

# IVADAS INTRODUCTION

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## Fish oil, polyphenols, and physical performance

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### Summary

Due to dietary changes since 1900, including reduced intakes of oily fish and the commoditisation of plant oils, Omega 6/3 ratios rose consistently from around 1-2:1 and now the average is 15:1 in the United Kingdom and 25:1 in the United States of America. These abnormally high ratios create an increased tendency towards chronic inflammation and provide a significant cause of chronic degenerative diseases. As chronic inflammation involving skeletal muscle and articular tissues hampers sporting and athletic performance, we identified a Norwegian professional team of football players, which had a significant absenteeism rate due to infection and injury, as a candidate for a pharmaconutritional program designed to reduce the 6:3 ratio. We hypothesised that such a change would reduce players' burden of chronic inflammation and contribute to various types of performance enhancement.

Initially, we tested the blood of all players in Lillestrøm Sports Club (LSK) and found that their average Omega 6:3 ratio was 12.5:1. Then we implemented a dietary program, which included an Omega-3 / lipophile polyphenol blend and which was continued over a 6-month period. This duration was necessary as it was already known that changes in cell membrane lipid populations would take at least 3 months to achieve, due to the slow rate of turnover of the phosphatidyl phospholipid components in cell membranes.

By the end of the intervention period, we were able to reduce their average Omega 6/3 ratios from 12.5 to 3.5. Rates of absenteeism, due to infection and injury, were reduced by 85 and 57% respectively, contributing to improved performance, morale, and position in the league. The Omega 3 / lipophile polyphenol pharmaconutritional intervention provided an extremely cost-effective way of optimising individual and particularly team performance leading to expressions of interest from many other clubs both in Norway and abroad and from the representatives of many other team sports.

This initial study has inherent limitations as it was an open design without a control group and as such was vulnerable to the placebo and Hawthorne effects. It may be argued that the duration of the study is long enough to minimise such effects but, from a purist perspective, those potential confounders cannot be excluded. Accordingly, we are planning to follow up this initial study with more rigorously designed trial utilising placebo control and longer duration, possibly, as long as 12 months. We hope to be able to report on this trial in Q1 2017.

**Keywords:**  $\omega$ 3,  $\omega$ 6, polyphenols, lipophile, performance, chronic inflammation.

### Introduction

The Omega-3 ( $\omega$ 3) polyunsaturated fatty acids in our diet are critically important anti-inflammatory nutrients. After ingestion they are, like other dietary fats, subject to beta oxidation but they also are predominantly incorporated as phosphatidyl phospholipids into the membranes of all our cells. These are dominant structural membrane components but, when degraded by phospholipase A2 (PLA2), the fatty acid components become substrates for the immunoregulatory enzymes cyclooxygenase (COX) and lipoxygenase (LOX).

When these enzymes act on saturated fatty acids and  $\omega$ 6 fatty acids, they generate pro-inflammatory metabolites such as IL-1 beta, IL-2, IL-6, and TNF-alpha; when they act on Omega-6 ( $\omega$ 3) fatty acids, they form anti-inflammatory metabolites, including

Series 3 prostaglandins, resolvins, protectins, and maresins (Colin et al., 2003; Simopoulos, 2008). If  $\omega$ 3 fatty acids predominate in cell membranes we are less likely to suffer from chronic inflammation and, thereby, gain a degree of protection against degenerative disease. If  $\omega$ 3 fatty acids are in the minority and our cell membranes are dominated by saturated and  $\omega$ 6 fatty acids, we are more likely to suffer from chronic inflammation and degenerative disease. This is particularly true in individuals with specific genetic vulnerabilities such as variants of the enzymes delta-6-desaturase and delta-5-desaturase (Schaeffer et al., 2006).

The relative amounts of the different fatty acids in our cell membranes are determined by relative amounts of different fatty acids in our diet. This has changed dramatically over the last century or so

(Clayton, Rowbotham, 2009; Blasbalg et al., 2011). Between 1909 and 1999 per capita consumption of oily fish declined, while the estimated consumption of plant oils such as soybean oil increased more than 1000-fold (Blasbalg et al., 2011). Accordingly, intakes of the  $\omega 6$  fatty acid Linoleic acid (LA) increased from 2.79% to 7.21% of energy; and the 6:3 ratio in our diet and cell membranes increased dramatically reaching an average 15:1 in Europe and 25:1 in the USA (Simopoulos, 2002; St Olav, 2015).

