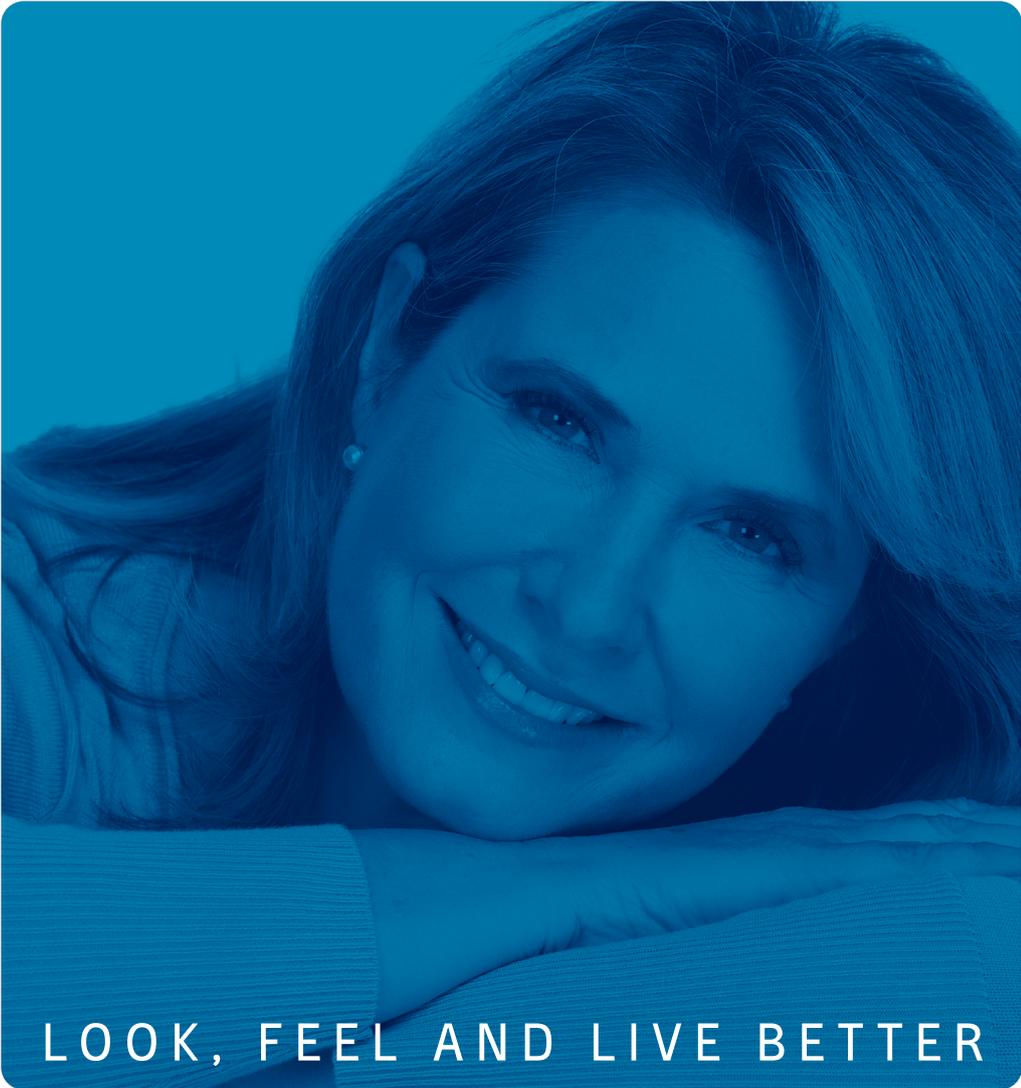


**PYCNOGENOL®**

Menopause





## Pycnogenol® for Menopause

Every year millions of women in the world enter the menopausal transition period, also referred to as perimenopause, ending a woman's fertile years. While menopause represents a normal stage of a woman's life, the transition period bears with it numerous bothersome and debilitating symptoms, which commonly greatly affect daily routines, life and health of affected women.

During menopausal transition women suffer from numerous symptoms which may greatly affect daily routines. Individual women may experience menopausal symptoms quite differently. Moreover women perceive symptoms differently in the world, with women in western countries having most commonly hot flashes, whereas Asian ladies consider joint pain the most bothersome symptom [Geller et al., 2006]. Furthermore, the menopausal life stage goes along with deterioration of endothelial function, putting women at elevated risk for cardiovascular health issues [Moreau et al., 2015]. Physiologic changes occurring during menopause are manifold and manifest also in dryer and less elastic skin.

