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# HerbClip™

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**FILE:: Pycnogenol®  
Pine bark ( *Pinus maritime* )  
Antioxidant activity  
Antiinflammatory activity**

**HC 052511 - 206**

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**RE: Pycnogenol® French Maritime Pine Bark Extract Shows Antiinflammatory Activity  
In Lab Testing**

Cho KJ, Yun CH, Yoon DY, Cho YS, Rimbach G, Packer L, Chung AS. Effect of bioflavonoids extracted from the bark of *Pinus maritime* on proinflammatory cytokine interleukin-1 production in lipopolysaccharide-stimulated RAW 264.7. *Toxicology and Applied Pharmacology*. 2000; Vol. 168:64-71.

There is increasing interest in the biological activities of plant extracts such as that obtained from the bark of the French maritime pine *Pinus maritime* (Pycnogenol®). Pycnogenol® (PYC) is the trade name for a unique, patented mixture of phenols and polyphenols, broadly divided into monomers such as catechin, epicatechin, and taxifolin and condensed flavonoids such as procyanidins. PYC also contains phenolic acids such as caffeic, ferulic, and *p*-hydroxybenzoic acid as minor constituents. Bioflavonoids are known to have strong antioxidant capabilities and efforts have been made to identify their potential usefulness based on these capabilities. Studies indicate that PYC participates in the cellular antioxidant network as indicated by its ability to prolong the lifetime of the ascorbyl radical and to protect endogenous vitamin E and glutathione in human endothelial cells from oxidative stress. However, little is known about the antiinflammatory properties of PYC.

Interleukin-1 (IL-1) is a multifunctional cytokine that is responsible for mediating a variety of processes in host defense, inflammation, and response to injury. Cytokines such as IL-1 can have beneficial or detrimental effects, depending on the context and amount in which they are produced. IL-1 is produced by macrophages and many other cell types by the actions of various stimuli such as viruses, lipopolysaccharides, and phorbol esters. During infection, IL-1 is mostly beneficial, but in cases of cancer and chronic inflammatory diseases, it may be detrimental. Therefore, cellular manipulation of the production of IL-1 and other proinflammatory cytokines are of importance in determining the outcome of the inflammatory response. Since IL-1 is a highly proinflammatory cytokine, agents that reduce its production and/or activity might be of a particular pharmacological and clinical interest.

Biologically active IL-1 acts as a growth factor for several cell types, including fibroblasts and keratinocytes and its gene promoter, which contains a lipopolysaccharide-responsive enhancer region, possesses binding sites involved in the expression of a variety of genes in response to oxidative stress.

This study examined the mode of action of bioflavonoids in the proprietary extract Pycnogenol® (Horphag Research Ltd, Guernsey, France) on free radical formation, activation of redox sensitive transcription factors, as well as lipopolysaccharide-induced IL-1 gene expression in murine macrophage cell lines.

A series of analytical assays, including ELISA, immunoblot analysis and competition RT-PCR demonstrated for the first time that the complex mixture of bioflavonoids found in *P. maritima* significantly affect both IL-1 gene expression and production. In H<sub>2</sub>O<sub>2</sub>-challenged macrophages, PYC exerts a potent dose-dependent radical scavenging activity.

Such antioxidant properties might also be an important determinant in down-regulating IL-1 gene expression and production. In the same cells, it was found that PYC blocked the activation of major factors (nuclear factor kappa and activator protein-1) involved in IL-1 gene expression.

The authors concluded that this study, using two representative murine macrophage cell lines, clearly demonstrated that the actions of PYC may down-regulate proinflammatory cytokine IL-1 gene expression and production in macrophages. The findings may contribute to the understanding of how bioflavonoids play an important role either as free radical scavengers or as preventive agents in contributing to the normalization of some pathophysiological conditions characterized by inflammation and may also support the possibility that bioflavonoids, including PYC, can be used as antiinflammatory and immunosuppressive agents based on their radical scavenging activities.

—Densie Webb, Ph.D.

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