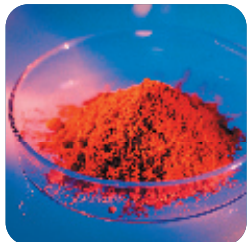
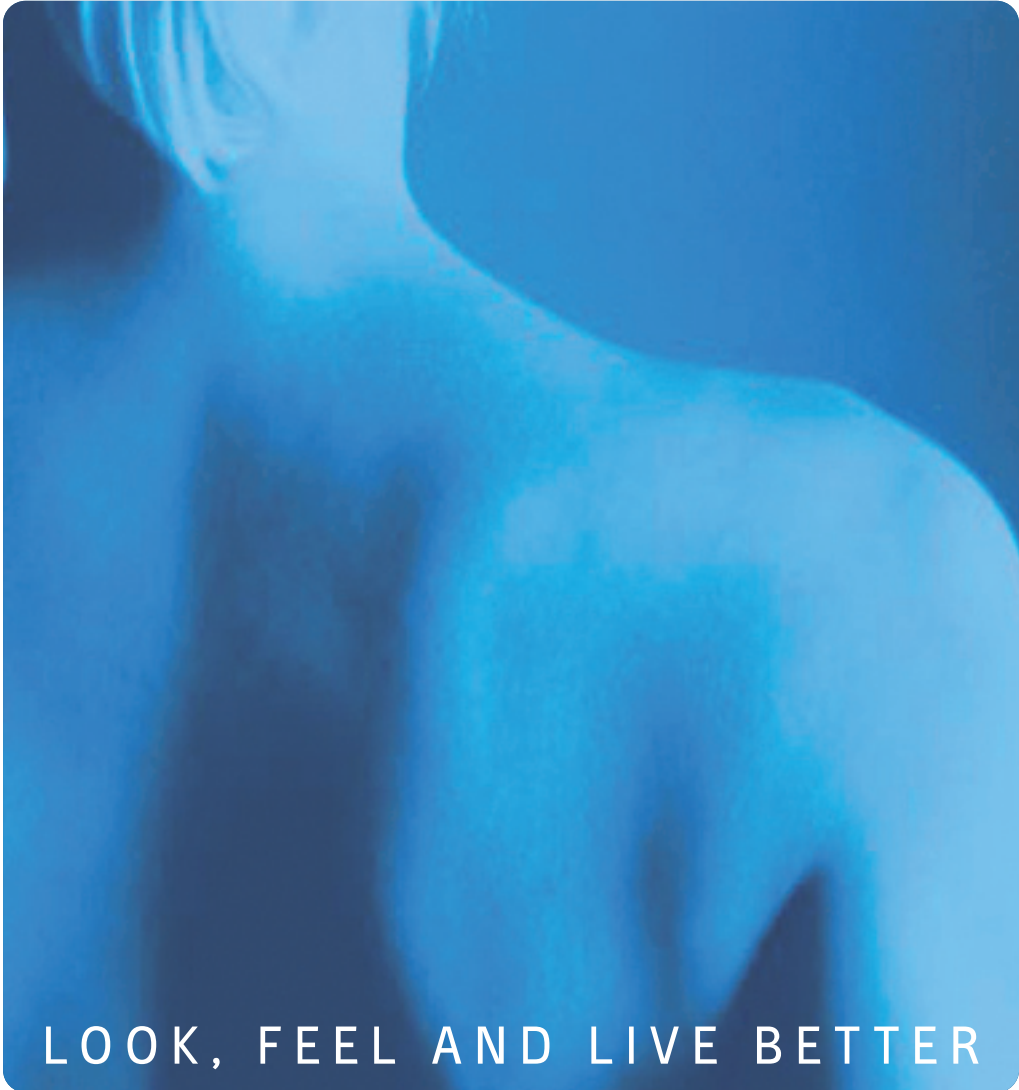


