-predicted maximal heart rate for the 2 exercise groups and 6 grams of oil per day were given to the two HiDHA® tuna oil groups (and 6 grams sunflower oil to the two control groups).

The results were pretty amazing! The people on tuna oil showed lower triglycerides, increased HDL (good) cholesterol, and improved blood vessel health. Also of benefit was a reduction in heart rate and improved heart rate variability. HiDHA® tuna oil and exercise helped reduce body fat and risk factors for heart disease.

This study's conclusion:

The authors stated that **tuna oil supplements and regular exercise both reduce body fat and improve cardiovascular and metabolic health.** Increasing intake of Omega-3s could be a useful adjunct to exercise programs aimed at improving body composition and decreasing cardiovascular disease risk.

Table 1: Summary of research outcomes

	TREATMENT		BENEFITS		
	Type of oil	+ Exercise	Increased Omega-3 DHA levels	Effects on weight	Benefits for cardiovascular health
Group 1	HiDHA® tuna oil	No	Yes		Lowered TGs Raised HDL Improved FMD Reduced heart rate Improved HRV
Group 2	HiDHA® tuna oil	Yes	Yes	Decreased body fat	Lowered TGs Raised HDL Improved FMD Improved SAC Reduced heart rate Improved HRV
Group 3	Sunflower oil*	No	No		
Group 4	Sunflower oil	Yes	No		Improved SAC

* Sunflower oil - (containing no Omega-3s and acting as a control or placebo)

- TGs** Plasma triglycerides (high levels increase risk of cardiovascular problems)
- HDL** High density lipoprotein ('good' cholesterol – higher levels decrease risk of cardiovascular problems)
- FMD** Flow-mediated dilatation (indicator of blood vessel function)
- HRV** Heart rate variability (a predictor of cardiac death)
- SAC** Small arterial compliance (indicator of small blood vessel function)

References:

- Hill AM, Buckley JD, Murphy KJ, Howe PR. Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors. *Am J Clin Nutr.* 2007;85:1267-74.
- Ninio DM, Hill AM, Howe PR, Buckley JD, Saint DA. Docosahexaenoic acid-rich fish oil improves heart rate variability and heart rate responses to exercise in overweight adults. *Br J Nutr.* 2008 Mar 13;1-7 [Epub ahead of print]



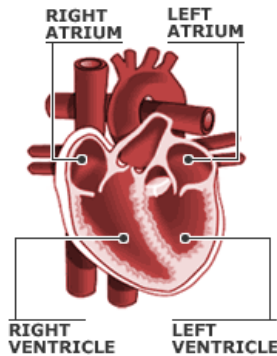
HiDHA® and the heart

Cardiac arrhythmias

Sudden death due to a heart attack is generally caused by a blockage in a coronary artery which leads to ventricular fibrillation (VF). This means that instead of regular beats of the heart, which pump blood around the body, the heart flutters ineffectively and blood is no longer pumped properly. Previous studies have shown that long chain Omega-3s help suppress ventricular arrhythmias such as VF.

The heart is divided into 4 chambers – the smaller two at the top are called the right and left atrium. The ventricles are the larger, lower chambers of the heart. Ventricular fibrillation, if not stopped quickly, causes death. Fibrillation of the atria (AF) can cause palpitations, lack of energy, fainting, chest pain or, more seriously, heart failure.

The Heart



The researchers in this study wanted to investigate the effects of fish oil on atrial arrhythmias – the upper chambers of the heart.

HiDHA® tuna oil fed animals were compared to animals fed sunflower oil in their diet and those with a standard diet. AF was more difficult to induce and sustain in the tuna oil group compared to the sunflower oil and standard diet groups.

Also, red blood cell, atrial and ventricular Omega-3 fatty acid levels were significantly higher in the tuna oil group. The ratio of atrial Omega-6s/Omega-3s was much lower in the tuna oil group – 1.5 compared to 13 in the sunflower oil group – not surprising as sunflower oil contains no Omega-3s.

This study's conclusion:

Incorporation of dietary Omega-3 fatty acids into atrial tissue reduces stretch-induced susceptibility to AF.

Reference: Ninio DM, Murphy KJ, Howe PR, Saint DA. Dietary fish oil protects against stretch-induced vulnerability to atrial fibrillation in a rabbit model. *J Cardiovasc Electrophysiol.* 2005 Nov;16(11):1189-94

Do the cardiovascular benefits apply to elite athletes?

