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1. Review Articles

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<td>Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested for strengthening capillary walls to decrease capillary filtration.</td>
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Recurrence of retinal vein thrombosis with Pycnogenol® or Aspirin® supplementation: a registry study.
Panminerva Med 57: 121-125, 2015

Ref. 271  CLINICAL STUDY: Pycnogenol® taken at early stages of diabetic retinopathy may partially restore vision further to strengthening retinal capillaries.
Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.

Ref. 227  Pycnogenol® in combination with Lutein provides synergistic antioxidant activity for protecting retinal lipids from oxidation.
Nakanishi-Ueda T, Kamegawa M, Ishigaki S, Tsukahara M, Yano S, Wada K, Yasuhara H
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.
J Clin Biochem Nutr 38: 204-210, 2006

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Kamuren ZT, McPeek CG, Sanders RA, Watkins JB
Effects of low-carbohydrate diet and Pycnogenol® treatment on retinal antioxidant enzymes in normal and diabetic rats.

Ref. 156  Pycnogenol® either alone or in combination with other antioxidants stimulates antioxidant enzyme activities in the retina of diabetic rats.
Dene BA, Maritime AC, Sanders RA, Watkins JB
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Ref. 092  CLINICAL STUDY: The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.
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Pycnogenol® for diabetic retinopathy: A review.

Ref. 075  CLINICAL STUDY: Pycnogenol® shows beneficial effects in retinopathy.
Spada L, Balestrazzi E
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Preventive effect of natural and synthetic antioxidants on lipid peroxidation in the mammalian eye.
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A standardized bark extract of Pinus pinaster Aiton (Pycnogenol®) attenuated chronic obstructive pulmonary disease via Erk-sp1 signaling pathway.

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Pycnogenol attenuates the release of proinflammatory cytokines and expression of peripilin 2 in lipopolysaccharides-stimulated microglia in part via inhibition of NF-kB and AP-1 activation.
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Sahbaz A, Aynioglu O, Isik H, Gun BD, Cengil O, Erol O
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Ref. 413  Pycnogenol® is suggested to protect from ventilation-pulmonary oedema in preclinical research.
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Pycnogenol, a compound isolated from the bark of pinus maritime mill, attenuates ventilator-induced lung injury through inhibiting NF-kB-mediated inflammatory response.

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Effects of Pycnogenol® on endothelial dysfunction in borderline hypertensive, hyperlipidemic, and hyperglycemic individuals: the borderline study.

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Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
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Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).
Biomed Pharmacother 60: 5-9, 2005

Ref. 107  Pycnogenol® as well as its metabolites found in blood of humans potently inhibit matrix metalloproteinases, enzymes involved in cartilage destruction.
Grimm T, Schäfer A, Högger P
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
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Pycnogenol® is shown in preclinical research to help manage allergic rhinitis.  
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CLINICAL STUDY: Pycnogenol® helps to deal with allergic asthma symptoms and allows for lowering medication dosage.  
Pycnogenol® improvements in asthma management.  
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**CLINICAL STUDY:** Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children.  
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Pycnogenol® as an adjunct in the management of childhood asthma.  
*J Asthma* 41: 825-832, 2004

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Pycnogenol® blocks release of histamine from mast cells *in vitro* to the same extent as the antiasthmatic drug DNCG.  
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Pycnogenol® inhibits the release of histamine from mast cells.  

Ref. 077  
**CLINICAL STUDY:** Pycnogenol® reduces asthma symptoms and improves lung function of asthmatic patients in a placebo-controlled, cross-over study.  
Pycnogenol® in the management of asthma.  
*J Med Food* 4: 201-209, 2001
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**Ref. 453**

CLINICAL STUDY: Further to alleviating menopausal symptoms, Pycnogenol® significantly improves blood sugar and -lipids, and supports healthy blood pressure, CRP- and homocysteine values.
Luzzi R, Belcaro G, Hosoi M, Feragalli B, Cornelli U, Dugall M, Ledda A
Normalization of cardiovascular risk factors in peri-menopausal women with Pycnogenol®.
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**Ref. 449**

A review on the efficacy of Pycnogenol® to alleviate climacteric symptoms by improving endothelial function and antioxidative status.
Rohdewald P
Relief from Menopausal Symptoms by Non-hormonal Treatment with Pycnogenol® (French Maritime Pine Bark Extract).
J Gend Syst & Disor 5: 4, 2016

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Pycnogenol® treatment inhibits bone mineral density loss and trabecular deterioration in ovariectomized rats.

