Summary of Key Scientific Studies: Antioxidant Benefits

Free radicals have gained a lot of attention in recent years because of their role in the pathogenesis of several diseases such as inflammation, atherosclerosis, arthritis, neurodegenerative conditions and cancer. Since endogenous antioxidants are frequently insufficient to protect against free radical-induced cellular damage, diet-derived antioxidants are important in maintaining health. There is sufficient epidemiological evidence correlating higher intake of certain foods or food-components rich in antioxidants with a lower incidence of various human diseases (Halliwell, 1996; Riccioni et al, 2007; Williams and Hord, 2005). One such major class of dietary antioxidants are the flavanols. Flavanols, particularly the single flavan-3-ols (catechins) and oligomeric flavan-3-ols (oligomeric proanthocyanidins or OPCs), are an integral part of the diet and are found in fruits such as apple, pear, and grapes, and in chocolate, wine, and tea. Scientists have proposed that the antioxidant activity of flavan-3-ols (catechins and OPCs) might be responsible for their beneficial effects in reducing risk of cardiovascular disease, cancer, inflammation, diabetes, neurological disorders and disorders of the eyes and skin (Tapiero et al, 2002; Urquiaga and Leighton, 2000).

The antioxidant and free-radical scavenging effects of the well-characterized, bioavailable (LaParra, 1978) OPCs-rich product, MASQUELIER's OPCs have been scientifically demonstrated in peer-reviewed journal articles and described in a monograph published in *Alternative Medicine Review* (Oligomeric Procyanidins. Monograph, 2003).

Scientific investigations have revealed that MASQUELIER's OPCs is a very efficient and stable scavenger of superoxide radicals generated *in vitro* (Masquelier, 1988; Meunier, 1989), exhibiting a scavenging effect 20-times more powerful than vitamin C, and also more powerful than several bioflavonoids (Masquelier, 1988). MASQUELIER's OPCs was also found to scavenge DPPH radicals *in vitro* (Barbier et al, 1988), and to exhibit high antioxidant capacity as observed in ORAC analysis (Independent analysis by ORAC Europe BV). Interestingly, MASQUELIER's OPCs was found to protect vitamin C from copper-induced oxidation (Masquelier, 1951), indicating a capacity to scavenge free radicals generated by metal ions and an antioxidant-sparing effect. Further studies demonstrated that MASQUELIER's OPCs inhibits peroxidative damage to cellular lipids induced by various pro-oxidants, suggesting a protective effect on cellular membranes (Bos et al, 1996; Meunier et al, 1989, de Haan et al, 2006b). Importantly, MASQUELIER's OPCs, at levels reported in human plasma after oral intake, was shown to significantly inhibit oxidation of human LDL *in vitro,* while a much higher level of vitamin E was required to similarly inhibit LDL oxidation (de Haan et al, 2008). MASQUELIER's OPCs also protected vascular endothelial cells from oxidative stress-induced cell death (de Haan et al, 2006a). These findings suggest a possible application in maintaining a healthy cardiovascular system and reducing risk of disease.

An independent single-blinded, controlled, human intervention study conducted by Hughes-Formella, et. al. demonstrated that MASQUELIER's OPCs dietary supplement in combination with a topical application containing ester-OPCs (cream or lotion) significantly reduced UV-induced skin erythema. UV-induced skin erythema has been indicated to be caused by an inflammatory process mediated by free radicals, and has been suggested to contribute to photoaging and photocarcinogenesis of skin (Trautinger, 2001). The study investigators proposed that MASQUELIER's OPCs (in the form of dietary supplement + topical application) can significantly reduce UV-induced skin erythema, likely through scavenging of free radicals (Hughes-Formella et al, 2007), and thereby have possible benefit in maintaining healthy skin and reducing risk of damaging effects of UV exposure.

Additional support for a probable anti-inflammatory effect for MASQUELIER's OPCs came from the observation that it reduces the "respiratory burst" in leucocytes *in vitro,* a process physiologically associated with inflammation (Barbier et al, 1988). MASQUELIER's OPCs was also found to partially rescue experimental animals from disorders induced by deficiency of vitamin C which exerts a well-established free radical-scavenging activity (LaParra et al, 1979), further indicating an antioxidant effect of MASQUELIER's OPCs *in vivo.*

Summarizing the currently available scientific evidence, *in vitro* and *in vivo,* animal and human investigations offer support for the free radical scavenging and antioxidant activity of MASQUELIER's OPCs, which can

contribute to maintaining health and reduce risk of developing degenerative diseases. MASQUELIER's OPCs have also been found to offer protection from UV- and chemical-induced oxidative stress in animals and exhibit strong free radical scavenging activity in various *in vitro* experimental systems, suggesting MASQUELIER's OPCs to be significantly effective in reducing UV-induced oxidative damage to human skin that can lead to photoaging and skin cancer.

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