### Pycnogenol® soothes climacteric symptoms

Pycnogenol® pine bark extract has been tested in numerous controlled studies with the aim to identify good health maintenance in women who are going through the menopausal life stage. The virtues identified so far for Pycnogenol® reach from general improvement of essentially all menopausal symptoms, to cardiovascular health protection and also improved skin health with elevated skin-hydration and -elasticity.

Three separate controlled clinical investigations have all ascribed Pycnogenol® to be efficacious and safe

for alleviating women's climacteric symptoms [Yang et al., 2007; Errichi et al., 2011; Kohama et al., 2013]. Pycnogenol® has natural anti-inflammatory activities, as well as vascular function improvement virtues, related to improvement of endothelial function [Nishioka et al., 2007]. Fortunately, Pycnogenol® does not appear to have any phytoestrogen-like activities nor promote hormonal alterations in peri-menopausal women participating in Pycnogenol® clinical trials [Kohama et al., 2013].



### The categories of the Women's Health Questionnaire (WHQ) as initially defined by Myra Hunter in 1992.

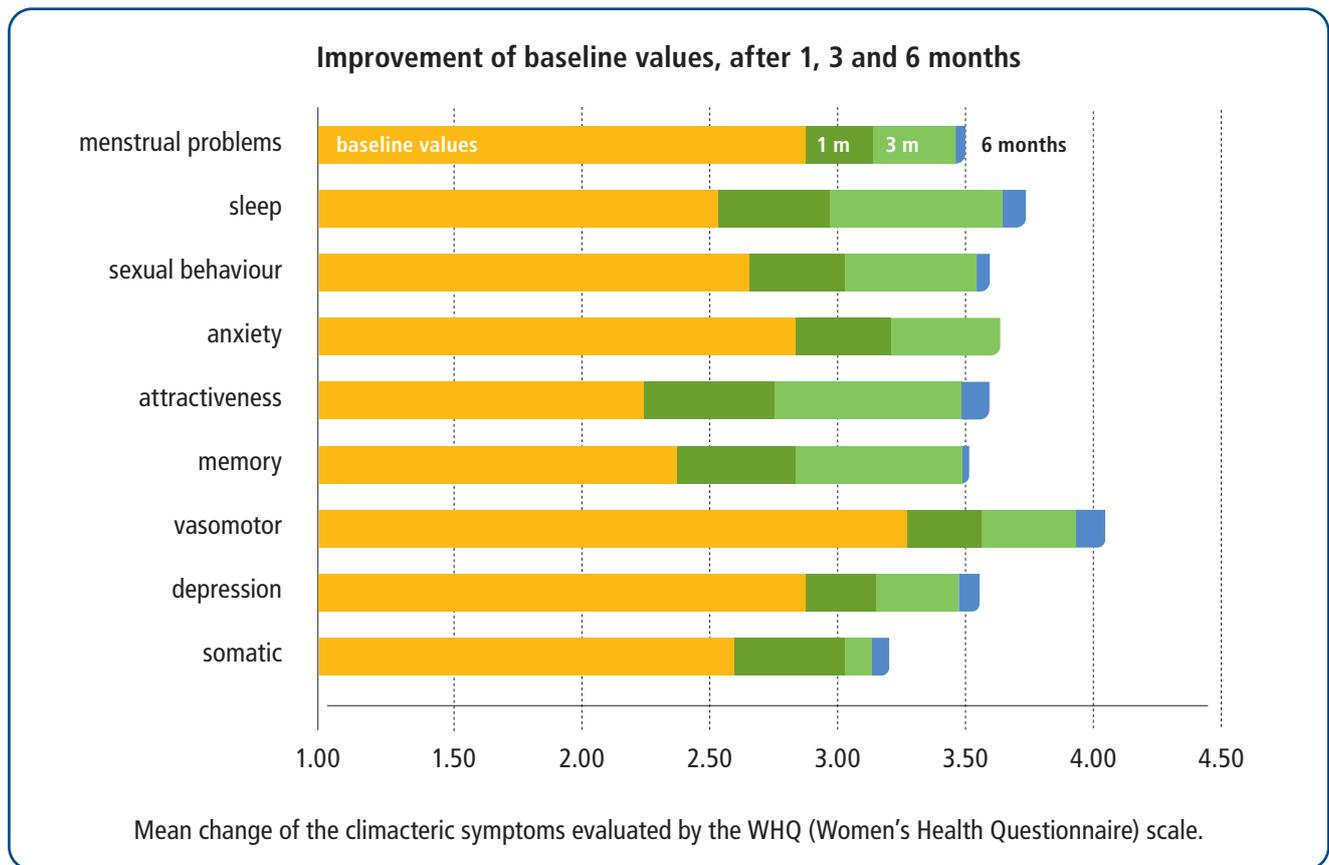
This questionnaire is most commonly used to identify improvement of menopausal symptoms in clinical

trials and was also applied for Pycnogenol® menopause studies.