Australian Rules football players were given either HiDHA® tuna oil or sunflower oil daily (control) during 5 weeks of training. Compared to the control group, the subjects in the tuna oil group showed the following benefits after 5 weeks:

- **red blood cell Omega-3s:** increased
- **triglycerides:** decreased
- **diastolic blood pressure:** decreased
- **heart rate during submaximal exercise:** decreased

Reference: Buckley JD et al, unpublished data

Synergy with cholesterol medication

The aims of this study were to evaluate the effects of a high DHA fish oil on people with high triglyceride levels who were already being treated with statin drugs for their high cholesterol levels.

The volunteers were given either HiDHA® tuna oil or olive oil (placebo) for 6 months.

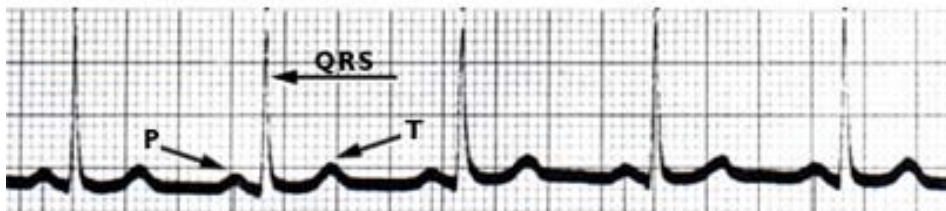
By 3 months there was a 27% reduction in triglyceride levels in the tuna oil group compared to the olive oil group which was maintained at 6 months. The total cholesterol was already well controlled by the statin treatment but there was a further reduction with HiDHA® tuna oil supplementation. The researchers stated that the results demonstrate that DHA-rich fish oil supplementation (2.16 g DHA/day) can improve plasma lipids in people taking statins and these changes were achieved by 3 months.

This study's conclusion:

Fish oil in addition to statin therapy may be preferable to drug combinations for the treatment of high blood cholesterol and triglycerides.

Reference: Meyer BJ, Hammervold T, Rustan AC, Howe PR. Dose-dependent effects of docosahexaenoic acid supplementation on blood lipids in statin-treated hyperlipidaemic subjects. *Lipids.* 2007 Mar;42(2):109-15.

ECG: Normal Heartbeat



ECG: Ventricular Fibrillation



More synergies - HiDHA® tuna oil and plant sterols

People with high blood cholesterol and triglycerides were given either HiDHA® tuna oil (1.5g/day Omega-3 DHA+EPA) or a placebo with or without a margarine-type spread enriched with plant sterols (2g/day). The combination of Omega-3s and plant sterols provided the greatest reduction in risk of cardiovascular disease by 14% and a marker of inflammation by 46%. These factors were reduced by plant sterols alone by almost 12% and 7% and by tuna oil alone by over 9% and 40% respectively.

This study's conclusion:

Long chain Omega-3s and plant sterols may have a synergistic effect in reducing cardiovascular risk and inflammation in people with high blood fats.

Reference: Micallef MA, Garg ML. Synergistic effects of phytosterols and long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA) on cardiovascular risk reduction in hyperlipidemic subjects. *AsiaPacClinNutr* 2007;16(Suppl 3):S101.

Dose effect of Omega-3 consumption

Intake of long-chain Omega-3s, particularly DHA, has been shown to improve cardiovascular risk factors. In this study the researchers looked at the amount required to achieve these benefits. This high quality study gave volunteers either 2, 4 or 6 grams/day of HiDHA® tuna oil or a placebo (Sunola oil).

For every 1 gram/day increase in DHA intake, there was a 23 % reduction in triglyceride levels, a 4.4 % increase in HDL-cholesterol and 7.1 % increase in LDL-cholesterol (only in the 4g/d group). Red blood cell (erythrocyte) DHA content increased in proportion to the dose of DHA consumed.

This study's conclusion:

The close association between incorporation of DHA in erythrocytes and its effects on serum lipids highlights the importance of erythrocyte DHA as an indicator of cardiovascular health status.

