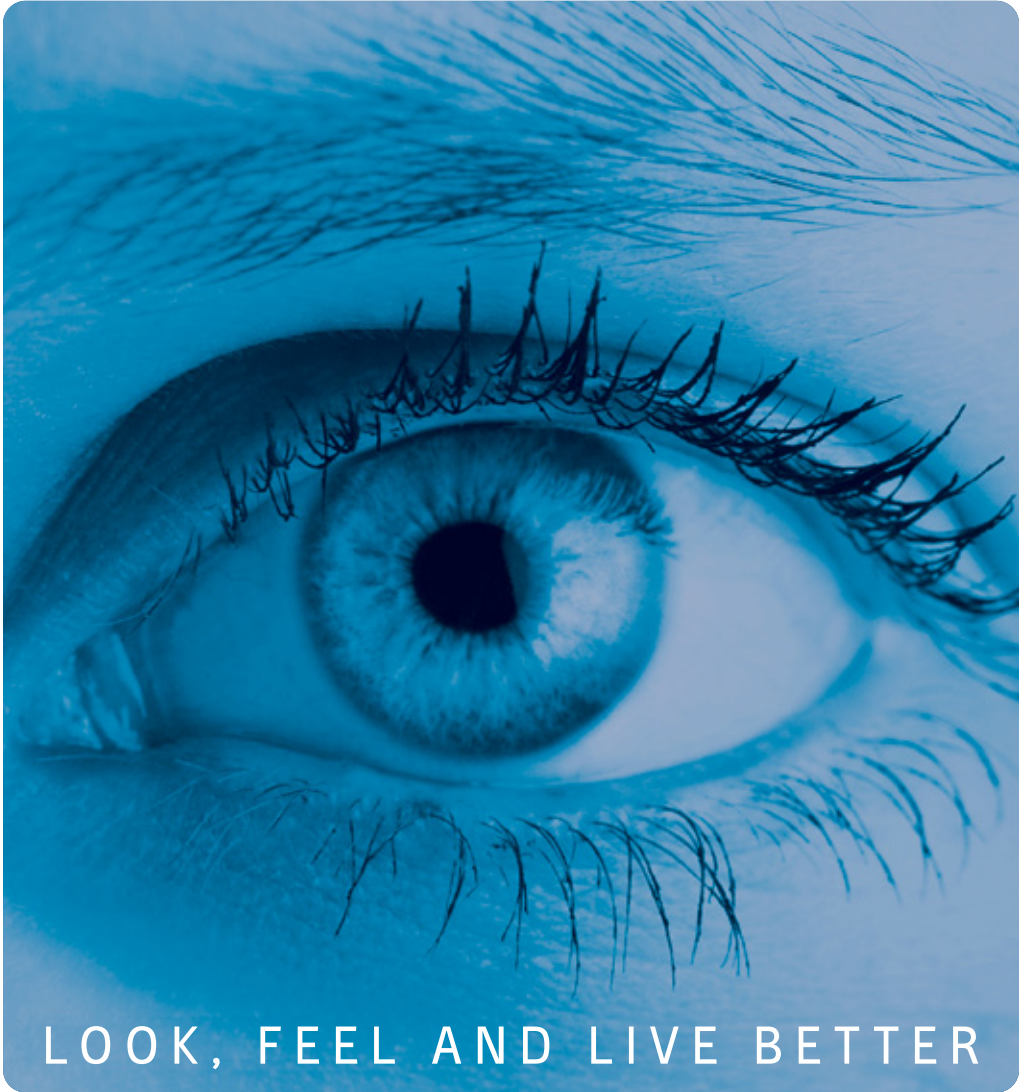


**PYCNOGENOL®**

Eye Health



LOOK, FEEL AND LIVE BETTER

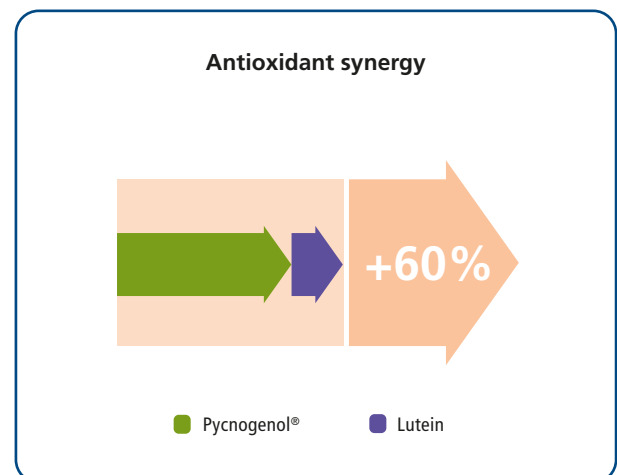


## Pycnogenol® for Eye Health

The natural ageing process affects the sharpness of vision, everyone experiences decreased accommodation of the lens to see clearly at near at higher age. Apart from the stiffening the lens will develop opacities and, furthermore, light sensing cones and rods may lose function with increasing age. The progression may occur more rapidly in some individuals than others and further to hereditary factors, predominantly lifestyle and dietary factors define the speed with which oxidative stress and metabolic factors cause cumulative damage to ocular tissues. The retina is the tissue with the highest metabolic turn-over in the body, with the consequence of generating the highest oxidative stress. Furthermore, ocular tissues are exposed to energetic UV rays which generate reactive oxygen species. Metabolic conditions such as diabetes involve a pathologic oxidative stress known to deprive antioxidant vitamins.

### Pycnogenol® provides potent antioxidant protection to the eyes

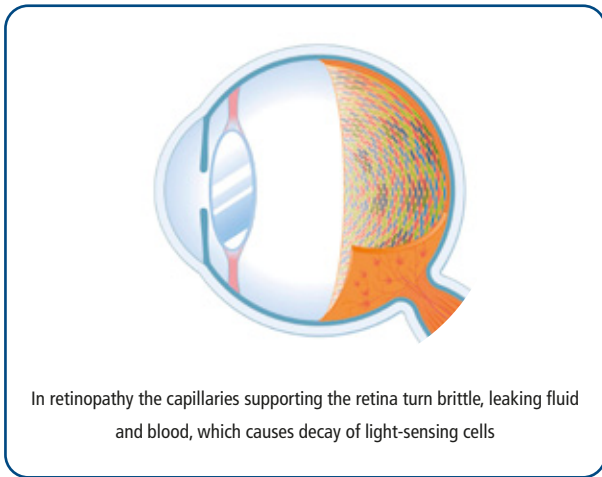
The eye is characterised by a unique aqueous-lipid phase barrier which requires water-soluble antioxidants for the aqueous phase such as the humour and lipophilic antioxidants, predominantly carotenoids, for the polyunsaturated fatty acid-rich retina. Pycnogenol® was found to protect retinal lipids more potently than vitamin C, vitamin E, CoQ10, lipoic acid and grape seed extract [Chida et al., 1999]. Especially the carotenoid Lutein has been found to