These abnormally high  $\omega 3/\omega 6$  ratios increase the tendency to chronic inflammation and are involved in the pathogenesis of all the chronic inflammatory diseases including cardiovascular disease, cancer, depressive illness, and the autoimmune diseases (Colin et al., 2003; Simopoulos, 2002, 2008). Conversely, a lower ratio enhances the functions of many tissues such as the eyes, immune system, and the CNS and reduces or stops chronic inflammation as well as improves or reduces the risk of many disease states. For example, whereas  $\omega 6/\omega 3$  ratio of 10:1 or higher exacerbates asthma, a ratio of 5:1 reduces asthmatic patients' symptoms and a ratio between 3:1 and 2:1 suppresses inflammation for related symptoms in patients with rheumatoid arthritis (Simopoulos, 2008; von Schaky, 2011).

As chronic inflammation results in tissue damage, which impacts negatively on physical performance, one might expect the omega 3's to have some beneficial effects on physical performance. Although a number of studies have assessed the efficacy of  $\omega 3$ PUFA supplementation on red blood cells deformability, muscle damage, inflammation, and metabolism during exercise, only a few studies have evaluated the impact of  $\omega 3$ PUFA supplementation on exercise performance. Some studies do show performance-related benefits in elderly subjects (Smith et al., 2008; Clayton, Rowbotham, 2009) or in young persons and athletes (Lembke et al., 2014; Lewis et al., 2015) but there are as many negative results (Krzywińska-Siemaszko et al., 2015). Discrepant outcomes such as these have led for calls (Shei et al., 2014) for more specific and more powerful studies designed to narrow down exactly what performance benefits  $\omega 3$  supplementation might have and in which sub-groups (age, sex, nutritional status, fitness level) those benefits might be most apparent.

Our approach was somewhat different. Taking as starting point, the concept that the anti-inflammatory effects and health benefits of the Inuit diet were not

solely attributable to the  $\omega 3$ 's but to the Inuit's dietary combination of  $\omega 3$ 's and lipophilic polyphenols (Clayton, Ladi, 2015), we set out to measure the effects of an  $\omega 3$  / lipophile polyphenol combination in a closely defined group of professional football players.

## Materials and methods

A standardised blend of 30% fish oil and high polyphenol olive oil was administered in doses calculated per body weight; for the majority of players it resulted in a dose of 12.5 ml/day. Lipid profiles were measured using dried blood spot technology, enabling the assay of the predominant 11 fatty acids in erythrocyte cell membranes. This was carried out by St Olav's certified analytical laboratory at Trondheim University (Norway).

### *Preventative Health at Lillestrøm Sports Club (LSK), Norway*

During preparations for the 2008/2009 season, a high incidence of infection and injuries in players, which was causing 65.8 man/days of absence per month, encouraged Lillestrøm Sports Club ([www.lsk.no](http://www.lsk.no)) to set up a preventative health program in October '09. The objective was to improve players' diet in a way predicted to reduce infection, injury, and recovery time. If successful, this would lead to increased time for players to collaborate in training and in competition and, possibly, contributing to a higher league rating.

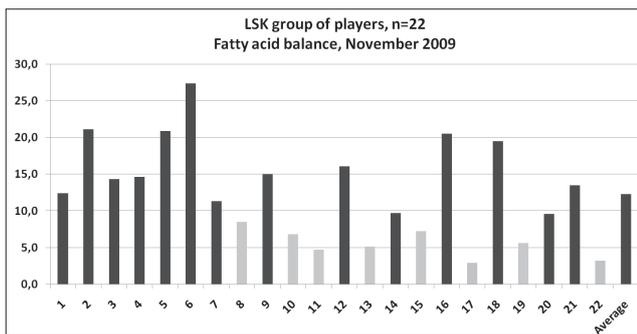
Targeted dietary adjustment was achieved through common breakfast and lunch for the group of players involving a general reduction in dietary Glycemic Load (GL) and at least two fish-based lunches per week plus the obligatory use of a blended fish oil / high polyphenol olive oil called Balance oil.

## Results

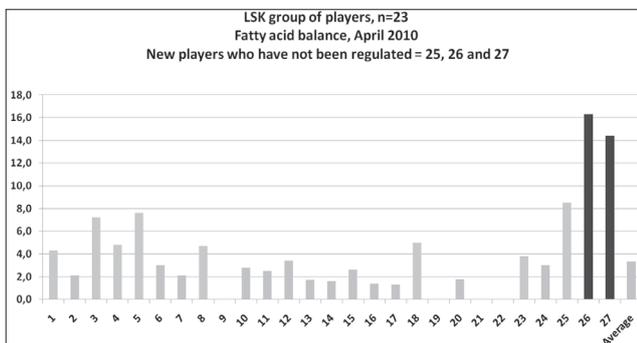
In November 2009, the fatty acid profile of all players in the elite group at LSK was measured. The results showed an average 6:3 ratio of 12.5:1 for the group (Fig. 1), with an average  $\omega 3$  level of 5.1 and an average  $\omega 6$  level of 64.2.

