Roles of Dietary Lipids in Development of Atherosclerosis: LDL Oxidation.

Dra. Mª del Carmen Ramirez-Tortosa
Dpto Bioquímica y Biología Molecular, Instituto de Nutrición y Tecnología de los Alimentos, Universidad de Granada, Spain, email: mramirez@ugr.es

Cardiovascular diseases (CVD) are considered as a group of multifactorial conditions associated with atherosclerosis, hypertension and thrombosis. These pathologic entities are closely related to both genetic factors and environmental influences. Atherosclerosis is the underlying pathology in most CVD. This multifactorial disease is modifiable by dietary components and lifestyle practices. Main risk factors are involved, including elevated low and very low-density lipoproteins (LDL and VLDL), hypertension, smoking, overweight and obesity, diabetes mellitus, and sedentary lifestyle. Atherosclerosis has a high incidence and prevalence in western countries, but the origin of the disease is not clear. In Mediterranean countries, this incidence is far from occidental countries, differences that could be explained because of the dietary pattern. It is widely accepted that lipids, especially cholesterol, are involved in the development of CVD. A number of studies have indicated an association between dietary fat, elevated serum cholesterol and lipid levels, and atherosclerosis. However, recent research has emphasized the importance of other macronutrients and micronutrients as modulators implicated in the development of CVD.

Low-density lipoprotein is formed in the liver, and carries about two thirds or more of the plasma cholesterol. High levels of this lipoprotein signify a higher risk for atherosclerosis, but pathogenic mechanisms remain unclear. Both genetic predisposition and dietary components play important roles in the modification of plasma levels of LDL. Moreover, LDL infiltration into the arterial wall is also increased by smaller particle size, mechanical and immunological alterations to the endothelium, blood pressure and by a decrease in the flow rate in specific places susceptible to the development of atheromatous plaques.

Once inside the intima, LDL undergoes oxidative modification to become oxidised LDL (oxLDL), and together with changes in lipoprotein charge and the glycation of these particles, LDL becomes recognized by scavenger receptors, contributing to foam cell formation. The oxidizability of LDL depends on its fatty acid profile and on the antioxidant content, determined by dietary components. MUFAs have the advantage that they are unsaturated but more stable than polyunsaturated fatty acids (PUFAs). Many studies have demonstrated that diets rich in MUFAs, such as the Mediterranean diet, generate LDL
which is less susceptible to oxidation, reflecting a protective mechanism of olive oil in the prevention of atherosclerosis.

The beneficial effect of virgin olive oil in the prevention of chronic diseases such as atherosclerosis is widely accepted. It is known that the resistance to lipid oxidation within lipoproteins can be altered by the dietary fatty-acid profile and antioxidant content. Other researchers observed that VLDL and LDL fractions isolated from animals fed olive oil were much more resistant to oxidation than were those fed with sunflower oil. In addition, the generation of conjugated dienes was significantly lower in the LDL of the olive-oil group. In turn, this LDL incubated with endothelial cells was degraded to a lesser extent by the macrophages. Since then, numerous research teams have studied whether a MUFA-rich diet truly prevents oxidative alteration of lipoproteins more than does a PUFA-rich diet, generating lipoproteins with marked resistance to oxidation.

In our research team, we have demonstrated that a diet rich in virgin or refined olive oil in rabbits with experimental atherosclerosis protects the LDL particles from oxidation. Moreover our group has reported that the intake of a diet rich in MUFA by rabbits with experimental atherosclerosis leads to a decrease in the plasma-lipid content and a lower susceptibility of LDL to oxidation, whereas diets rich in PUFA also decrease the plasma-lipid fraction but increase LDL susceptibility to oxidation. We reported the same results in patients with peripheral vascular disease fed a diet rich in olive oil. Thus, oleic acid itself protects LDL against oxidation.

Many studies suggest that when dietary saturated fats are replaced by n-3 PUFA, LDL becomes susceptible to oxidation. In humans, the susceptibility to LDL oxidation is related to the degree of coronary stenosis). In addition, a study on the impact of different fatty acids on endothelial cell cultures and their possible influence on the lipid peroxidation of LDL reported significant increases in LDL peroxidation mediated by cells supplemented with PUFA.

The studies by our research group using a model of experimental atherosclerosis in rabbits coincide with the above results. Thus, LDL enrichment with n-3 PUFA increases the susceptibility to oxidation, in comparison with n-6 PUFA and MUFA. However, we have also found that the oxidative alterations of LDL with a high percentage of n-3 PUFA patients with peripheral vascular pathology can be reduced by the simultaneous intake of extra-virgin olive oil, since lower uptake of LDL by macrophages and lower electrophoretic mobility of LDL was demonstrated in patients who ingested 40 g of extra-virgin olive oil daily together with a 16-g supplement of fish oil for 3 months, in comparison to a control group of patients without dietary treatment.