

# **OLIVE OIL, FROM FATTY ACIDS TO ANTIOXIDANTS**

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The low-density lipoproteins are the means to transport the most part of cholesterol to plasma. It is widely recognized that a low-density proteins' increase has a key-role for the development of arteriosclerosis or cardio-coronary disease. It seems that these proteins, recognized as harmless in the "origin", represent a real danger inside the artery walls, when they are altered by an oxidation process. The possibility of oxidation for the low-density lipoproteins depends both on internal (endogenous) and on external (exogenous) factors. For the latter the food agents are extremely important, over all as regards the kinds of fatty acids and the antioxidant vitamins, present in our food. This document examines the mechanism of the low density proteins-oxidation and the role of food factors in the prevention of this process.

## **The oxidation of the low-density proteins**

Half the cholesterol present in our blood is carried by low-density lipoproteins, round particles composed by fats and proteins and formed by an external monolayer containing triglycerides and/ or esters of cholesterol (non polar-fats). One particle of these lipoproteins contains about 3600 fatty acids, half of them is polyunsaturated. The low-density lipoproteins contain also antioxidants among which Alpha-tocopherol (vitamin E).

The oxidation of the low-density proteins (per-oxidation) is a chain-reaction caused by the free radicals, that react over all when they are in touch with the oxygen. The polyunsaturated fatty acids are particularly fit for the per-oxidation of the lipids and for the division into a series of products joining the APO-B of the low-density lipoproteins.

These can be oxidated in a laboratory joining them to the macrophages (derived from the big cells called monocytes), with the smooth muscle cells and the endothelial or with the metal ions (iron or copper). The oxidation process alive is not well known and it is thought that it can be limited by the presence of antioxidants in the blood, as for example the ascorbic acid (vitamin C). The oxidation of these low-density proteins is more likely to take place in the artery walls than in the blood circle. The low-density proteins containing vitamin E, instead, are less subject to this process of oxidation, that takes place probably only when the anti-oxidant defences are scarce and over all when there is lack of alpha-tocopherol.

### **The oxidation of the lipoproteins and the arteriosclerosis**

The development of arteriosclerosis starts basically when the lipoproteins enter the artery wall and are trapped inside, where they have oxidative changes. The macrophages ( these cells are formed only when the monocytes, coming from the circle, pass through the artery wall) swallow eagerly these modified low- density lipoproteins rendering them frothy cells. The accumulation of frothy cells inside the lipoproteins causes lipid layers. These are not an important obstacle of the artery, but they are converted, as it happens with scars , into fibre plaques, that on their turn, gradually transform into arteriosclerotic lesions responsible of many diseases.

### **The olive oil and the oxidation of the lipoproteins**

The fatty acids can influence the oxidation of the low-density lipoproteins in various ways. The composition and the quantity of the saturated food fats, for example, help to determine the quantity of these lipoproteins inside the artery wall. It has been proved that the substitution of alimentary saturated fats with the polyunsaturated reduces the low- density lipoproteins , decreasing the quantity of these particles inside the artery wall and consequently the quantity( and composition) of available proteins for the oxidation. Thanks to its high content of monounsaturated fatty acids, the olive oil prevents the process of oxidation( see the section entitled “ effects of the fatty acids on the oxidation of low-density lipoproteins”) and through powerful antioxidants, as the vitamin E and phenol compounds, described here below, gives the low- density lipoproteins a further and valid protection.

### **The effects of fatty acids on the oxidation of low-density proteins**

The real link between the use of monounsaturated and polyunsaturated fatty acids and the reduction of this predisposition to oxidation of the low-density proteins has been widely analysed. Experiments on rabbits show that low- density lipoproteins rich in oleic acid( the key-fatty acid of the olive oil) are resistant to oxidation. These data are confirmed by studies on food : in fact it was demonstrated that there is a close link between the content of low density lipoproteins in linoleic acid ( the key-polyunsaturated fatty acid that is to be mainly found in the vegetal oils) and the process of oxidation. This process is particularly put in evidence when the food is rich in polyunsaturated fatty acids more than in a food-style based on monounsaturated fatty acids. Researchers have then tried to understand if this effect is caused by the catalyzing action of the polyunsaturated fatty acids or by the inhibitive action that the monounsaturated fatty acids have on this low-density lipoproteins' oxidation. It has been observed that when the

olive oil is added to our food habits, there is a decrease of the content in linoleic acid of low-density lipoproteins, the reduction of the phagocytosis by the macrophages and a minor availability to the low density lipoproteins.

