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Review Article

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Pycnogenol®, a Plant Extract for Women's Health

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Abstract

The extract from the bark of the French maritime pine (Pinus pinasterAiton, subsp. atlantica), marketed as Pycnogenol® (Horphag Research, Ltd.), offers a wide range of benefits for women's health and well-being. The present review summarizes results of clinical studies related to sex-specific diseases and troubles, affecting the reproductive system, as well as to some sex related diseases, which are more prevalent in women compared to men.

The sex-specific diseases and troubles, which could be ameliorated by Pycnogenol, comprise dysmenorrhea, endometriosis, and low-back pain during pregnancy, post-partum hemorrhoids, menopausal symptoms and sexual behavior.

The sex-related diseases, manifesting themselves predominantly in women, and having successfully treated with Pycnogenol, are venous diseases, as chronic venous insufficiency (CVI) and ulcers, osteoarthritis (OA) and cosmetic problems.

The review reports significant results from clinical studies listed above and discusses the findings in brief.

Results suggest that Pycnogenol, grace of its improvement of endothelial health and its anti-inflammatory properties, contributes to an improvement of women's health in a non-hormonal way. Pycnogenol presents a safe and versatile food supplement.

Keywords: Cosmeceutical, Dysmenorrhea, Endometriosis, Menopause, Osteoarthritis, Pycnogenol®, Sunburn, Veins

Introduction

Consisting of polyphenolic substances as phenolic acids, catechin, taxifolin and procyanidins, Pycnogenol and its active metabolites are scavengers of free radicals and antioxidants [1, 2]. The specific pine bark extract inhibits inflammatory mediators as cyclooxygenases, TNF-α, interleukins, prostaglandin-E2, C-reactive protein and matrixmetallo proteases [3]. Therefore, Pycnogenol's anti-inflammatory actions provide an analgetic effect and reduce oxidative stress [4].

In addition to the anti-inflammatory action, Pycnogenol improves endothelial health by stimulating synthesis of endothelial NO and reducing the blood levels of the vasoconstrictors endothelin-1, thromboxane A2 and angiotensin II [4]. The balance between vasodilators and vasoconstrictors in the endothelium is of outstanding importance for a healthy circulation.

The anti-inflammatory potential of Pycnogenol and its positive influence on endothelial health contribute both to the beneficial effects of the extract on women's diseases.

The anti-inflammatory component comes to the fore in case of dysmenorrhea, endometriosis, osteoarthritis and oxidative stress. The improvement of endothelial health is important for treating menopausal symptoms, CVI, hemorrhoids, and, not specific for women, for cardiovascular problems.

Improvement of sex-specific diseases

Low back pain during last 3 months of pregnancy

80 Japanese women received 30mg a day Pycnogenol to ameliorate low back pain, pelvis or calf cramps during the third trimester of pregnancy [5]. Women's reported pain relief just after 2 weeks, no effect was observed in the placebo groups, the supplementation was well tolerated.

Low back pain, dysmenorrhea and endometriosis

In an open study with Japanese women, intake of 60mg Pycnogenol a day reduced menstrual pain from high to low pain after 2 cycles [6]. A multi-center study with 116 women could demonstrate that the use of 60mg Pycnogenol a day halved the use of analgesics in the double-blind, placebo-controlled study [7].

In endometriosis, 60mg Pycnogenol a day could reduce pain from severe to moderate in a study with 58 women [8]. In combination

with oral contraceptives, 100mg Pycnogenol a day resulted in a total disappearance of pain in 54-57% of the women, with the oral contraceptives alone none of the women was free of pain. Biopsies showed a reduction of vascular endothelial growth factor and of aromatase, both are involved in development of endometriosis [9,10]. The reduction of use of analgesics is important for minimizing unwanted effects of therapy with analgesics or anti-rheumatic substances. Less pain under Pycnogenol increases quality of life without unwanted effects.

Relief from menopausal symptoms

Treatment of menopausal symptoms was subject of 3 randomized, placebo-controlled, double-blind studies.