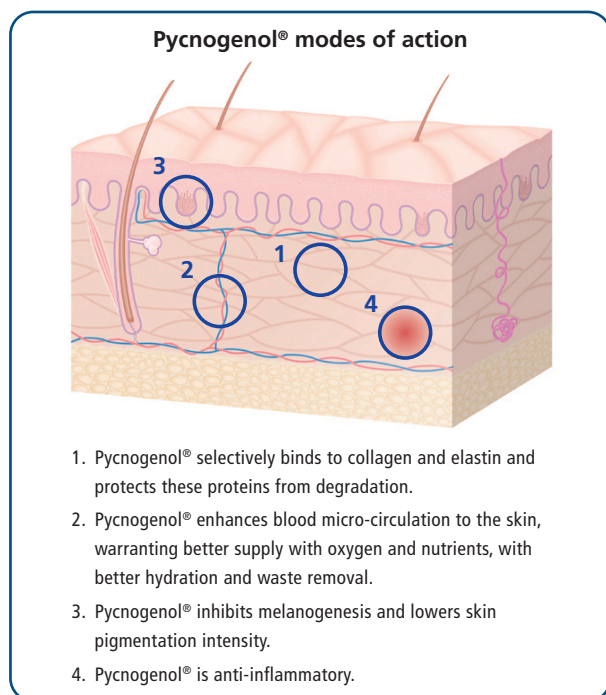
# PYCNOGENOL

Oral Skin Care



## Pycnogenol® in Oral Skin Care

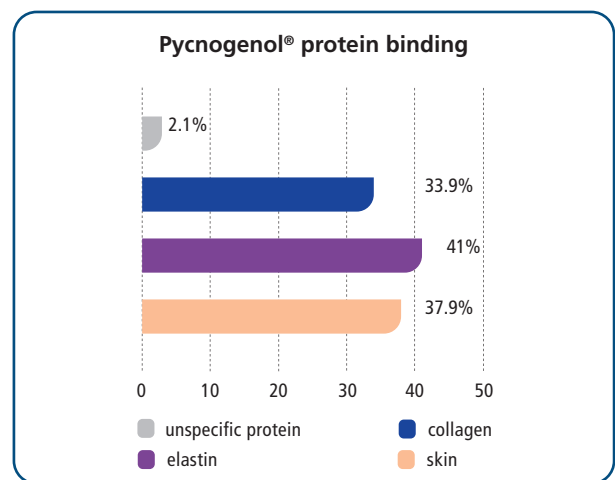
Pycnogenol® is widely used in topical and oral applications for various dermatological indications. A unique combination of pharmacological functions of Pycnogenol® provides an unmatched variety of health benefits for skin health.



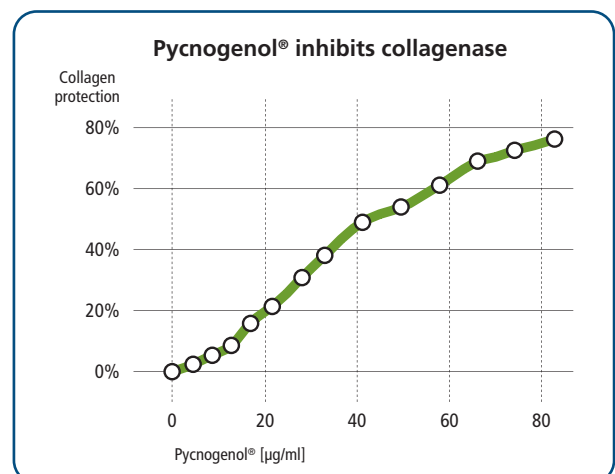
### Pycnogenol® binds and protects collagen and elastin

Pycnogenol® has a high affinity to proteins rich in the amino acid hydroxyl-proline. These are predominantly the matrix proteins in the skin, collagen and elastin. When Pycnogenol® is added to collagen or elastin, a high amount remains tightly bound. In consequence, Pycnogenol® also tightly binds to the skin. To other proteins such as albumins Pycnogenol® has little affinity [Grimm et al., 2004].