### **Activities of alimentary fatty acids**

Some alimentary fatty acids can modify the composition of the cellular membrane of the monocytes increasing the production of free radicals and favouring pro-oxidant effects. A study has compared the effects of a diet rich in monounsaturated fatty acids and polyunsaturated omega 3 (present in fish oil) or omega6 (linoleic acid) on the production of superoxide anion (a free radical) in the monocytes and the macrophages. Only the omega-3 fatty acids have determined a reduction in the production of free radicals, while the monocytes have presented no meaningful change and no increase in the levels of this parameter though monounsaturated or polyunsaturated fatty acid of omega-6 series have been introduced. The mechanism of this phenomenon are still unknown, and these results haven't been reproduced anymore. Further researches on the role of the different fatty acids will be necessary to find out the hidden mechanisms of the pro-oxidant cellular activity; anyway, the cells containing a major quantity of monounsaturated fatty acids are less sensible to the oxidative damage (compared to omega-6 polyunsaturated fatty acids), probably due to the composition of the cellular membrane of such substances.

### **The anti-oxidant components of the olive oil**

The oxidative stress can play an important role in the development of different chronic diseases such as cardio-coronary pathologies and cancer. The possibility that alimentary anti-oxidants, such as the ones present in the olive oil, can have a protective action against the oxidation of low density lipoproteins, gave birth to a series of epidemiologic studies and sanitary actions.

### **The vitamin E**

Some epidemiologic studies have demonstrated that high quantities of vitamin E, assumed for a two years' period at least, effectively reduce the risk of cardio coronary diseases (31-65%); these have not given the same results in short-term experiments done with minor quantities. The most random researches providing the assumption of vitamin E have had the same results. These studies had not been planned to check cardiologic data: their duration was too limited and the advised quantities of vitamin were suboptimal. Today some great studies are being made; this

could bring to a final conclusion. Only the study called 'Cambridge Health antioxidant Study'(CHAOS) has been concluded so far. The results of this research, controlled through a placebo, made on 2000 patients with documented cardio coronary pathologies, have found out that the assumption of high quantities of vitamin E can concretely reduce the non-fatal heart attack but it has no effect on the global mortality.

The studies on the sanitary activities have been strongly criticized, because a few years' assumption is supposed not to be sufficient to show the positive effect of the antioxidants: in fact it could be necessary at least 20 years' assumption of these substances before checking positive clinic effects. Furthermore it has been shown that the assumption of vitamin E determines an increase of alpha-tocopherol both in the plasma and in the low- density lipoproteins, which turn to be more resistant to the oxidation. There is also a direct relation between the resistance of such particles and the assumed quantity of vitamin. The resistance to oxidation is higher even in elements not assuming supplementary quantities of vitamin, but that have higher plasmatic levels of tocopherol, compared to others having inferior basal levels.

**The phenol components:** the simple phenols and the phenol acids, as for example the flavonoids can remove the free radicals and the low- density lipoproteins that are more resistant to oxidation, they can also inhibit the lipid peroxidation. The phenol elements have also an anti-inflammatory and anti- haemorrhagic effect.

The benefits on health provided by the phenol flavonoids have been registered in the course of the studies "Seven Countries" and " Zuthe Elderly": in fact it was observed that the average assumption of flavonoids is linked only in an indirect way to cardiovascular disease. Further researches will be necessary to confirm the cardio protective properties of these substances.