**Ref. 400**

CLINICAL STUDY: In combination with low-dose oral contraceptives Pycnogenol® effectively decreases pain and number of bleeding days.
Maia H, Haddad C, Casoy J
The effect of Pycnogenol® on patients with dysmenorrhea using low-dose oral contraceptives.
Int J Women’s Health 6: 1019-1022, 2014

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CLINICAL STUDY: The use of Pycnogenol® improves signs and symptoms of postpartum varicose veins and venous function. Veins regain shape faster.
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Oral administration of Pycnogenol® associated with sunscreen improve clinical symptoms of melasma.
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CLINICAL STUDY: The oral administration of Pycnogenol® combined with daily sunscreen application should be added as an adjuvant to other treatments of melasma.
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CLINICAL STUDY: The combination of oral contraceptives with Pycnogenol® shows a positive synergetic effect on the eutopic endometrium of endometriosis patients.
Pycnogenol® in postpartum symptomatic hemorrhoids.
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CLINICAL STUDY: In the months after pregnancy, Pycnogenol® appears to positively affect hemorrhoid signs and symptoms.
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CLINICAL STUDY: Pycnogenol® taken with oral contraceptives alleviates endometriosis related pain.
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Ref. 046

CLINICAL STUDY: Pycnogenol® improves the morphology of spermatozoa. The percentage of non-deformed sperms in sub-fertile men was increased by 99% after supplementation with Pycnogenol®.
Roseff S, Gulati O
Improvement of sperm quality by Pycnogenol®.
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Ref. 045

CLINICAL STUDY: Pycnogenol® helps in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
Kohama T, Suzuki N
The treatment of gynaecological disorders with Pycnogenol®.
Eur Bull Drug Res 7: 30-32, 1999
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Pycnogenol protects CA3-CA1 synaptic function in a rat model of traumatic brain injury.  
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| Ref. 368 | CLINICAL STUDY: Pycnogenol® reduces oxidative stress and improves physical performance in athletes.  
Evaluation of the effects of supplementation with Pycnogenol® on fitness in normal subjects with the Army Physical Fitness Test and in performances of athletes in the 100-minute triathlon.  
| Ref. 230 | CLINICAL STUDY: Pycnogenol® consumption increases vasodilatation by 42% in young healthy men, which warrants sufficient blood and oxygen supply to performing muscle.  
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.  
Hypertens Res 30: 775-780, 2007 |
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Cramps and muscular pain: prevention with Pycnogenol® in normal subjects, venous patients, athletes, claudicants and in diabetic microangiopathy.  
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Improved endurance by use of antioxidants.  
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Ref. 431 CLINICAL STUDY: Pycnogenol® supplementation for 12 months improves cognition and quenches oxidative stress in normal subjects aged 55 to 70 years.
The COFU3 Study: Improvement in cognitive function, attention, mental performance with Pycnogenol® in healthy subjects (55-70) with high oxidative stress.

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Belcaro G, Luzzi R, Dugall M, Ippolito E, Saggino A
Pycnogenol® improves cognitive function, attention, mental performance and specific professional skills in healthy professionals aged 35-55.

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Pycnogenol® supplementation improves cognitive function, attention and mental performance in students.
Panminerva Med 53: 75-82, 2011

Ref. 241 CLINICAL STUDY: Pycnogenol® significantly improves memory in 101 senior citizens with memory deficits and saves their poly-unsaturated fatty acids, such as from neuronal membranes, from oxidative destruction.
Ryan J, Craft K, Wesnes K, Stough C
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.

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Urinary catecholamines in children with attention deficit hyperactivity disorder (ADHD): modulation by a polyphenolic extract from pine bark (Pycnogenol®).