A double-blind, placebo-controlled study with 200 participating healthy peri-menopausal women, who were not exposed to any hormonal therapy, showed

that Pycnogenol®, taken over a time period of six months, improved all investigated climacteric symptoms [Yang et al., 2007].



Women presented with moderately severe menopausal symptoms at trial start, with symptoms gradually improving already after one month supplementation with Pycnogenol®. Further improvement was identified following three months of continuous daily supplementation with Pycnogenol®. The alleviation of menopausal symptoms persisted and moderately further improved following supplementation with Pycnogenol® for another three months until trial completion after six months [Yang et al., 2007].

Benefits of Pycnogenol® for menopausal women were then investigated in 80 Caucasian women, in a controlled study in Italy. The findings confirmed the virtues of daily supplementation with Pycnogenol® for soothing typical symptoms related to the peri-menopausal transition period [Errichi et al., 2011]. This study pointed to significant symptom improvements manifesting already after eight weeks of Pycnogenol® supplementation in the morning and the evening.



## Menopause

score range 0–4	score at inclusion	after 8 weeks Pycnogenol®
hot flushes	3.1	1.1
nightly sweating	3.1	2.1
irregular periods	3.7	2.1
loss of libido	2.1	1.1
vaginal dryness	2.2	1.2
mood swings	1.9	1.1

Pycnogenol® was found to significantly also improve fatigue, concentration and memory problems in addition to improvements in hair loss, dizziness, weight gain, bloating, brittle nails, irregular heart-beat, depression, anxiety, irritability and panic disorder.

Furthermore, Pycnogenol® proved to be helpful with several pain sensations which commonly occur with some women during menopause.

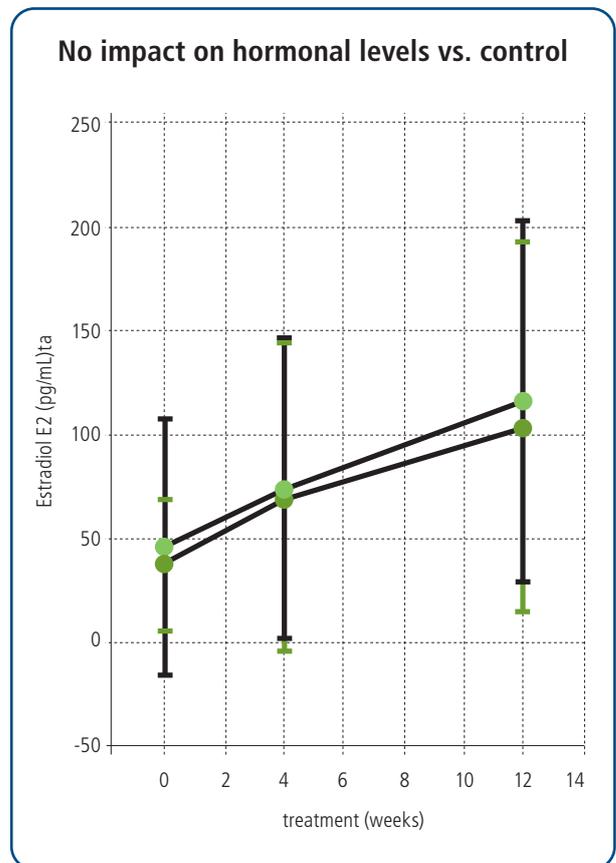
score range 0–4	score at inclusion	after 8 weeks Pycnogenol®
breast pain	2.6	1.3
head aches	3.2	2.2
joint pain	2.7	0.9
electric shocks	2.5	0.6
gum problems	2.2	1.2
muscle tension	2.8	1.1
itchy skin	2.9	1.2
tingling extremities	2.2	1.1

Most importantly, menopausal women participating in clinical trials with Pycnogenol® did not experience side effects. On the contrary, Pycnogenol® was very well tolerated by women participating in the trial. Blood samples collected from women showed that Pycnogenol® supplementation significantly lowered oxidative stress.