Symptoms were scored according to Women's Health Questionnaire [11]. The Taiwanese study with 200 peri-menopausal women tested the effect of 200mg Pycnogenol a day over a period of 6 months [12]. All menopausal symptoms were significantly ($p<0.001$) ameliorated, improvement increased time-dependently. Under placebo, effects were not significant superior compared to Pycnogenol (data not shown) (Table.1)

Table 1: Mean change of the climacteric symptoms evaluated by the WHQ scale (12)

	Pycnogenol® group (n=80)			
	Enrollment	**1 month**	**3 months**	**6 months**
Somatic problems	2.61	3.05**	3.14**	3.21**
Depressed	2.89	3.16*	3.21**	3.29**
Vasomotoric problems	3.28	3.57*	3.64**	3.76**
Memory/ concentration	2.39	2.85**	3.03**	3.06**
Attractiveness	2.26	2.77	2.98**	3.09**
Anxiety	2.85	3.22**	3.27**	3.27**
Sexual behaviour	2.67	3.04*	3.18**	3.23**
Sleep	2.55	2.98**	3.22**	3.31**
Menstrual problems	2.89	3.15**	3.21*	3.25**

All means of symptoms were stat. sign. different to enrollment for the Pycnogenol® group ($p>0.001$). Significant differences to placebo are indicated by *$p<0.01$, **$p<0.001$

In an Italian study, 38 menopausal women received 100mg Pycnogenol a day, 32 women remained untreated formed the control group [13]. Also in this study, hot flushes, bloating, irregular heart beat and digestive problems improved significantly vs. control.

In a Japanese study, running over 12 weeks, 170 women received 60mg Pycnogenol a day or placebo [14]. Vasomotoric items, sleep problems and feeling tired were significantly improved vs. placebo.

The 3 studies demonstrated a time- and dose-dependent effect of Pycnogenol in relieving climacteric symptoms.

Thus, the supplementation with Pycnogenol compensates for the loss of estrogens antioxidative effects and the fading NO production following estrogen decline.

Pycnogenol relieves menopausal symptoms in a non-hormonal way. It did not alter estradiol levels during a treatment with 60mg a day Pycnogenol for 6 months and did not alter concentrations of estrogen, follicle stimulating hormone, dehydroepiandrosterone after intake of 60mg Pycnogenol for 3 months [8,14]. It acts by his antioxidative activity, as registered in two of the climacteric studies and by the enhancement of NO production, thus minimizing oxidative stress and regulating vascular and vasomotoric problems [12,13,15]. The observed improvement of psycho-social climacteric symptoms reflects most probably the better quality of life because of diminished pain, hot flushes and night sweats. Enhancement of concentration and memory by Pycnogenol, as observed in other studies [16-19] may also contribute to well-being.

Sexual behavior

Some items from the Menopause questionnaires were focused on sexual problems as vaginal dryness or loss of libido.

Also for these symptoms, the possibility to produce a better blood circulation in genital organs in combination with the anti-inflammatory actions effect may assist to improve sexual wellness.

Improvement of sex-related diseases

Venous disorders

Although data for prevalence of chronic venous disorders indicate no clear sex difference, women develop with a high frequency varicose veins on the lower limbs during pregnancy [20]. These post-partum veins disappear normally during 6 months after delivery, but in about 25% of the women varicose veins persist [21].

The chronic venous insufficiency (CVI) presents for women an esthetic problem besides the symptoms of pain and edema formation, especially young women try to get free from varicose veins and swollen ankles.

Women screened for presence of varicose veins were treated either with stockings (n=69) or with stockings plus 100mg Pycnogenol for a period of 12 months [22]. Most signs and symptoms were lowered in both groups. However, after 6 months the number of dilated veins was significantly ($p< 0.05$) lower in the Pycnogenol group. Spider veins did not significantly disappear in the group treated with stockings only, but decreased significantly in the Pycnogenol group. The study extension to 12 months did not improve results from the foregoing 6 months.

Pycnogenol has been found superior to elastic stockings and produces a better symptom relief from CVI as most of the venotonic drugs [23]. An ex-vivo experiment could demonstrate that Pycnogenol intake increases significantly the elasticity of varicose veins [24].

The clinical studies showing reduction of number of varicose veins and reduced formation of edema point to a favorable role of Pycnogenol in treating CVI [23].

Venous or diabetic ulcers present a serious problem for patients. They are difficult to treat and need a long period of time for healing. The intake of Pycnogenol and the application of Pycnogenol as powder externally could accelerate the healing process very significantly [25-26].

Post-partum hemorrhoids

60 women with hemorrhoids after their second pregnancy were treated either with standard management or with standard management plus 150mg Pycnogenol for 6 months, starting following the third month of pregnancy [27].

Most women with 3rd degree hemorrhoids were symptom free at 6 months. The reduction of symptoms was better in the Pycnogenol group: 18/24 subjects symptom free versus 14/25 in the control group. Also for 4th degree hemorrhoids, more subjects were symptom free (7/10) in comparison to 4/11 in the group under standard treatment. No unwanted effects were reported [27].

