

COMMENTARIES

The Prevention of Atherosclerosis by Food Components: Polar Lipids versus Omega-3 PUFAs

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Background

Since the study of the seven countries [1], some unanswered questions still remain as to why cohorts in Greece and Italy had coronary heart disease (CHD) at low frequencies but high levels of serum cholesterol. Although preventable, cardiovascular diseases (CVDs) remain the top global cause of death and stroke [2]. For this reason, the prevention of atherosclerosis is a major objective of modern medical and biochemical investigations into the mechanism of atherosclerosis and how the structure of food components determines their role in the mechanism(s) involved.

Atherosclerosis is a chronic inflammatory condition caused by the deposition of cholesterol and other cellular constituents in the intima of large and medium arteries [3], that can lead to an acute clinical event through plaque rupture and thrombosis where platelet activating factor (PAF) [4] plays a crucial role [5].

Polar Lipids

Lipid microconstituents of specific food that constitute important ingredients of the Mediterranean diet have been found to exert *in vitro* important biological activities, namely, anti-inflammatory and antithrombotic activity which inhibits PAF actions. PAF is the most potent inflammatory lipid mediator, a well-recognized agonist of platelet aggregation that plays a crucial role in atherosclerosis. These lipid microconstituents could thus inhibit the onset of atherosclerosis and the development of CVDs. Such lipids have been found in a wide range of

food such as red and white wine [6], yoghurt [7], fish [8-10], olive oil [11], and olive pomace [12].

Further *in vivo* studies of olive oil [11,12], olive pomace [12,13], and fish [14] have re-confirmed that it is the polar lipid fraction of these two food sources that can reduce the thickness of atherosclerotic lesions in hypercholesterolemic rabbits and/or cause regression of the already formed atherosclerotic lesions. In a further mechanistic study, it has recently been demonstrated that the polar lipids of sea bream have modulated in blood the PAF metabolic enzymes in blood (by down-regulating PAF biosynthesis and up-regulating PAF catabolism) upon atherosclerosis and also maintained low levels of PAF [15].

These results are further reinforced by *in vivo* studies, where the consumption of traditional Greek Mediterranean meals, rich in lipid PAF inhibitors with *in vitro* action, has been found to reduce platelet activity in healthy subjects and in patients suffering from type 2 diabetes mellitus [16,17]. In addition, the results from an intervention study in metabolic syndrome patients, has shown that different lipid microconstituents, which act as PAF and/or ADP inhibitors *in vitro*, contribute to the observed variation in their postprandial anti-aggregatory action [18].

Omega-3 PUFAS

According to some studies, the consumption of oily fish leads to increased levels of omega-3 polyunsaturated fatty acids (omega-3 PUFAs) and thereafter a favorable cardiovascular prognosis, this statement was supported with epidemiological data evaluated by meta-analyses [19-22], and it was linked to higher levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [23]. Clinically, men who consume oily fish at least once a week had a 50% lower incidence of coronary heart disease (CHD) and sudden cardiac death (SCD) [19-21,24].

Mechanistically, though, it is not clear how omega-3 PUFAs work. Their postulated mechanism in preventing atherosclerosis could be through lowering the levels of triacylglycerol, preventing arrhythmias, decreasing platelet aggregation, or lowering blood pressure [25].

On the other hand, the association of omega-3 PUFAs and CVDs has been revised recently by evaluating all randomized trials on the supplementation of omega-3 PUFAs to adults [26]. In this review, the results of 20 studies on 68,680 patients were evaluated and omega-3 PUFAs were not found to be statistically significantly associated with CVDs in various patient populations.

Evaluation of Current Knowledge and Future Research Avenues

Despite the significant progress in understanding the mechanism of atherosclerosis and the factors implicated in CVDs pathology, well-designed intervention and clinical trials in human are still needed. CVDs are multifactor diseases and a reduction in LDL cholesterol and triacylglycerols alone, cannot provide either a satisfactory biochemical explanation or protection of humans. A healthy eating pattern can modify cardiovascular risk factors and its beneficial effect against atherosclerosis has been demonstrated.

From this point of view, omega-3 PUFAs that demonstrate their beneficial effect mainly through reducing plasma cholesterol and triacylglycerol levels [27] or by inhibiting some of the individual stages of atherogenesis [28-30] can neither explain satisfactorily the findings of the seven countries study [1] nor address the corresponding questions mentioned above. The supplementation of omega-3 PUFAs has not shown satisfactory results on lowering the risk for the development of CVDs [26].

It could be, thus, suggested that atherosclerosis is not primarily associated to high or low cholesterol and triacylglycerol levels, since *in vivo* studies, using experimental animals, the development of atherosclerotic lesions was not influenced by the levels of cholesterol and triacylglycerol levels but by the action of polar lipids that acted as PAF inhibitors [11-14]. This is one research avenue: the mechanism by which atherosclerosis is developed.

Another research avenue could be on studies relating the structure of compounds (with antiatherogenic properties) to their biological activity. Given that some dietary phospholipids and glycolipids exhibit beneficial effects against CVDs [31,32], future research could be focused on correlating the structure of these polar lipids to specific modes of actions and mechanisms in the development of atherosclerosis in experimental animals and also humans.

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