### Large double-blind, placebo-controlled study with 170 women

A large double-blind study with 170 Japanese perimenopausal women finds that Pycnogenol® improves symptoms without affecting women’s growth- and sex- hormone levels [Kohama et al., 2013].

After four and twelve weeks of daily supplementation blood was drawn and compared to baseline values prior to Pycnogenol intake. IGF-1 (insulin-like growth factor type 1) did neither rise significantly over baseline values prior to Pycnogenol® intake, nor in comparison to a placebo-treated comparative control group. Estradiol E2 did marginally and insignificantly increase in both groups, placebo- and Pycnogenol®-treated. No alterations related to follicle-stimulating hormone nor dehydro-epiandrosterone occurred.

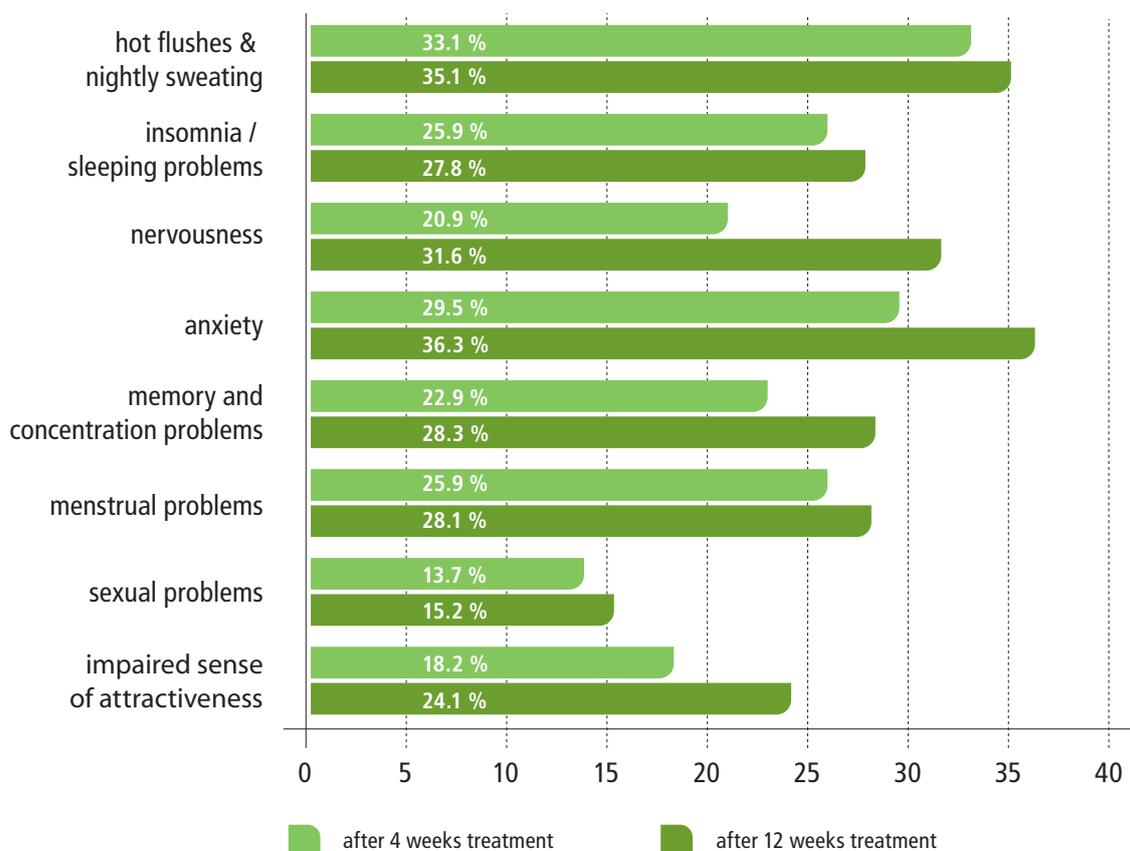


**In conclusion, Pycnogenol® does not exert hormonal or phyto-oestrogenic activities.**

This study identified significant menopausal symptom improvement, using two questionnaires in parallel, the “Women’s Health Questionnaire” and “Kupperman Index”. The symptoms responding particularly well to supplementation with Pycnogenol® were vasomotor-related items: “hot flushes”, “easy sweating”, “cold sensation of body and limbs” and “shortness of breathing”. These vasomotor related symptoms rely on

healthy endothelial function, allowing blood vessels to constrict and relax, to control blood flow as required. Pycnogenol® exerts significant support for improving endothelial function, allowing arteries to expand, such as for directing blood supply to needy tissues, or to the dermis with the aim to radiate off excess body heat. Moreover, this study proved that the applied daily total Pycnogenol® dose of 60 mg is effective for soothing climacteric symptoms, as illustrated below.