protect the retinal macula from oxidative damage. Under laboratory conditions Lutein and Pycnogenol® were investigated for their antioxidant protective effect of the retina. Further to their potent individual antioxidant contributions the combination of Lutein and Pycnogenol® showed additional synergistic protection of retinal lipids from oxidation by 60% [Nakanishi-Ueda et al., 2006]. Further to the pronounced antioxidant potency in aqueous environments Pycnogenol® appears to exhibit synergistic effects with lipophilic antioxidants along the water-lipid interface of tissues.



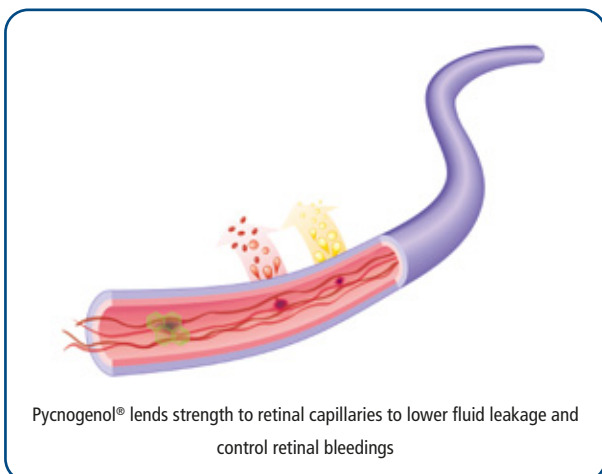
### Pycnogenol® protects retinal capillaries

Further to the integrity and functioning of light sensing cells the condition of the vascular system supporting the retina plays a pivotal role for healthy vision. Cardiovascular risk factors, predominantly hyperglycaemia, involve serious harm to retinal capillaries. In diabetes the retinopathy involves leakage of plasma into the retina causing macular oedema and spot-like bleedings. Lipid constituents of plasma may remain in the retina as insoluble "hard" exudates. Retinopathy

is considered a “stealth disease” as it progresses unnoticed and symptom-free while it leads to gradual, largely irreversible loss of vision. Left untreated retinopathy may progress to the proliferative stage which is characterised by growth of new capillaries to compensate for the lack of oxygen in the retina. These vessels grow uncontrolled and interfere with normal eye vision and, furthermore, tend to cause severe bleedings. The proliferative stage of retinopathy may lead to complete blindness.