Further experiments showed that Pycnogenol® as well as its metabolites, developing after oral con-



sumption in humans, protects collagen and elastin from enzymatic degradation. These enzymes, matrix metalloproteinases (MMPs), influence the equilibrium between collagen degradation and renewal. The inhibitory concentrations (IC50) of Pycnogenol® metabolites were lower than that of a known MMP-inhibitor

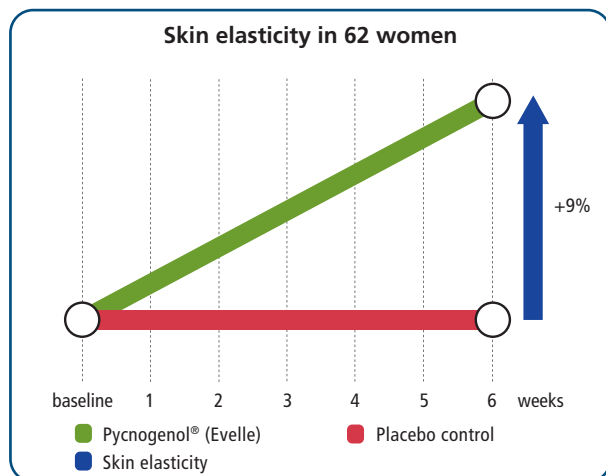


Captopril. As an example, inhibition of collagen degradation by collagenase in presence of Pycnogenol® is shown below.

### Pycnogenol® increases skin elasticity humans

In a double-blind, placebo-controlled clinical study with 62 women a complex formulation with Pycnogenol® as lead active ingredient was shown to significantly increase skin elasticity after 6 weeks oral treatment by 9% as compared to placebo [Segger et al., 2004]. In addition to Pycnogenol® this complex formulation (Evelle™) bears various natural antioxidants, minerals and vitamins.

Continuous intake of Pycnogenol® as formulated into Evele™ for 12 weeks was shown to improve skin smoothness significantly by 6% as compared to placebo.

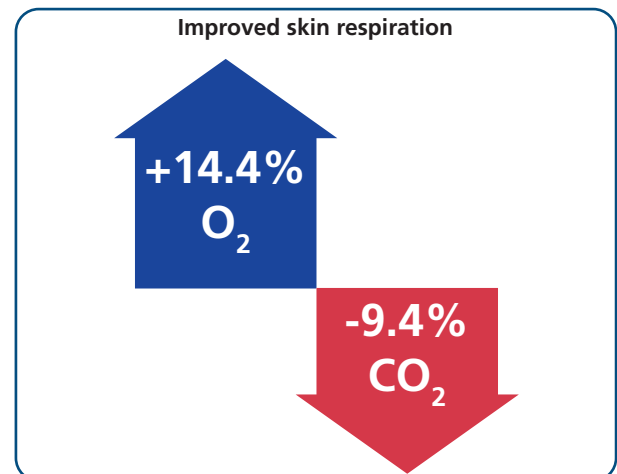


### Pycnogenol® enhances blood micro-circulation to the skin

Pycnogenol® enhances generation of endothelial nitric oxide (NO) which is the key mediator facilitating arterial relaxation and consequently allows for optimal blood flow [Fitzpatrick et al., 1998]. Oral Pycnogenol® supplementation was found to increase blood perfusion of the skin and oxygen partial pressure increased and, conversely, carbon dioxide concentration decreased [Belcaro et al., 2005]. This study

demonstrated an improved healing of wounds (ulcers) in individuals with micro-circulatory disorders.

An improved blood perfusion of the skin warrants optimal supply with all important nutrients as well as better hydration to support skin vitality.