Osteoarthritis (OA)

OA afflicts preferably women. In Germany, 48% of women over the age of 65 suffer from OA versus 31% of men [28]. The incidence of OA for women increases sharply in menopausal transition [29]. Because of this anti-inflammatory and cartilage regenerating effects, Pycnogenol has been found to reduce significantly symptoms of OA as pain, stiffness and swelling, thus increasing mobility [3, 30].

3 Placebo-controlled, double-blind studies could show that supplementation of OA patients with Pycnogenol reduced the intake of analgetic or anti-rheumatic drugs, thus minimizing unwanted effects of medication [31-33]. The increased mobility under Pycnogenol has a great positive impact on daily life, as ascending stairs, social life is less restricted, so that general well-being is reinforced, resulting in less anxiety and depression [33]. These effects advocate the use of Pycnogenol early during development of knee, hip or hand OA.

Skin health

External application

Health and appearance of skin are of outmost importance for most women. Pycnogenol helps to protect and to renew the skin. Pycnogenol containing gels or ointments preserve the skin against UV radiation by inactivating free radicals and by reducing the inflammation following UV exposure. Damage of the skin by UV radiation does not only accelerate skin ageing, intense radiation may produce skin cancer. A lotion containing 0.2% Pycnogenol, applied after UV radiation, was able to reduce the number of tumors and to prolong the time for appearance of tumors in nude mice significantly [34]. This experiment demonstrates that Pycnogenol does not act simply as a sunscreen, but as a powerful anti-inflammatory agent.

Further to skin health, Pycnogenol-containing gel reduced dose-dependently scar formation and accelerates wound healing in an animal experiment [35].

Far more important for skin health as the external application in cosmetic are the findings with Pycnogenol applied orally as tablets or capsules.

Pycnogenol taken orally as a cosmeceutical

The oral intake of Pycnogenol is able to reduce the consequences of sunburn, protecting the skin from inside against the inflammation produced by UV radiation [36]. The minimum dose of UV to produce erythema was increased following supplementation with Pycnogenol in a dose-dependent fashion in 21 white volunteers.

In addition to the protection against UV damages, Pycnogenol counteracts the weakening of skin structure by lytic enzymes, destroying essential structure elements of the skin. Following intake of 200mg Pycnogenol, the damaging matrix metalloproteases, as collagenase and elastase are inhibited in plasma of volunteers [37]. Remarkably, Pycnogenol does not only protect structure elements of the skin against UV or lytic enzymes, it is also able to stimulate the renewal of skin elements. Biopsies from skin of 20 healthy women revealed an increased gene expression for collagen synthesis and hyaluronic acid synthase following intake of 75mg Pycnogenol for 6 weeks [38].

Corresponding to the 40% higher gene expression of the collagen producing enzyme, women's skin elasticity, measured by means of a cutometer, was increased by 25% after 6 weeks daily intake of 75mg Pycnogenol. Simultaneously, caused by the increase of hyaluronic acid synthesis, skin hydration, evaluated by a corneometer, was significantly improved by 21% [38].

This improvement of skin elasticity and hydration by Pycnogenol was accompanied by a lower expression of genes synthesizing melanin [39]. This reduced gene expression provided the explanation for Pycnogenol's effects in reducing over-pigmentation of the skin. In a clinical study, intensity and area of over-pigmentated spots were significantly lower by 37% and 22% respectively following intake of 75mg Pycnogenol for 4 weeks. So Pycnogenol exerted a bleaching effect [40].

Finally, a healthy microcirculation is important for the nutrition of the skin.150mg Pycnogenol accelerated the uptake of oxygen and the elimination of carbon dioxide from skin surface [25].

In conclusion, acting as a cosmeceutical, Pycnogenol has been shown to be of great value for skin care, improving women's skin elasticity, hydration, microcirculation and amelioration of skin color.

Safety

Pycnogenol has been affirmed as GRAS (generally recognized as safe) in self affirmation process by toxicology experts.

Pycnogenol has been tested in 145 clinical studies, involving more than 13.500 patients. The rate and nature of mild unwanted effects as troubles in the digestive tract, headache and skin problems was 1.9%, very near to the rate of 2% for placebo registered in these studies.

Conclusion

Pycnogenol promotes women's health with a plethora of benefits. The non-hormonal amelioration of gynecological problems, starting from relief from menstrual pain, going further to pregnancy-associated effects and ending on improvement of climacteric symptoms, are the important sex-specific benefits.

Venous disorders and osteoarthritis, more common in women compared to man, could be successfully treated with Pycnogenol. Last not least, preservation and renewal of women's skin, documented in clinical studies, complete the picture of a supplement, seemingly designed from nature just for women.

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