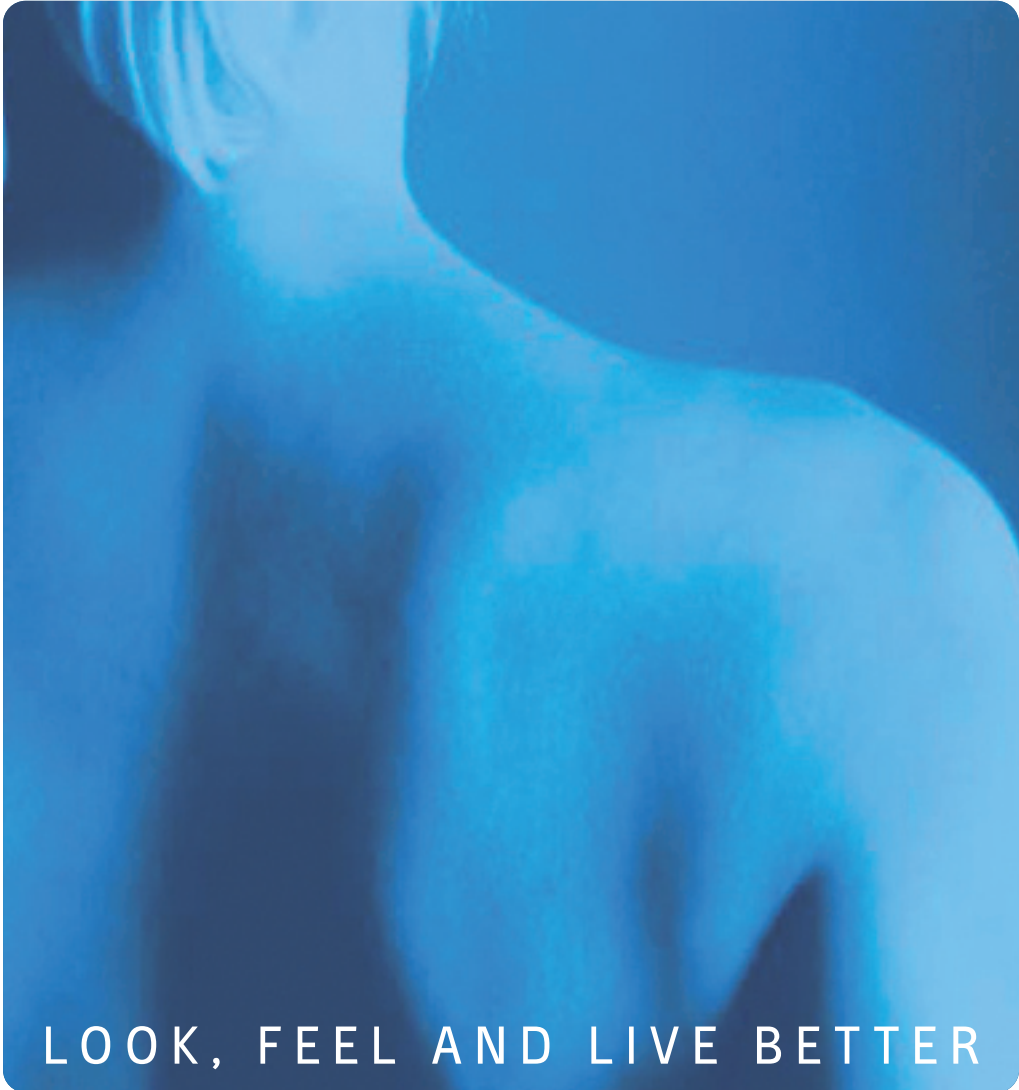


PYCNOGENOL

Topical Skin Care

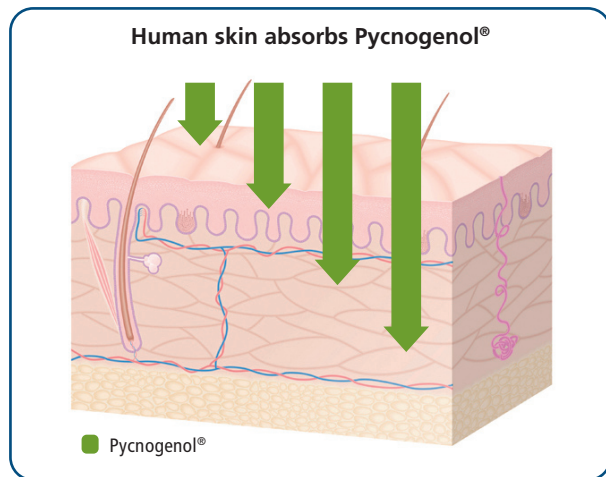


Pycnogenol® in Topical Skin Care

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.