Reference: Milte CM, Coates AM, Buckley JD, Hill AM, Howe PR. Dose-dependent effects of docosahexaenoic acid-rich fish oil on erythrocyte docosahexaenoic acid and blood lipid levels. *Br J Nutr*. 2007 Oct 31;116



Menopause and the heart

Before menopause women have a lower risk of heart disease than men of the same age, possibly due to the protective effects of oestrogen. After menopause, women's heart disease risk increases. This preliminary study looked at an animal model to see if supplementation with fish oil (HiDHA® tuna oil) could reduce the risk of heart disease in females after simulated menopause.

So far the researchers have found that ovarian oestrogen withdrawal (as occurs in menopause) alters the cardiac membrane Omega-6:Omega-3 ratio and that tuna oil alters the recovery of the heart in response to a period of oxygen deprivation (as occurs in a heart attack) which may be a protective mechanism for prolonged survival.

Reference: Delbridge L et al, unpublished data

HiDHA® and the brain

Depression

Increasing levels of DHA in the body associated with reduced depression. A/Professor Barbara Meyer and colleagues gave volunteers who were receiving treatment for major depression either HiDHA® tuna oil or olive oil (placebo) for 4 months. Their depression was scored by a psychodiagnostician using several different measures during this time.

With HiDHA® supplementation, red blood cell Omega-3 DHA content increased by almost 90% but there was no change with the placebo group. Red blood cell levels of Omega-3 fatty acids are an indication of body levels of these nutrients.

A statistical analysis indicated that there was a significant association between the change in red blood cell DHA and the depression scores.

Reference: BJ Meyer BJ, Grenyer B, Crowe T, Owen AJ, Howe PRC. Improvement of major depression is associated with increased erythrocyte DHA - subset analysis in a double-blind Omega-3 supplementation trial. Presented at ISSFAL conference, 2004.

This study's conclusion:

HiDHA® tuna oil is effective in raising levels of DHA in the body. Further study of the relationship between DHA and depression is warranted.

More research underway...

Another group of researchers is currently looking at the effects of HiDHA® tuna oil on bipolar disorder with preliminary findings looking positive.

Eye health and HiDHA®

Eye health with increasing age

Researchers from the University of Melbourne looked at the effects of dietary Omega-3s on the pressure of fluid in the eye. Increased pressure is a risk factor for glaucoma, a common eye disorder which can lead to vision loss and blindness if untreated. This is due to permanent damage to the optic nerve.

Long chain Omega-3 DHA is found in concentrated amounts in the retina where it plays an important role in sending signals between the eye and brain.

The researchers compared animals fed either a high Omega-3 (using HiDHA® tuna oil) or low Omega-3 diet. They found that increasing dietary Omega-3s with age reduced the pressure of fluid in the eye by 13%. This was associated with a 56% increase in fluid flow and a 59% decreased rigidity of the cornea.



This study's conclusion:

...dietary manipulation may provide a modifiable factor for intraocular pressure regulation. However, further studies are needed to consider whether this can modify the risk for glaucoma and can play a role in treatment of the disease.

Reference: Nguyen CT, Bui BV, Sinclair AJ, Vingrys AJ. Dietary Omega 3 fatty acids decrease intraocular pressure with age by increasing aqueous outflow. Invest Ophthalmol Vis Sci. 2007 Feb;48(2):756-62.

HiDHA® and performance

Performance – heart and muscles

Professor Peter McLennan from the University of Wollongong has been studying the effects of DHA-rich fish oil (HiDHA® tuna oil) on the heart and other muscles. He has demonstrated a strong relationship between the heart cell membrane composition of Omega-3s and prevention of the fatal heart rhythm disturbance, ventricular fibrillation, under conditions mimicking human sudden heart attack death. The anti-arrhythmic effect can be achieved with low supplementation and after a relatively short time but only in association with the incorporation of Omega-3 DHA into the membranes of heart muscle cells.

Further studies using an animal model show another cardioprotective effect. Animals fed Omega-3s use oxygen more efficiently and have a slower heart rate giving them a reserve capacity during exercise or trauma.

Similarly, trained cyclists have a lower heart rate and lower oxygen consumption during exercise after tuna oil supplementation.



Conclusion:

The experimental animal data indicate that Omega-3s are essential for normal heart function and provide cardioprotection as a direct consequence of their incorporation into heart cell membranes. Omega-3 s may offer a new approach to the optimization of heart function and reduction in cardiac disease mortality and morbidity.

