

President's Page

Olive and Oleuropein

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Cardiovascular disease is one of the leading causes of morbidity and mortality in both men and women in the western world. In the United States, it accounted for approximately 40% of all deaths in the year 2000.¹ Epidemiological data indicate that cardiovascular diseases in the Mediterranean area are considerably less common than in the rest of Europe.² This finding has been attributed to the traditional Mediterranean diet with its high consumption of olive oil and olives.

At the end of the 1950s, the Seven Countries Study was designed to investigate relationships between diet and cardiovascular diseases. Sixteen cohorts were selected in Finland, Greece, Italy, Japan, the Netherlands, the United States and Yugoslavia. The baseline survey was followed up after 5 and 10 years by repeat surveys.³ The cohorts differed in average diets. Death rates were related positively to average percentage of dietary energy from saturated fatty acids, negatively to dietary energy percentage from monounsaturated fatty acids, and were unrelated to dietary energy percentage from polyunsaturated fatty acids, proteins, carbohydrates, and alcohol. All death rates were negatively related to the ratio of monounsaturated to saturated fatty acids. Oleic acid accounted for almost all differences in monounsaturates among cohorts. All-cause and coronary heart disease death rates were low in cohorts with olive oil as the main fat.⁴

Olive products constitute a rich source of polyphenols like oleuropein and its derivatives, such as hydroxytyrosol, which have the ability to scavenge free radicals and inhibit the chemical oxidation of low density lipoproteins.^{5,6} Diets rich in olive oil reduce tissue oxidative stress and enhance the glutathione antioxidant defence system in atherosclerotic rabbits,⁷ while diets

rich in polyphenols are currently recommended for the prevention of atherosclerosis.⁸

The major constituent of the leaves and unprocessed olive drupes of *Olea europaea* is oleuropein and the majority of polyphenols found in olive oil or table olives are derived from its hydrolysis. Oleuropein has high antioxidant activity *in vitro*, comparable to a hydrosoluble analogue of tocopherol.⁹ Oleuropein scavenges superoxide anions, hydroxyl radicals and inhibits the respiratory burst of neutrophils and hypochlorous acid-derived radicals.⁵ The heart is the most susceptible organ to premature ageing and free radical mediated oxidative stress. Basic and clinical research has clearly documented the role of free radical damage and the progression of cardiovascular disease. Oxidative stress may be the result of myocardial ischaemia, acute ischaemia-reperfusion injury, endothelial damage, as well as acute or chronic oxidative damage, such as in the case of anthracyclin cardiotoxicity.¹⁰ We summarise recent investigations into the role of oleuropein in the prevention of myocardial reperfusion injury and acute cardiotoxicity induced by doxorubicin.

In light of the increasing interest in the Mediterranean diet, we investigated the impact of oleuropein *in vivo* in normal and hypercholesterolaemic rabbits subjected to ischaemia and reperfusion.¹¹ Treatment with oleuropein for 3 or 6 weeks considerably reduces the infarct size in normal rabbits subjected to 30 min of regional ischaemia followed by 3 hrs of reperfusion, while a higher dose reduces the infarct size in hypercholesterolaemic rabbits. Oleuropein protects reperfused myocardium from oxidative damage *in vivo*, and decreases total cholesterol and triglyceride levels. It also influences the metabolic profile of normal subjects, restoring the mechanisms of aerobic glycolysis and providing

cardioprotection before the onset of ischaemia. The reduction in infarct size brought about by oleuropein may occur as a result of several mechanisms, such as the elimination of reperfusion injury (because of less oxidative stress), the improvement of endothelial function, either directly or because of hypolipidaemia, or by a possible activation of intracellular mediators that render the heart more tolerant toward a subsequent lethal ischaemic insult.

The potential cardioprotective activity of oleuropein in acute cardiotoxicity induced by doxorubicin treatment was determined *in vivo* in rats.¹² It successfully treats doxorubicin-induced cardiotoxicity by inhibiting lipid peroxidation products, decreasing oxidative stress and reducing iNOS in cardiomyocytes. Histopathological results confirm the beneficial effect of oleuropein. Our results have given us greater insight into how to develop novel therapeutic strategies against DXR cardiotoxicity.

Oleuropein is a novel, naturally occurring antioxidant compound, which may possibly be used to resolve a problem of clinical relevance, such as DXR-induced cardiotoxicity. Oleuropein exhibits anti-ischaemic effects, and its therapeutic activity appears to be more extensive than previously indicated in clinical trials.

There are 4 formulations of olive leaf extracts on the market that contain oleuropein from 15 to 62.5 mg. Among the commercially available preparations, Oliceutic Acid contains the highest concentration of oleuropein (60-62.5 mg). Olive Leaf Liquid contains olive leaf extract in liquid and the daily dose is 7.5 mg oleuropein, while the formulations Olive Leaf caps and Olive Leaf Vegicaps contain 15 mg of oleuropein as recommended daily dosage.

References

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