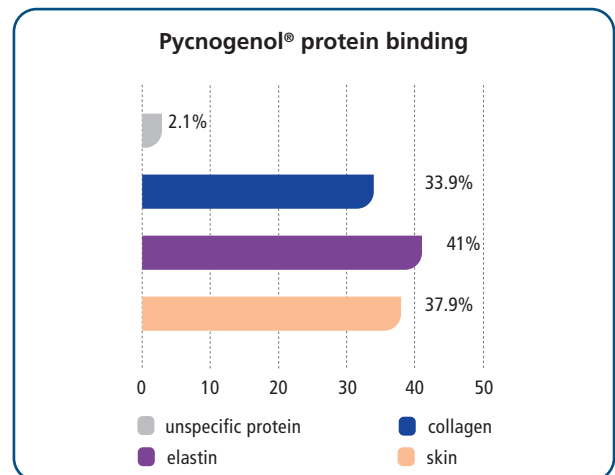
Human skin absorbs Pycnogenol®

Pycnogenol® was tested for the ability to be absorbed by human skin [Sarikaki et al, 2004]. A Pycnogenol® solution was applied to a viable human skin patch and molecules penetrating the skin were identified. Smaller constituents such as phenolic acids were identifiable already 30 min after application. Many constituents, including catechin, showed the highest concentration after 4 hours. Many constituents of Pycnogenol® were measurable in significant quantities even 12 hours after application.



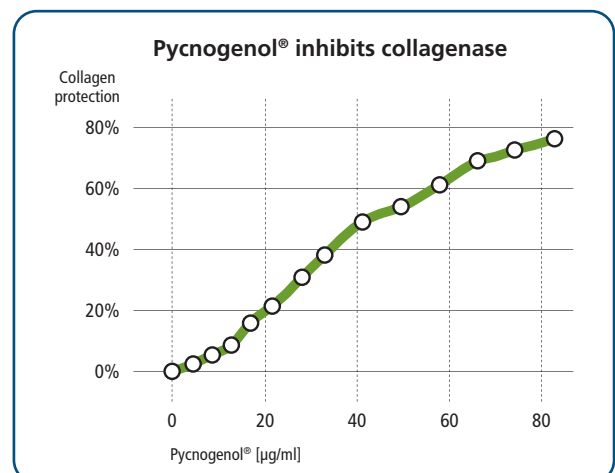
Pycnogenol® binds and protects collagen and elastin

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].

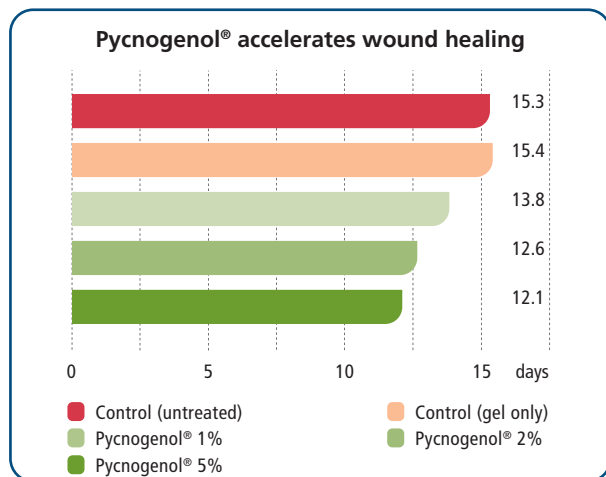
Further experiments showed that Pycnogenol® as well as its metabolites, developing after oral consumption in humans, protects collagen and elastin from enzymatic degradation. These enzymes, matrix metalloproteinases (MMPs), influence the equi-



librium 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® accelerates wound healing and lowers scar formation