References:

Pepe S, McLennan PL. Cardiac membrane fatty acid composition modulates myocardial oxygen consumption and postischemic recovery of contractile function. Circulation. 2002 May 14;105(19):2303-8.

McLennan PL. Presentation at Pacific Lipids, Auckland, 2004

HiDHA® and asthma – the Childhood Asthma Prevention Study (CAPS)

Observational studies have linked dietary fatty acid intake with asthma in childhood. This 5 year study looked at the effects of supplementation with Omega-3s (from HiDHA® tuna oil) on asthma and related symptoms in children. Pregnant women with a family history of asthma were randomly divided into groups who either received Omega-3 dietary intervention or not. The dietary intervention consisted of low Omega-6 oils and canola margarines in the family diet and tuna oil capsules added to the formula of non-breast-fed babies and at 6 months of age, 500mg tuna oil added to their food.

At 18 months of age, children with additional Omega-3s had a 9.8% reduction in the prevalence of any wheeze and a 7.8% reduction in prevalence of wheeze lasting more than 1 week.

Conclusion 1: Increasing dietary omega-3 fatty acids might have a beneficial effect on the prevalence of wheeze during the first 18 months of life.

At 3 years there was a significant 10.0% reduction in the prevalence of cough

in atopic children in the Omega-3 group but no significant differences in wheeze were found.

Conclusion 2: These results suggest that the intervention may have a role in preventing the development of allergic sensitization and airways disease in early childhood. This offers the prospect of reducing allergic disease in later life.

516 children (84% of the original group) were evaluated at age 5 years. The ratio of Omega-6 to Omega-3s in plasma was lower in the active diet group. However, the prevalence of asthma, wheezing, eczema, or atopy did not differ between the groups.

Conclusion 3: Further research is required to establish whether other interventions can be recommended for the prevention of asthma and allergic disease. Dietary fatty acid modification, as implemented in this trial during infancy and early childhood, did not prevent the onset of asthma, eczema, or atopy in high-risk children.

References:

Mihrshahi S, Peat JK, Webb K, Tovey ER, Marks GB, Mellis CM, Leeder SR. The childhood asthma prevention study (CAPS): design and research protocol of a randomized trial for the primary prevention of asthma. *Control Clin Trials*. 2001 Jun;22(3):333-54.

Mihrshahi S, Peat JK, Marks GB, Mellis CM, Tovey ER, Webb K, Britton WJ, Leeder SR; Childhood Asthma Prevention Study.

Eighteen-month outcomes of house dust mite avoidance and dietary fatty acid modification in the Childhood Asthma Prevention Study (CAPS). *J Allergy Clin Immunol*. 2003 Jan;111(1):162-8. Erratum in: *J Allergy Clin Immunol*. 2003 Apr;111(4):735.

Mihrshahi S, Peat JK, Webb K, Oddy W, Marks GB, Mellis CM; CAPS Team. Effect of omega-3 fatty acid concentrations in plasma on symptoms of asthma at 18 months of age. *Pediatr Allergy Immunol*. 2004 Dec;15(6):517-22.

Peat JK, Mihrshahi S, Kemp AS, Marks GB, Tovey ER, Webb K, Mellis CM, Leeder SR. Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. *J Allergy Clin Immunol*. 2004 Oct;114(4):807-13.

Marks GB, Mihrshahi S, Kemp AS, Tovey ER, Webb K, Almqvist C, Ampon RD, Crisafulli D, Belousova EG, Mellis CM, Peat JK, Leeder SR. Prevention of asthma during the first 5 years of life: a randomized controlled trial. *J Allergy Clin Immunol*. 2006 Jul;118(1):53-61. Epub 2006 May 30.



Oral health and HiDHA®

This study assessed the effects of HiDHA® tuna oil on periodontitis, an oral disease which is thought to result from an inflammatory response to certain bacteria living between the teeth and gums. If untreated it destroys the soft tissue and bone that support the teeth, and eventually may cause tooth loss.

Mice fed tuna oil had significantly higher Omega-3 levels in oral soft tissues and 54-72% less bone loss when inoculated with bacteria compared to the control group.

This study's conclusion:

The bone loss was inversely related to Omega-3 tissue levels indicating that Omega-3-rich fish oil may have potential benefits in the prevention and/or management of periodontitis.

Reference: Bendyk A et al, unpublished data