Blood values during the trial period changed from a clear  $\omega 6$  dominance to a balanced distribution between  $\omega 3$  and  $\omega 6$  fatty acids. After 16 weeks of Balance oil, the average  $\omega 6:3$  balance for the group of players fell from 12.5:1 to 3.4:1 (Fig. 2). Individual players, who initially had extremely unfavorable blood values during the period, were adjusted to better than the average values for the whole of the group of players.

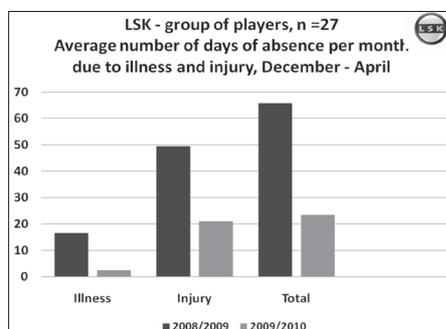
The effect on player performance was remarkable. Comparing the preparation period for the 2009/2010 season with the same period in 2008/2009 (November-April), absence due to illness fell by 85%, while absence due to injury fell by 57% (Fig. 3). Overall, this gave the team an extra 42 player/days per month to train together. During this same period, players demonstrated a clear improvement in physical tests. The reduction in absenteeism was highly significant; LSK now enjoyed the fewest days of absence than any other club in the league.



**Fig. 1.** Fatty acid ratios of LSK players before supplementation.  $\omega 6:3 > 9:1$  designated in black,  $\omega 6:3 < 3:1$  designated in gray



**Fig. 2.** Fatty acid ratios of LSK players after supplementation for 6 months.  $\omega 6:3 > 9:1$  designated in black,  $\omega 6:3 < 3:1$  designated in gray



**Fig. 3.** Impact of Balance oil on player health over 2 seasons

## Discussion

Studies at the University of Tromsø in Norway have shown that the industrial processes used to extract fish oil destroy or remove the trace ingredients

in fish (such as the polyphenols) that likely played a critical role in conferring their original health benefits and certainly greatly reduced anti-inflammatory effects of the oil (Elvevoll, Osterud, 2003). In fact, the removal of antioxidants and other trace compounds creates a situation where the purified fish oils can become pro-oxidative (Sanders, Hinds, 1992; Sen et al., 1997; Umegaki et al., 2001; Vericel et al., 2003; Schubert et al., 2010), pro-inflammatory (Mata et al., 1996; Berstad et al., 2003), and cause increased DNA damage (Schubert et al., 2010). Worryingly, there is evidence that older subjects – the bulk of those who take  $\omega 3$  supplements – are intrinsically more vulnerable to its pro-oxidative effects (Cazzola et al., 2007) probably because they are not eating enough of the appropriate antioxidants to compensate for the  $\omega 3$ 's (Umegaki et al., 2001).

A series of studies have shown multiple negative effects of purified fish oils, ranging from biochemical markers such as increased inflammatory cytokines and oxidative stress (Johansen et al., 1999; Seljeflot et al., 1999; Burr et al., 2005; Cunane, 2013) to clinical end-points including increased angina and atheroma (Simpoulos, 2008). The DART 2 trial, the only clinical trial lasting more than four years, showed that fish oil capsules increased the risk of heart disease and sudden death (Burr et al., 2005). A large meta-analysis (which reviewed 20 studies involving 68,680 patients) showed that supplementing with purified omega-3 PUFA's was not associated with a lower risk of all-cause mortality, cardiac death, sudden death, myocardial infarction, or stroke based on relative and absolute measures of association (Burr et al., 2003). There is a general consensus, however, that eating oily fish reduces all-cause and coronary heart mortality (Mozaffarian et al., 2013) so there is an apparent discrepancy between the effects of fish and the effects of fish oil.

We believe that some of the discrepancy is due to poorly formulated fish oil.

Vitamin E, the antioxidant most commonly used in fish oil capsules, is not the right candidate. It may protect the oils while they are in the capsule, but it does not protect them once they have been consumed. Supplementing the diet with purified  $\omega 3$  fatty acids increases lipid peroxidation as measured by plasma MDA release and lipid peroxide products and this is not effectively suppressed by vitamin E supplementation (Allard et al., 1997). Even more worrying, when  $\omega 3$ 's and meat are consumed together (as they were in the Inuit diet), vitamin E

acts as a pro-oxidant and increases the oxidation of the  $\omega$ 3's (Tirosch et al., 2015).

Lipophile polyphenols such as the phlorotannins present in the marine algae which are the source of all  $\omega$ 3 PUFA's; and the secoiridoids found in olive oil are far more effective in stabilising  $\omega$ 3's than vitamin E (AOCS, 2010). In addition, they have potent anti-inflammatory effects of their own. Our results indicate that the administration of a standardised blend of fish oil and lipophile polyphenols reliably improved  $\omega$ 6:3 ratios in the cell membranes of young professional sportspersons and significantly improved their overall health and performance.