Pycnogenol® strengthens retinal capillaries to help control leakage of fluids and blood into the retina. Furthermore, Pycnogenol® improves the endothelial function of retinal microvessels which supports better blood micro-circulation in the retina.



### Clinical studies with Pycnogenol®

Six clinical studies with more than 1200 diabetic patients have shown that Pycnogenol® is effective to stop further progression of retinopathy and save the eye sight of diabetics. Pycnogenol® stabilises and seals leaky capillaries of the retina, stopping further outflow of blood. In some cases even an improvement of visual acuity was evident.

### Early exploratory studies for treatment of retinopathies with Pycnogenol®

Two open case studies were carried out in France to explore the possibility to use Pycnogenol® for treatment of eye diseases resulting from capillary bleeding, mostly diabetic retinopathy. These studies were reported and published in French, the results have been reviewed in English [Schönlau & Rohdewald, 2002].

### Double blind comparative study

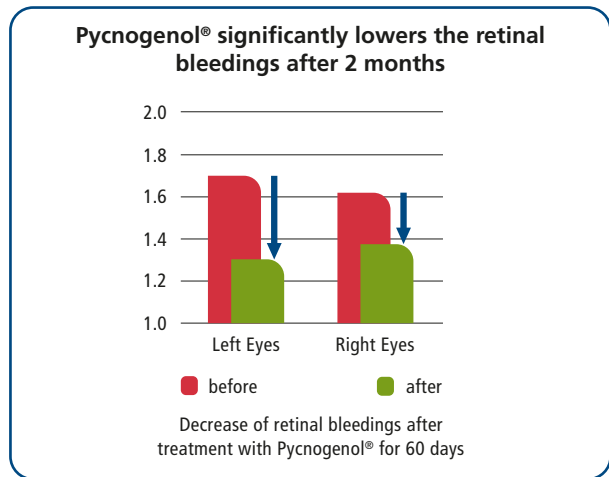
The efficacy of Pycnogenol® was compared in a double blind study design with another compound commonly utilised for slowing the progression of diabetic retinopathy: calcium dobesilate (Dexium). Two groups with 16 diabetic retinopathy patients each were treated with either Pycnogenol® (120 mg/day for 6 days, then 80 mg/day) or Dexium (2-3 tablets equivalent to 1000-1500 mg calcium dobesilate per day) over a period of 6 months at the Ophthalmology Department of the University Clinic of Würzburg, Germany [Leydhecker, 1986].

Particular emphasis was given in this study to obtain an objective judgement of the treatment efficacy. Panoramic photos of the whole retina were taken of all patients before and after treatment. Further to bleedings a primary focus in this study was the investigation of exudates, lipid depositions remaining in the retina from fluid leakages from capillaries. Seven ophthalmologists independently from one another judged the improvement of both bleedings and exudates, without knowing which medication the patient received. Both the retinal bleedings as well

as the exudates improved in the majority of patients taking Pycnogenol®. The study outcome suggests a higher efficacy with Pycnogenol as compared to Dexium.