### Pycnogenol® helps prevent UV damage and photo-ageing

Exposure of the skin to UV-light generates oxygen radicals which in turn damage skin cells and connective tissues. In an advanced stage the destructive processes can initiate an immune response which is grossly visible as sunburn. Activated immune cells cause significant damage to the skin, as they discharged even more reactive oxygen species as well as MMPs which further degrade collagen and elastin. Altogether, the immune response adds significant more harm to the skin than caused by UV-rays alone.

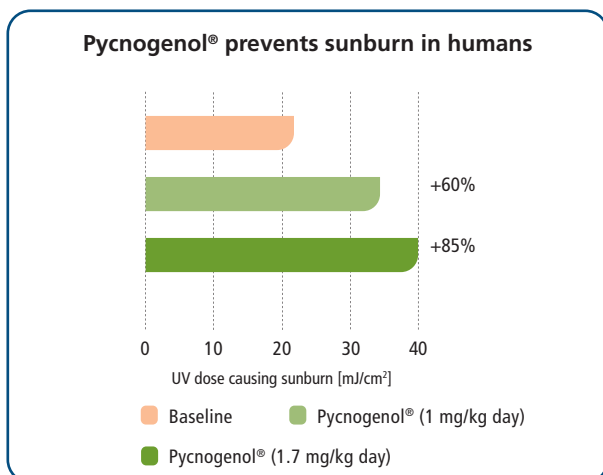
Pycnogenol® displays anti-inflammatory potency, as it inhibits the trigger (NF-kB), which governs the pro-inflammatory machinery in immune cells. Oral application of Pycnogenol® to human volunteers was shown to significantly inhibit the trigger NF-kB by 15% [Grimm et al., 2006]. For details on inflammation please refer to PYCNOGENOL® AS ANTI-INFLAMMATORY.

Oral supplementation of healthy volunteers with

Pycnogenol® was shown to inhibit the inflammation caused by UV-exposure and consequently protected from sunburn [Saliou et al, 2001].

The individual UV-dose causing the first reddening of the skin (minimal erythema dose; MED) was measured at baseline and again after 4 weeks supplementation with 1 mg Pycnogenol® per kg body weight. This increased the UV-dosage necessary for causing sunburn by in average 60%.

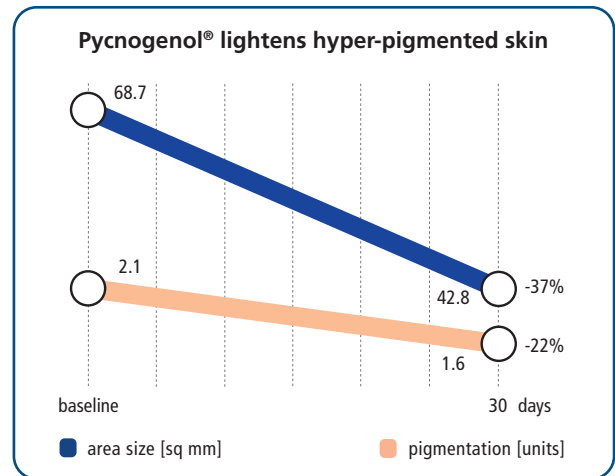
Increasing the oral Pycnogenol® dosage to 1.7 mg per kg body weight for another 4 weeks consequently further increased the MED to 85% compared to baseline values.



In pre-clinical trials orally applied Pycnogenol® was demonstrated to be protective also against chronic UV-exposure induced skin malignancies. These findings point to a significant photo-protective and anti-photo-ageing effect of Pycnogenol®.

### Pycnogenol® inhibits melanogenesis and lowers pigmentation intensity

In vitro experiments have suggested that Pycnogenol® inhibits tyrosine kinase in melanocytes and thus lowers generation of skin pigments [Yasumuro et al., 2006]. A clinical study has demonstrated that Pycnogenol®



is effective to lighten-up over-pigmented areas of the skin in humans.

