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Editorial

Fish Phospholipids: Dietary Components with Anti-Atherogenic Potentiality

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Background

Epidemiological studies have demonstrated the protective role of fish and fish oil consumption against Coronary Heart Diseases (CHD), while the nutritional benefits of fish consumption were mainly attributed to omega-3 polyunsaturated fatty acids (PUFAs) [1]. Clinically, men who consume oily fish at least once a week had a 50% lower incidence of CHD and sudden cardiac death [2-4]. Although the mechanism of action remains unclear, omega-3 PUFAs cardioprotective activity could be through lowering the levels of triacylglycerol, preventing arrhythmias, decreasing platelet aggregation, or lowering blood pressure [5].

On the other hand, the association of omega-3 PUFAs and cardiovascular diseases (CVDs) has been revised recently by evaluating all randomized trials on the supplementation of omega-3 PUFAs to adults [6]. In this review, the results of 20 studies on 68,680 patients were evaluated and omega-3 PUFAs were found to have no statistically significant association with CVDs in various patient populations. Additionally scientific data suggest that other substances, apart from omega-3 PUFAs, may be responsible for the anti-atherogenic properties of marine fish [7,8].

Fish Phospholipids

Lipid micro-constituents present in fish have been found to exert *in vitro* biological anti-inflammatory and antithrombotic activity which inhibits platelet activating factor (PAF) actions [9-12]. PAF represents a highly active lipid mediator produced and released by various stimulated cells [13], while it promotes, through its receptor [14], a wide range of biological responses such as oxidation, inflammation and thrombosis that have been linked to the pathogenesis of many inflammatory chronic diseases such as atherosclerosis [15].

The presence of PAF antagonists in fish muscle, such as mackerel (*Scomber scombrus*) has been shown for the first time by Rementzis et al. (1997). The lipid components that were identified in the aforementioned fish muscle were gangliosides; complex glycolipids that are found in the outer half of the membrane bilayer with their sugar groups exposed at the cell surface, suggesting some role in the interactions of the cell with its surroundings [12].

A more recent study regarding the impact of grilling and brining on the cardio-protective properties of sardine (*Sardina pilchardus*), in terms of PAF-antagonist content, revealed that phospholipids (e.g. sphingomyelin and phosphatidylethanolamine) of all specimens (raw, grilled and brined) have been found to exert strong inhibitory activity against PAF activity indicating that grilling and brining have not diminished the cardio-protective properties of sardine [9]. These lipid micro constituents could thus inhibit the onset of atherogenesis and the development of CVDs.

Furthermore an *in vivo* study of gilthead sea breams (*Sparus aurata*) [16] have reconfirmed that it is the fish phospholipids that can reduce the thickness of atherosclerotic lesions in hypercholesterolemic rabbits. More specifically, twelve healthy male New Zealand rabbits of specific weight were randomly divided into two groups of six animals each and were given specific diets for 45 days. Group A was given atherogenic diet 1% cholesterol, while group B was given atherogenic diet fortified with gilthead sea bream phospolipids (0.06% w/w) [16]. The obtained results showed that diet supplementation with fish phospholipids, in hypercholesterolemic rabbits has been found to developed early atherosclerosis lesions of significantly lower degree compared to control group receiving the atherogenic diet [16].

These data could be explained on the basis of the elevated activity of the main catabolic enzyme of PAF; PAF-Acetylhydrolase (PAF-AH) in the plasma of rabbits of group B, in combination with the decreased platelet aggregation of group B. The decreased platelet aggregation of group B could be attributed to the presence of PAF-inhibitors in gilthead sea bream phospholipids. In addition, earlier scientific data has underlined the *in vitro* inhibition of the main regulatory enzyme of de novo PAF biosynthetic pathway; PAF-cholinephosphotransferase (PAF-CPT), on human mesangial cells by gilthead sea bream phospholipids [17].

A further mechanistic study performed on the specific activities of four PAF metabolic enzymes in leukocytes, platelets and plasma of the male New Zealand white rabbits of group A and B of the aforementioned *in vivo* experiment demonstrated decreased PAF-CPT activity in leukocytes of group B along with decreased activities of both PAF biosynthetic enzymes: PAF-CPT and Lyso PAF-acetyltransferase (Lyso PAF-AT) in platelets of group B [18]. Therefore it has been underlined that gilthead sea bream phospholipids have modulated PAF metabolic enzymes in blood (by down-regulating PAF biosynthesis and up-regulating PAF catabolism) upon atherogenesis and also maintained low levels of PAF [18].

Research Perspectives

The steadily increase of global population results in higher food consumption and increased demand for processed food, meat, dairy and fish [19]. At the same time the biggest challenge is the development of environmentally sustainable procedures of food

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production reinsuring food security and suppressing environmental pollution.

In terms of food security in aquaculture, it is necessary to overcome the obstacle of fish oil dependence on the sustainable production of fish feed. Currently, one million tonnes of fish oil are produced on an annual basis [20], while 40% and 60% of the global production of fish meal and fish oil, respectively, are used in aquaculture [21]. These data suggest that the diminishing levels of available wild fish worldwide combined with the fact that aquacultured carnivorous species require large amounts of wild fish in their feed [22] create an emerging necessity to improve the resource management practices.

Over the past few years, significant breakthroughs have occurred in the partial replacement of fish oil by plant oils, such as soybean, linseed, rapeseed, sunflower, palm oil, olive oil and Olive Pomace (OP) (a major by-product of the olive oil extraction industry) in compounded fish feeds and several studies have been carried out to investigate certain vegetable oils as possible sustainable partial substitutes for fish oils in compounded fish feeds [21].

Recent scientific data demonstrated that the partial replacement (8 %) of fish oil with OP in the fish feed induced a satisfactory growth performance in gilthead sea bream (*Sparus aurata*) at the end of the on-growing period (90 days), while the antithrombotic activity of the fish lipids obtained from the fish fed with the OP diet has been found to be significantly increased in comparison with the fish fed with the conventional fish diet [23].

Similar observations obtained from the partial replacement (4 %) of fish oil with OP in the fish feed of sea bass (*Dicentrarchus labrax*) at the end of the on-growing period (180 days) [24]. The structural characterisation of fish phospholipids obtained from sea bass fed with OP diet underlined that the phosphatidylcholine derivatives identified could serve as natural precursors, where upon phospholipase A_2 activities allow liberation of free DHA and EPA fatty acids [24].

Given that some fish phospholipids exert beneficial effect against CVDs, future research could be focused on correlating the structure of these phospholipids to specific mechanisms in the development of atherogenesis.

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