In a pharmacological study the ability of skin to heal wounds was investigated [Blazsó et al., 2003]. Wounds were inflicted by heat treatment followed by topical application of Pycnogenol® gel once a day until healing. In absence of treatment the healing process took 15.3 days and application of gel without Pycnogenol® had no effect on the healing time. Gel with 1% Pycnogenol® was found to accelerate the healing process by 1.6 days as compared to gel without Pycnogenol®. Pycnogenol® was found to dose-dependently shorten the period required for wound healing. Furthermore, scar size was lowered with increasing Pycnogenol® concentration.



In two clinical trials topically applied Pycnogenol® was shown to improve healing of ulcers in individuals with venous disorders or diabetes [Belcaro et al., 2005 & 2006]. Application of Pycnogenol® powder directly onto ulcers in 30 diabetic patients allowed complete healing in 84% of patients, whereas the

control group receiving standard treatment only had 61% with completely healed ulcers.

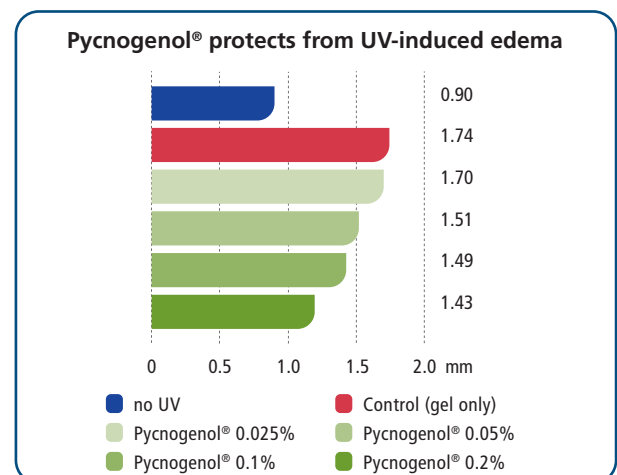
Pycnogenol® is a potent antioxidant

Pycnogenol® was demonstrated to be a very potent antioxidant with the ability to neutralize every naturally occurring oxygen radical species [Rohdewald 2002]. Pycnogenol® can recycle oxidized (spent) vitamin C to restore its activity. This supports the availability of vitamin C as co-factor for the enzymatic activity of prolyl hydroxylase, which synthesizes functional collagen and elastin. For more details on the antioxidant activity of Pycnogenol® please refer to PYCNOGENOL® AS SUPER ANTIOXIDANT.

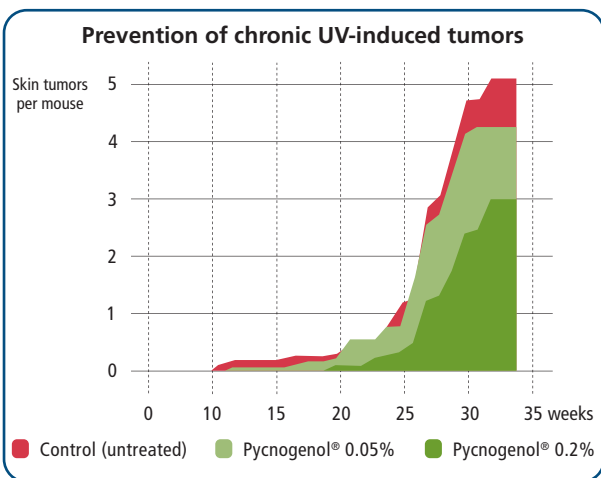
Pycnogenol® helps prevent UV damage and photo-ageing

Exposure of the skin to UV-light generates reactive oxygen radicals and triggers pro-inflammatory processes which may cause sunburn. Pycnogenol® was shown in preclinical studies to effectively counteract sunburns [Sime et al., 2004].