These brownish spots or patches often develop particularly in the face of women, much less frequently on other parts of the body. This type of hyper-pigmentation of certain areas of the skin is known in dermatology as chloasma, or melasma. Dermatologists have noticed that this phenomenon often occurs to young mothers or women taking contraceptive hormones. Moreover, it has been noted that oxidative stress is involved in over-production of skin pigments and exposure to sunlight greatly contributes to further oxidative stress. Often aggressive chemical peeling agents are applied to the skin, even though some are known to cause irreversible skin damage.

Oral supplementation of 30 women with Pycnogenol® for one month reduced the size of skin affected by hyper-pigmentation significantly by 37% [Ni et al., 2002]. And, more importantly, the average pigmentation intensity of women taking part in the trial was lowered by about 22%. In this study Pycnogenol® was found to be effective to achieve a fair skin without any side-effects.

### Pycnogenol® is a very potent antioxidant

Pycnogenol® has been shown in laboratory testing as well as in humans to provide significant an-

tioxidant potency to the body [Chida et al., 1999]. Pycnogenol® is effective for neutralizing a broad range of oxygen radical species. Moreover, it protects vitamin E from oxidation and recycles oxidized (spent) vitamin C back to the bioactive form [Rohdewald, 2002]. Pycnogenol® thus contributes to the antioxidant network in the body. Following oral consumption of Pycnogenol® over a period of three weeks the blood oxygen radical capacity (ORAC) of 25 volunteers increased significantly by 40% [Deveraj et al.,

2002]. For more details on the antioxidant activity of Pycnogenol® please refer to PYCNOGENOL® AS SUPER ANTIOXIDANT.

Pycnogenol® represents a very potent cosmeceutical which offers a broad range of clinically substantiated health benefits for the skin:

- Antioxidant potency
- Increased skin elasticity
- Anti-inflammatory activity
- Improved skin micro-circulation
- Anti-photoaging and sun-protection
- Lowered skin pigmentation

Pycnogenol® supports skin health best when applied topically in addition to oral uptake. Each delivery form has unique advantages. Both delivery forms in combination provide optimal supply with nutrients from within and warrant highest efficacy particularly for photo-protection and improved skin elasticity. Please check for more details: PYCNOGENOL® IN TOPICAL SKIN CARE.

## References

- Belcaro G et al.* Venous ulcers: microcirculatory improvement and faster healing with local use of Pycnogenol®. *Angiology* 56: 699-705, 2005.
- Blazsó G et al.* Pycnogenol® accelerates wound healing and reduces scar formation. *Phytother Res* 18: 579-581, 2004.
- Chida M et al.* In vitro testing of antioxidants and biochemical end-point in bovine retinal tissue. *Ophthalmic Res* 31: 407-415, 1999.
- Devaraj S et al.* Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters the plasma lipoprotein profile. *Lipids* 37: 931-934, 2002.
- Fitzpatrick et al.* Endothelium-dependent vascular effects of Pycnogenol®. *J Cardiovas Pharmacol* 32: 509-515, 1998.
- Grimm T et al.* Antioxidant activity and inhibition of matrix-metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®). *Free Rad Biol Med* 36: 811-822, 2004.
- Grimm T et al.* Inhibition of NF-κB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®). *J Inflamm* 3: 1-15, 2006.

*Segger D et al.* Supplementation with Evelle improves skin smoothness and elasticity in a double-blind, placebo-controlled study with 62 women. *J Dermatol Treat* 15: 222-226, 2004.

*Rohdewald P.* A review of the French maritime pine bark extract (Pycnogenol®), a herbal medication with a diverse pharmacology. *Int J Clin Pharmacol Ther* 40(4): 158-168, 2002.

*Saliou C et al.* Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by a French maritime pine bark extract. *Free Rad Biol Med* 30: 154-160, 2001.

*Yasumuro M et al.* Inhibition of melanogenesis by pine (*Pinus pinaster*) bark extract containing procyanidins. Manuscript in preparation 2006.