Summary of Key Scientific Studies: Cardiovascular/Circulatory System

The beneficial effects of the phytonutrient MASQUELIER's OPCs on the structure and function of blood vessels (veins, arteries, capillaries and lymphatic vessels), and thereby on the circulatory and cardiovascular systems, have been indicated through sixty years of continuous scientific study, in many published peer-reviewed journal articles, and reviewed in a monograph published in *Alternative Medicine Review* (Oligomeric Procyanidins. Monograph, 2003).

In initial studies testing bio-availability and tissue localization of MASQUELIER's OPCs, Masquelier and co-scientists demonstrated that when radio-labelled and administered orally to mice, the radioactivity rapidly appeared in the plasma, localized to various body tissues, particularly those rich in collagen and glycosaminoglycans such as blood vessels and connective tissues. This indicated that MASQUELIER's OPCs is highly bio-available and biologically active in the vascular and connective tissues (LaParra et al, 1978). The vasculo-protective effects of MASQUELIER's OPCs were further investigated and established in a series of *in vitro,* animal and human studies.

Evidence of beneficial effects of MASQUELIER's OPCs from *in vitro* and animal studies

In studies conducted in animals, it was observed that MASQUELIER's OPCs, at an oral dose of 50 mg/kg/day, significantly decreased vascular permeability induced by collagenase in rats (Gavignet-Jeannin et al, 1988). MASQUELIER's OPCs was also demonstrated to bind collagen and elastin in blood vessel walls, promote collagen synthesis and polymerization and inhibit degradation of collagen and elastin in a study conducted in guinea pigs (Pfister, 1982). Further *in vitro* studies revealed that this phytonutrient demonstrated a high percentage of binding to collagen fibres (Masquelier et al, 1981) and promoted synthesis of collagen and elastin, and inhibited their proteolytic degradation, (Gavignet-Jeannin et al, 1988; Tixier et al, 1984).

Based on the observed beneficial effects in strengthening and protecting blood vessels, it was hypothesized that MASQUELIER's OPCs might also have beneficial effects on the cardiovascular system. Interestingly, in a cholesterol-fed rabbit model of atherosclerosis, MASQUELIER's OPCs (50mg/kg/day oral administration for 10 weeks) significantly decreased the amount of cholesterol bound to elastin in the aortic wall, indicating a potential role for this compound in reducing risk of atherosclerosis and cardiovascular disease (Wegrowski et al, 1984). Scientific investigations also demonstrated that MASQUELIER's OPCs exerted strong antioxidant activity *in vitro* (Masquelier, 1988), and significantly protected endothelial cells from lipid peroxidation and free radical-induced cell death (Meunier et al, 1989; de Haan et al, 2006). Oxidative damage to endothelial cells can lead to endothelial dysfunction, which increases the risk of cardiovascular disease.

Evidence of beneficial effects of MASQUELIER's OPCs from human intervention studies

The positive effects of MASQUELIER's OPCs on blood vessel structure and function were also observed in several human intervention trials.

In double-blind, placebo-controlled studies, MASQUELIER's OPCs was found to induce a statistically significant decrease in capillary fragility, permeability and other age-associated microcirculatory anomalies (Dartenuc et al, 1980; Dubos et al, 1980). In an open-label study in 78 subjects with venous abnormalities, MASQUELIER's OPCs was shown to significantly decrease vascular fragility in 79.4% of the subjects (Beylot and Bioulac, 1980).

Additionally, it was shown that MASQUELIER's OPCs improved lymphatic circulation and thereby decreased risk of edema more effectively than placebo in a double-blind study in 20 subjects (Pecking et al, 1987). MOOPCs was demonstrated in double-blind and open-label studies to be highly effective in ameliorating venous abnormalities and associated indicators such as edema, restlessness, deregulated venous tone and varicoses in the legs, and thereby decrease risk of developing chronic venous insufficiency (Delacroix, 1981; Henriet, 1994; Thebaut, 1985).

In double-blind, controlled studies (Arne, 1982) and open-label studies (Fromantin, 1981), it was also demonstrated that MASQUELIER's OPCs significantly reduced microvascular abnormalities such as increased capillary permeability, aneurysms and exudates that are risk factors for developing retinopathy in the eyes of diabetic or hypertensive subjects.

Conclusion

In summary, the totality of the scientific evidence from *w* animal and human intervention studies described above suggests that MASQUELIER's OPCs have a strong structural and functional vascular-reinforcing and vascular-protective effect, might considerably reduce risk of many types of vascular anomalies and can significantly contribute to the health of the circulatory and cardiovascular systems.

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