Ref. 205 CLINICAL STUDY: Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).
Dvorakova M, Sivonova M, Trebaticka J, Skodacek I, Waczulikova I, Muchova J, Durackova Z
Research Article: The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).
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Pycnogenol® protects neurones from amyloid β peptide-induced apoptosis.
Brain Res Mol Brain Res 104: 55-65, 2002

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Pycnogenol® protects vascular endothelial cells from β-amylloid-induced injury.

Ref. 052  Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.
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Impact Communications Inc., Green Bay, WI, USA, 17-19, 1999

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Pycnogenol® shows pigmentation reduction in human skin.  
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Ex vivo study for evaluating the whitening activity of Pycnogenol® after exposure to ultraviolet and infrared radiations, and visible lights.  

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CLINICAL STUDY: This article reviews earlier clinical Pycnogenol® research of the group, identifying improved skin elasticity and hydration, highlighting new findings on oral Pycnogenol® supporting fairer skin complexion, as well as improved skin barrier function.  
Grether-Beck S, Marini A, Jaenicke T, Krußmann J  
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CLINICAL STUDY: The study describes significant reduction of skin pigmentation with Pycnogenol® supplementation, taken in addition to the use of sunscreens, in 31 women with melasma.  
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The use of Pycnogenol® in the treatment of melasma.  

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CLINICAL STUDY: Research demonstrates that Pycnogenol® in combination with pomegranate extract brightens skin and helps decrease blotches in European and Asian women.  
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**Ref. 388**  
CLINICAL STUDY: Most common clinical aspects of psoriasis could be improved by Pycnogenol® supplementation.  
Improvement in signs and symptoms in psoriasis patients with Pycnogenol® supplementation.  

**Ref. 348**  
CLINICAL STUDY: Pycnogenol® increases women’s skin elasticity and hydration which coincides with significantly new collagen and hyaluronic acid synthesis in their skin.  
Pycnogenol® Effects on Skin Elasticity and Hydration Coincide with Increased Gene Expressions of Collagen Type I and Hyaluronic Acid Synthase in Women.  

**Ref. 243**  
Pycnogenol® inhibits pigment formation in skin cells four times more potently than kojic acid, a compound commonly used in skin-whitening products.  
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| Ref. 195 | CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers in humans.  
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| Ref. 185 | CLINICAL STUDY: Pycnogenol® inhibits release of enzymes involved in breaking-down collagen and elastin in inflamed skin in humans.  
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).  
J Inflamm 3: 1-6, 2006 |
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In vitro percutaneous absorption of pine bark extract (Pycnogenol®) in human skin.  
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Pycnogenol® accelerates wound healing and reduces scar formation.  
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| Ref. 132 | CLINICAL STUDY: Supplementation with Pycnogenol® in combination with vitamins, minerals improves skin smoothness and elasticity in women.  
Segger D, Schönlau F  
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Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.  
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Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).

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The cosmeceutical Pycnogenol®.
J Appl Cosmetol 20: 241-246, 2002

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Ni Z, Mu Y, Gulati O
Treatment of melasma with Pycnogenol®.
Phytother Res 16: 567-571, 2002

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Solar ultraviolet-induced erythema in human skin and nuclear factor-kappa-B-dependent gene expression in keratinocytes are modulated by French maritime pine bark extract.

Ref. 073  Pycnogenol® favourably affects the gene expression profile in human keratinocytes, indicating a promising potential for improving inflammatory skin disorders such as psoriasis and dermatoses.
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From ancient remedies to modern therapeutics: Pine bark uses in skin disorders revisited.
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Pine bark extract Pycnogenol® down regulates IFN-γ - induced adhesion of T cells to human keratinocytes by inhibiting inducible ICAM-1 expression.

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ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.

Ref. 026  Pycnogenol® protects α-tocopherol from oxidation and extends its life-time in endothelial cells.
Virgili F, Kim D, Packer L
Procyanidins extracted from pine bark protect α-tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide peroxynitrite.

Ref. 019  Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
Biaso G, Gabor M, Rohdewald P
Anti-inflammatory activities of procyanidin containing extracts from Pinus pinaster Ait. after oral and cutaneous application.
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