manipulations of the utilization of metabolic substrates should result in an improvement of myocardial ischemia and of left ventricular function.

Therefore, the metabolic changes of diabetes alter myocardial metabolism reducing cardiac susceptibility to ischemic stimuli and cardiac performance. In diabetic coronary patients the episodes of transient myocardial ischemia coupled with the chronic myocardial hypoperfusion cause a progressive decline of left ventricular function. The inhibition of FFA oxidation improves cardiac metabolism at rest, increases the cardiac ischemic and therefore reduces the decline of left ventricular function due to chronic hypoperfusion and repetitive episodes of myocardial ischemia.

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Natural antioxidants: A novel approach for counteracting cardiometabolic risk

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Bergamot (Citrus Bergamia) is an endemic plant of Calabrian region in Southern Italy. To date, 95% of worldwide bergamot production occurs in the Ionic area of Calabria, where soil characteristics and pH (<6.5–7.5) are particularly suitable for its cultivation.

Bergamot essential oil (BEO) is made up of a volatile fraction and a non-volatile residue. Volatile components make up approximately 93–96% by weight of bergamot oil, while the non-volatile residue represents the remaining 4–7%. The non-volatile fraction is a mixture of monoterpene and sesquiterpene hydrocarbons (such as limonene, γ-terpinene, and β-pinene) and their oxygenated derivatives (linalool and linalyl acetate). The non-volatile (4–7% of total) fraction containing coumarins and psoralens [such as bergapten (5-methoxypsoralen) and bergamottine (5-geranyloxypsoralen)]. The non-volatile residue, which influences the olfactory properties of the oil, contains waxes and polymethoxylated flavones other than about 0.2% bergapten which is responsible for the phototoxicity of BEO. The bergapten-free extract of the essence (BEO-BF) together with a natural essence deprived of the hydrocarbon fraction and of bergapten (BEO-HF/BF) are prepared by extractive industries for perfumery and cosmetic uses [2,3].

Bergamot differs from other citrus fruits not only because of the composition of these flavonoids, but also because of their particularly high content. Some of the flavonoids such as naringin, present also in grapefruit, have already been shown to be active in animal models of atherosclerosis, while neoeriocitrin and rutin exhibited the strongest capacity to inhibit LDL oxidation. Importantly, bergamot juice is rich in 3-hydroxy-3-methylglutaryl neohesperidosides of hesperetin (brutieridine) and naringenin (melitidine) with ability to inhibit HMG-CoA reductase. These compounds most likely contribute to the important hypolipemic effects of bergamot juice and vasoprotective effects of bergamot oil derivatives in rats and in humans as demonstrated by recent clinical studies carried out in patients treated with bergamot-derived polyphenolic fraction (BPF) obtained concentrating bergamot juice in a form of powder, enriched in flavonoids.

Epidemiologic studies have demonstrated that a Mediterranean diet rich in olive oil is associated with decrease in risk for cardiovascular disease, obesity, and diabetes. Although some of the protection may be from the unsaturated fatty acid components of such a diet, additional small molecules found in olive oil and olive plants may confer protection, including the polyphenol oleuropein and hydroxytyrosol.

The two main sources of olive polyphenols are olive leaves and the waste from the olive oil industry. Olive leaves have the highest antioxidant and scavenging power among the different parts of the olive tree. There are five groups of phenolic compounds principally present in olive leaves: oleuropeosides (oleuropein and verbascoside); flavones (luteolin-7-glucoside, apigenin-7-glucoside, diosmetin-7- glucoside, luteolin, and diosmetin); flavonols (rutin); flavan-3-ols (catechin), and substituted phenols (tyrosol, hydroxytyrosol, vanillin, vanillic acid, and caffeic acid). The most abundant compound in olive leaves is oleuropein, followed by hydroxytyrosol, a precursor of oleuropein, the flavone-7-glucosides of luteolin and apigenin, and verbascoside, a conjugated glucoside of hydroxytyrosol and caffeic acid.

Oleuropein prevents cardiac disease by protecting membrane from lipid oxidation, by affecting coronary blood vessel dilation, by exerting antiarhythmic action, by improving lipid metabolism, by protecting enzymes, by preventing hypertensive cell death in cancer patients and by its antiviral properties.

In the current review, we want to highlight the potential beneficial effects of synergistic action of BPF and oleuropein.

There is evidence to suggest that the anti-hypertensive activity of the olive leaf extract lies probably in its content of oleuropein acting synergistically with other active substances to exert both ACE inhibitory and calcium channel blocking activities.

The anti-hypertensive and cholesterol-lowering actions hypothesized for oleuropein suggest its potential synergistically action with BPF, able to induce in patients both hypolipemic and hypoglycaemic effects other than an improvement of reactive vasodilatation. This latter action also underlines an improvement of endothelial function in patients at risk of atherosclerosis.

Since oxidative stress has been shown to reduce reactive NO-dependent vasodilatation, it is likely that BPF may well attenuate overproduction of oxygen reactive species in the vascular wall thereby restoring the imbalanced endothelial function in hyperlipemic patients.

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A modern approach in cardiometabolic risk — The role of oxidative stress and LOX-1 expression in endothelial dysfunction and cardiometabolic risk

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Background: Overproduction of oxidized-low density lipoproteins (oxyLDL) has been found to contribute in endothelial cell (EC) dysfunction thereby leading to atherosclerosis development and progression. In particular, oxyLDL lead to apoptotic cell death of EC via oxidative stress production, mostly subsequent to overexpression of the scavenger receptor LOX-1. Here, we hypothesize that LOX-1 expression in EC represents a crucial event which attenuates protective autophagic response, thereby enhancing programmed endothelial cell death.

Methods and results: Bovine aortic endothelial cells (BAEC) in culture were exposed to oxyLDL (1–100 μM). After 48 h incubation, oxyLDL produced apoptotic cell death of BAEC as detected by FACS analysis, an effect counteracted by antioxidant N-acetyl-cysteine (NAC) as well as by the NO-donor SNAP. OxyLDL-induced apoptotic cell death was also accompanied by reduced VEGF-dependent phosphorylation of constitutive NO synthase (cNOS) in BAEC and consistent attenuation of autophagic response as detected by expression of beclin-1 and LC3, two reliable biomarkers of autophagy. Moreover, silencing LOX-1 receptor significantly restored LC3 expression in oxyLDL-treated BAEC, thus suggesting a key role of LOX-1 overproduction in oxyLDL-induced endothelial dysfunction.