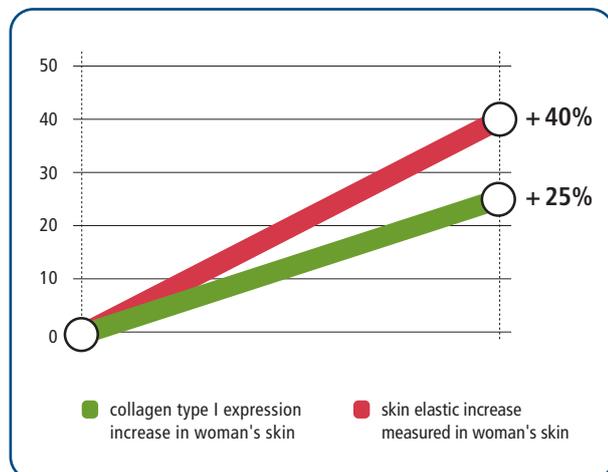
**Relative menopause symptom score improvement after 4 and 12 weeks treatment with 60 mg Pycnogenol® daily**



### Dermatologic virtues of Pycnogenol® identified for menopausal women

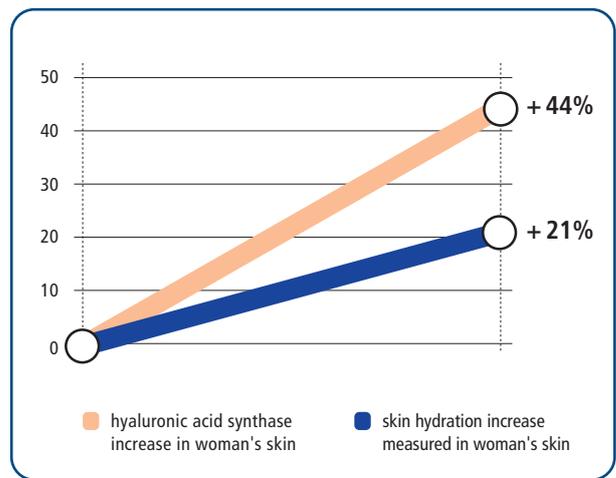
With the onset of perimenopause a progressive decline in skin appearance occurs. Women experience continuous changes occurring to their skin, with the dermis losing elasticity and commonly also increasingly getting dryer. Furthermore, the dermis progressively gets thinner at climacteric age and reduction in dermal collagen content leads to gradual loss of skin elasticity.

Twenty healthy menopausal women supplemented with Pycnogenol® daily for twelve weeks and collagen type I expression was established from skin tissue samples, collected before and subsequent to supplementation with Pycnogenol [Marini et al., 1012]. A significant collagen type I expression increase by 44% was identified already after six weeks. Correspondingly, women's skin was found to present with significantly elevated skin elasticity and ultrasound investigations suggest improved firmness.



Women participating in this study were also investigated for skin hydration and hyaluronic acid synthesis. The outcome presented with significantly increased expression of the enzyme hyaluronic acid synthase in

the dermis, which generates moisturising hyaluronic acid. Increased amounts of hyaluronic acid result in binding and retention of larger water quantities, especially in extracellular space, which correspondingly leads to more even, smoother and taut appearing skin.



### Pycnogenol® affects skin hyper-pigmentation

In some women during menopause the appearance of hyper-pigmented skin areas may occur, which is perceived as particularly bothersome. In many women such overly-pigmented skin-spots may be entirely absent, whereas other women experience particularly troublesome over-pigmented darker spots. A study carried out with menopausal women found that Pycnogenol inhibit activation of genes related to skin pigmentation, which is understood to arrest further progression of skin darkening [Grether-Beck et al., 2016].

Pycnogenol® is demonstrated to significantly alleviate menopausal symptoms in three controlled clinical trials with in total 450 menopausal women

Pycnogenol® is demonstrated to be safe and does not incur any hormonal alterations in menopausal women

Pycnogenol® defies visible signs of ageing, improving skin elasticity, smoothness and moisture, by elevation of collagen, elastin and hyaluronic acid synthase in menopausal women

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