## Conclusion

Typical sportspersons such as the professional football players at LSK Norway have  $\omega$ 6:3 ratios in their blood averaging 12.5. This is far higher than government recommendations and is known to increase the tendency to chronic inflammation and ill health. A course of relatively high dose  $\omega$ 3 fish oil blended with lipophile polyphenols reduced  $\omega$ 6:3 ratios to 3.5 and led to significant reductions in absenteeism due to infection and injury. This simple nutritional strategy encouraged significant gains in performance and productivity and was highly cost-effective. We consider this as preliminary study and plan to extend our research with more ambitious nutritional programs that also include the immune-regulatory 1-3, 1-6 beta glucans and a range of micro- and phyto-nutrients. We believe that such programs have the potential to achieve further significant improvements in individual and team sporting performance.

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## ŽUVŲ TAUKAI, POLIFENOLIS IR FIZINĖ VEIKLA

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### SANTRAUKA

Nuo 1900 m. dėl įvykusių mitybos pokyčių, su mažėjusio riebiųjų žuvų vartojimo ir augalinių aliejų paplitimo omega 6/3 santykis, nuosekliai didėdamas, išaugo nuo maždaug 1–2:1 iki vidutiniškai 15:1 Jungtinėje Karalystėje ir 25:1 Jungtinėse Amerikos Valstijose. Toks akivaizdžiai per didelis santykis sukuria didesnę polinkį lėtiniam uždegimams ir sudaro palankias sąlygas atsirasti lėtinėms degeneracinėms ligoms. Atsižvelgiant į tai, kad lėtiniai uždegimai, tarp kurių paminėtini griaučių raumenų ir sąnario audinių uždegimai, turi neigiamos įtakos sportinei ir judamajai veiklai apskritai, buvo pradėtas tyrimas taikant specialią mitybos programą, skirtą sumažinti 6/3 santykį. Tyrimo dalyviu buvo pasirinkta profesionali Norvegijos futbolo komanda, kurioje dėl žaidėjų patiriamų infekcijų ir traumų buvo praleidžiama gana daug pratybų ir varžybų. Buvo iškelta hipotezė, kad šio santykio pokytis palengvins žaidėjų dėl lėtinio uždegimų patiriamus sunkumus ir įvairiapusiškai pagerins jų sportinės veiklos kokybę.

Tyrimo pradžioje buvo paimti mėginiai ir ištirtas visų Lilestriomo (*Lillestrom*) sporto klubo (LSK) žaidėjų kraujas; nustatytas vidutinis omega 6/3 santykis buvo 12,5:1. Tolesniame etape buvo įgyvendinta mitybos programa, vartojant omega-3 / lipofilinį (sugeriantį riebalus) polifenolio mišinį. Programa truko šešis mėnesius. Jos įgyvendinimo trukmę lėmė tai, kad ląstelės membranos lipidų populiacijos pokyčiai dėl lėtos fosfatidiletanolamino fosfolipidų komponentų apykaitos ląstelės membranose trunka mažiausiai tris mėnesius.

Intervencinio laikotarpio pabaigoje mums pavyko sumažinti tiriamųjų vidutinį omega 6/3 santykį nuo 12,5 iki 3,5. Futbolo žaidėjų nedalyvavimas sportinėje veikloje dėl patiriamų infekcijų ir traumų sumažėjo atitinkamai nuo 85 iki 57 %, kartu pagerėjo žaidimo kokybė, o tai lėmė komandos patekimą į aukštesnę vietą lygoje. Omega-3 / lipofilinė polifenolio mitybos intervencija sudarė ypatingą galimybę optimizuoti individualų ir ypač komandinį darbą, su-

keldama didelį daugelio kitų sporto klubų Norvegijoje ir už jos ribų, taip pat ir kitų komandinių sporto šakų atstovų susidomėjimą.

Šis mūsų pirmasis tyrimas buvo ribotas, nes eksperimentas vyko atvirai, be kontrolinės grupės; dėl to egzistuoja placebo bei Hotorno efekto (*Hawthorne effects*) tikimybė. Dėl ilgo tyrimo laikotarpio šių efek-

tų pasireiškimas gali būti ginčytinas, tačiau, vertinant teoriškai, turi būti atsižvelgiama į šiuos efektus. Tikimės tęsti pradėtą darbą, tik labiau kontroliuoti placebo efektą ir naudoti ilgesnį tyrimo laiką (apie 12 mėnesių). Tyrimo rezultatus tikimės paskelbti 2017 m. pirmame ketvirtyje.

*Raktažodžiai:*  $\omega$ 3,  $\omega$ 6, polifenolis, lipofilinis (sugeriantis riebalus), sportinė veikla, lėtiniai uždegimai.

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