**Study demonstrating decreased bleedings by fluorangiography**

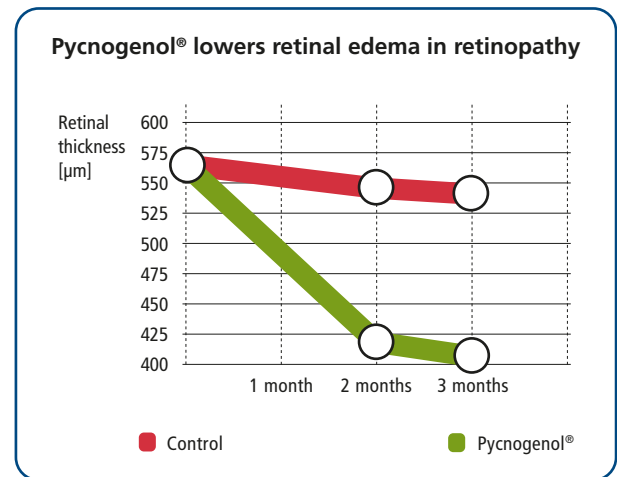
In another clinical trial 40 retinopathy patients received intravenous injection of fluorescein which allows for identification and quantification of momentary retinal bleedings by fluorescence intensity. A rapid sequence of fluorangiographs allows for recording the retinal blood flow dynamics as well as the integrity of the blood-retina barrier. The microangiopathy was scored using a semi-quantitative 4-score scale ranging from healthy (=0) to severe bleedings (=3). After two months of treatment with Pycnogenol retinal bleedings decreased significantly [Spadea et al., 2001].



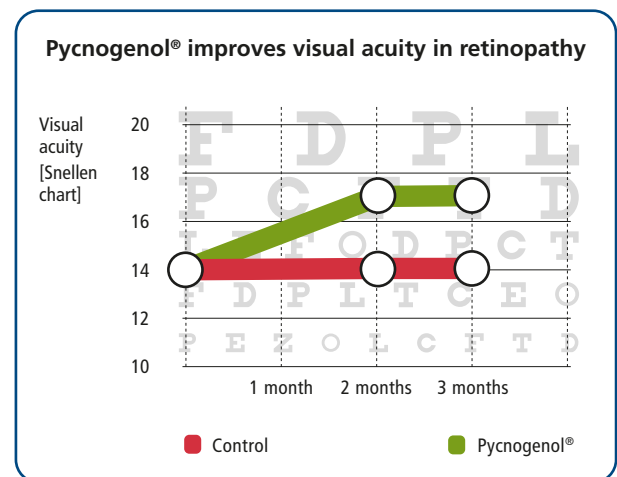
**Pycnogenol® improves visual acuity in early stage retinopathy**

A clinical study with 46 subjects suffering from early stage retinopathy characterised by mild to moderate retinal oedema showed significantly improved visual acuity after 3 months of treatment with Pycnogenol®, whereas no effect was found in a control group. With Pycnogenol® the visual acuity improved on a Snellen chart from baseline 14/20 to 17/20.

Moreover, this study showed a significantly relieved retinal oedema, a consequence of the increased capillary wall strength resulting from Pycnogenol® taken for 3 months.



The blood velocity was increased significantly by about 30% after taking Pycnogenol®, suggesting a better perfusion of retinal tissue which is understood to be the reason for increased visual acuity [Steigerwalt et al., 2009].



**Multi-centre study with 1169 retinopathy patients**

The most impressive evidence for the efficacy of Pycnogenol® for saving the eye sight of retinopathy patients stems from a multi-centre study in Germany.



In total 1169 subjects with diabetes I and II participated and took Pycnogenol® in dosages ranging from 20 to 160 mg, depending on the severity of retinal bleedings, for a period of 6 months. The outcome of the study showed that after 6 months in average no further vision loss occurred suggesting that Pycnogenol® effectively stops the progression of retinopathy [Schönlau & Rohdewald, 2001].

### German Multi-Centre study with 1160 patients

#### Patients:

- Diabetes type I and type II
- Diabetes since trial start to maximum 60 years; average 149 months
- Retinopathy since trial start to maximum 26 years; average 1130 days
- No previous treatment 51%, with previous treatment 49%

#### Treatment:

- Daily dosage 20mg Pycnogenol 1 to 8 times a day
- Treatment duration 6 months

#### Outcome:

- Pycnogenol successful for stopping the progression of retinopathy
- In average a moderate improvement of visual acuity

#### Study conclusion:

Pycnogenol has considerable therapeutic benefits for patients with diabetic retinopathy

Pycnogenol® provides potent antioxidant protection against oxidative-stress related degenerative processes in the eyes. The antioxidant properties of Pycnogenol® act in synergy with lipophilic antioxidants in the eye, such as with Lutein.

Pycnogenol's vascular benefits translate to considerable benefits for people suffering from retinopathy. This diabetic complication is improved with Pycnogenol® by supporting impaired capillary integrity and function. The capillary filtration and bleeding is significantly improved with Pycnogenol®. The better perfusion of retinal tissue owing to improved endothelial function with Pycnogenol® helps restore some of the vision lost in retinopathy.

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