### **Summary and conclusions**

There is some evidence that the oxidative modifications of low density lipoproteins have a key-role in the atherogenesis. The oxidation process of these particles starts with the per oxidation of the polyunsaturated fatty acids inside them. This means that the oxidation process of the low-density lipoproteins basically depends on their composition of fatty acids. This composition, determining the tendency to oxidation, can be influenced by the alimentary fatty acids: diets rich in monounsaturated fatty acids, for example, make these lipoproteins resistant to the oxidative modifications more than diets with polyunsaturated fatty acids, among them the linoleic acid. The food habits have some influence even on the composition into fatty acids of the cellular

membranes: a diet rich in monounsaturated fatty acids favours a high content of these substances in the cellular membranes, giving the cell a higher endurance against the oxidative damage.

A further protection against this oxidation is introduced by alimentary antioxidants such as the vitamins E and C, the flavonoids etc. Recent laboratory studies have demonstrated that not only the alpha-tocopherol, but also the phenolic elements, can inhibit the oxidation of the low-density lipoproteins and consequently reduce the risk of the atherosclerosis.

Further researches will be fundamental to find out the whole action of the phenolic elements. The most studies about the Mediterranean diet have mainly examined the positive effects as regards the cardiovascular system associated to an inferior assumption of saturated fats, and a higher level of monounsaturated fatty acids, but also complex carbohydrates and fibres. The recent data suggest that the protective effect on the cardiovascular system could be also provided by other substances characteristic of the Mediterranean diet, as for example the antioxidants contained in fruit, vegetable and olive oil.

A high assumption of monounsaturated fatty acids through the consumption of olive oil, can join the advantages of the cholesterol reduction with a decrease of low density lipoproteins and the inhibition of the cellular oxidation.

### **The olive oil and the atherosclerosis**

In 1833 Lobstein introduced the term "arteriosclerosis" to show a particular or general sufferance of the vascular system just before or during the old age, characterized by the vascular hardening. The term "atherosclerosis" was later created by Marchand (1904) to describe a form of arteriosclerosis causing a contemporaneous alteration of the inside and medium tunic of the arteries, using the term "atherome" coming from the Greek word "athere" which designed a skin spot containing pus. As analogy with the skin lesion, in 1940 Halter called "atheromes" the yellowish plaques of the arteries. Now the term "atherosclerosis" is universally accepted and its definition was conventionally established by the WHO (World Health Organization) in 1957 as a variable combination of inside modifications of the arteries consisting in a local deposit of lipids, blood and blood products, fibres tissue and calcium deposits with associated alterations of the medium tunic. The atherosclerosis is the main cause of death because it is one of the most widespread diseases in industrialized countries. The haemic-pathogenesis is complex and involves several factors.

Beyond some elements evidently linked to the genetic origin, there are some factors of risk which help the development of the lesion.

The most important are smoking, hypertension and cholesterol; besides all these factors, age must be taken into consideration (45-55), the male sex, diabetics, obesity, triglycerides, the oral contraceptives and the lack of physical activity. Some clinic researches, led in the last ten years, have put in evidence how the atherosclerosis is strictly connected to people's food-habits. There is in fact a higher presence in the developed countries than in developing countries; and inside the nations with a high life-style there is a sharp difference depending on regional food traditions. It is for this reason that a diet rich in animal fats was shown to favour the metabolic disorder (cholesterol) that is the basic of the atheromatic plaque; moreover how an increase of the cholesterol levels is one of the most important factors of risk for this disease. Several researchers have led systematic studies among different populations comparing their diets and checking the presence of this disease, to find out the pathogenesis' relations between the diet and the development of the atheromatic plaque. The most important among them is "Seven Countries Study" which witnessed a close relationship between the cardiovascular disease and the excessive use of animal fats that raise the cholesterol level because of their high content of saturated fatty acids. On the contrary this study demonstrated that vegetal oils, rich in unsaturated fatty acids, provide a protection against cholesterol and atherosclerosis. No effects, instead, were stressed for the monounsaturated fatty acids, as the oleic acid contained in the olive oil. It must be underlined that not all the plasmatic cholesterol is atherogeneous, but only the one linked with the low-density proteins (LDL) and particularly the one linked to LDL; while the part of cholesterol linked to HDL seems to have a protective action because these lipoproteins have the task to remove the free cholesterol from the cells, and bring it to the liver where it is taken away through the bile.