The skin thickness was evaluated after exposure of the skin to UV-light for three consecutive days, which serves as measure for the skin sunburn reaction. As compared to baseline, the UV exposure almost doubled the skin thickness, reflecting a significant reaction of the skin to the UV radiation. Application of lotions containing Pycnogenol® to the skin immediately after



each UV-exposure dose-dependently reduced edema. A concentration as low as 0.05% Pycnogenol® significantly inhibited the inflammatory sunburn reaction. Pycnogenol® was applied to skin after UV-exposure because the procyanidins in Pycnogenol® absorb UV-light. Application to the skin subsequent to UV-exposures ensures that exclusively the anti-inflammatory properties of Pycnogenol® are active.



Pycnogenol® was also shown to potently counteract the systemic immuno-suppressive effects of UV-radiation. Application of 0.1% Pycnogenol® lotion to exposed skin post irradiation restored the UV-affected immune response (evaluated as contact hypersensitivity to chemical irritants) to 87% of non-irradiated levels [Sime et al., 2004].

Pycnogenol® was demonstrated to protect from UV-radiation induced carcinogenesis [Sime et al., 2004]. In absence of Pycnogenol® treatment (0%) mice chronically exposed to UV began to develop benign papillomas after 11 weeks which thereafter progressed towards more malignant states. Pycnogenol® lotion applied after each UV-exposure prolonged the onset of tumors, this effect reached significantly when 0.2% Pycnogenol® was applied. Some mice treated with 0.2% Pycnogenol® never developed a tumor during this experiment. These findings suggest a significant photo-protective effect of Pycnogenol®.

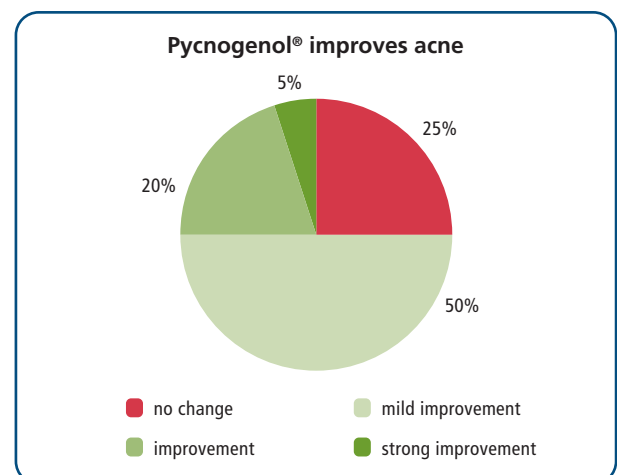
Pycnogenol® has broad anti-microbial activity

Pycnogenol® exerts anti-microbial activity against a broad range of micro-organisms: gram positive and negative bacteria, as well as yeast [Torras et al, 2005]. The minimum inhibitory dose ranged from 20 µg/ml, such as for Staphilococcus aureus, to 250 µg/ml as in the case of Campylobacter. The MID for Candida albicans was shown to be 30 µg/ml. Pycnogenol® does not have bacteriocidal activity. Upon dilution of Pycnogenol® concentration below MID, microbial growths will be restored. Formulations bearing at least 0.025% Pycnogenol® will possess anti-microbial activity towards both gram positive and negative bacteria as well as Candida albicans.

Pycnogenol® is effective for acne treatment

Pycnogenol® has been clinically tested in 40 women suffering from adult acne. A 0.5% Pycnogenol® lotion was applied twice a day after washing the face. The symptom severity was investigated at baseline and after 1 month treatment using an established symptom severity grading standard [Seki et al., 2006].

The results showed that the majority of women experienced an improvement of their acne. One in four women did experience any effect of the treatment. 75% of the women found an improvement and 5% had their acne dramatically improved.



Pycnogenol® was suggested to improve acne as a result of its anti-inflammatory activity, its anti-microbial activity as well as the improved wound healing properties. This study suggests that Pycnogenol® may be beneficial in a variety of skin conditions involving inflammatory and infectious components.

Pycnogenol® represents a very potent cosmetic ingredient which offers a broad range of clinically substantiated health benefits:

- Antioxidant potency
- Improved skin health and collagen renewal
- Anti-microbial activity
- Anti-inflammatory activity
- Anti-photoaging and sun-protection

Pycnogenol® is most effective for healthy skin when it is applied topically as well as taken as supplement. 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 ORAL SKIN CARE.

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