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1. Review Articles

Ref. 160  Review article - Update of Pycnogenol® until 2005
Rohdewald, P. (2005)
Pycnogenol®, French Maritime Pine Bark Extract.
Monograph in Encyclopedia of Dietary Supplements; Ed. Marcel Dekker, digital publisher, 2005, p 545-553

Ref. 169  Monograph on Safety and efficacy aspects of Pycnogenol®
Pycnogenol (French Maritime Pine Bark Extract) Pinus Pinaster Aiton subsp. atlantica.

Ref. 170  USP Monograph.

Ref. 171  USP Monograph.
Maritime Pine Bark Extract – USP 28. 2024-2025

Ref. 168  Pycnogenol as a neutraceutical in cardiovascular health and diabetes (Review).
The Nutraceutical Pycnogenol: its role in cardiovascular health and blood glucose control.
Biomedical Reviews 16: 49-57.

Ref. 085  Review article summarizing published data on Pycnogenol® until 2001.
A review of the French maritime pine bark extract (Pycnogenol®), a herbal medication with a diverse clinical pharmacology.

Ref. 114  Review of the positive effects of Pycnogenol® for cardiovascular health, based on the published clinical studies in the cardiovascular area.
Pycnogenol® and cardiovascular health.
Evidence Based Integrative Medicine, 1(1): 27-32.

Ref. 094  Review article: Summary of the positive effects of Pycnogenol® for skin care.
Schönlau, F. (2002)
The cosmeceutical Pycnogenol®.
Ref. 092  Review article: Summary of 5 clinical studies describing the effects of Pycnogenol® supplementation in patients with diabetic retinopathy.

Ref. 034  Review article: discusses in details the biological activities of Pycnogenol®, mainly focusing on its antioxidant and cardiovascular pharmacological profile in light of up to date available data on Pycnogenol®.

Ref. 039  Review article: describes cardiovascular pharmacologic profile of Pycnogenol®, mainly high lighting its inhibitory effects on the smoking-induced platelet aggregation in humans.

Ref. 054  Pharmacological and clinical actions of Pycnogenol® (Review).

Ref. 041  Review article: describes efficacy and safety profile of Pycnogenol® in venous disorders in humans. Mechanisms of reducing oedema are also discusssed.

Ref. 031  Review article: discusses the history of ancient pine bark uses to the present day development of Pycnogenol®.

Ref. 038  Review article: describes in addition to the antioxidant activity of Pycnogenol®, its effects on the immune system and modulation of nitrogen monoxide metabolism, the development of Pycnogenol®.
Ref. 180  Pycnogenol's beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc.
Nutritional supplements in clinical practice.
Prog. Med. 24: 1503-1510.
2. Cardiovascular System

**Ref. 177**  
Pycnogenol and Coenzyme Q10 enhance cardiovascular health synergistically.  
Nutraceutical Synergism: Pycnogenol® and Coenzyme Q10 Enhance Cardiovascular Health.  

**Ref. 168**  
Pycnogenol as a nutraceutical in cardiovascular health and diabetes (Review).  
The Nutraceutical Pycnogenol: its role in cardiovascular health and blood glucose control.  
*Biomedical Reviews* 16: 49-57.

**Ref. 114**  
Review of the positive effects of Pycnogenol® for cardiovascular health, based on the published clinical studies in the cardiovascular area.  
Pycnogenol® and cardiovascular health.  

**Ref. 080**  
Pycnogenol® reduces blood pressure, as shown in a randomized, double-blind, placebo-controlled study performed in mildly hypertensive patients.  
Furthermore, Pycnogenol® significantly decreases the level of the vasoconstrictor factor (thromboxane) in blood of these patients.  
A randomized, double-blind, placebo-controlled, prospective, 16 week crossover study to determine the role of Pycnogenol in modifying blood pressure in mildly hypertensive patients  

**Ref. 117**  
Pycnogenol® improves endothelial function of hypertensive patients and helps to lower the dose of the antihypertensive drug (Nifedipine) when administered simultaneously.  
Pycnogenol® French maritime pine bark extract, improves endothelial function of hypertensive patients.  
*Life Sciences,* 74: 855-862.

**Ref. 017**  
Pycnogenol® inhibits the angiotensin II converting enzyme (ACE) and produces a moderate hypotensive effect in rats.  
ACE inhibition and hypotensive effect of procyanidinins containing extract from the bark of Pinus pinaster Sol.  
**Ref. 036** Pycnogenol® inhibits smoking induced platelet aggregation in dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce increase in bleeding time.

Inhibition of smoking-induced platelet aggregation by Aspirin and Pycnogenol.
*Thrombosis Research,* **95**: 155-161.

**Ref. 053** Pycnogenol® inhibits smoking-induced increased levels of thromboxane B2, the noxious agent involved in the increased platelet reactivity/aggregation in smokers. These results explain the mechanism of anti-platelet aggregation activity of Pycnogenol® observed in smokers.

Pine bark extract reduces platelet aggregation.
*Integrative Medicine,* **2** (**2/3**). 73-77.

**Ref. 043** Pycnogenol® helps fighting against heart disease by inhibiting adhesion and aggregation of platelets and improving microcirculatory blood flow in humans.

The effect of Pycnogenol® on the microcirculation, platelet function and ischemic myocardium in patients with coronary artery diseases.

**Ref. 027** Pycnogenol® counteracts the constriction of blood vessels due to stress. The vaso-relaxant activity of Pycnogenol® is mediated through nitric oxide.

Endothelium-dependent vascular effects of Pycnogenol.
*Journal of Cardiovascular Pharmacology,* **32**: 509-515.

**Ref. 042** Pycnogenol® helps to maintain a healthy circulation through vasodilatation, anti platelet aggregation, free radical scavenging and capillary sealing effects. The role of endothelial nitric oxide (NO) is also discussed.

Rohdewald, P. (1999)
Reducing the risk for stroke and heart infarction with Pycnogenol®.

**Ref. 090** Pycnogenol® increases antioxidant capacity and lowers cholesterol in obese volunteers in a double-blind, placebo-controlled study.

Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
*Lipids* **37** (**10**): 931-934.
Ref. 140  Pycnogenol® increases red blood cell membrane fluidity and protects erythrocytes against oxidative stress.
The effect of Pycnogenol® on the erythrocyte membrane fluidity.

Ref. 176  Pycnogenol® inhibits the most important pro-inflammatory enzymes, signalizing Pycnogenol's bioavailability.
Inhibition of Cox-1 and Cox-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol)
*Biomedicine & Pharmacotherapy*, **60**: 5-9.
3. Venous Disorders

**Ref. 182** Pycnogenol® demonstrate superior activity versus Daflon® in treatment of chronic venous insufficiency in a comparative clinical study.

**Ref. 172** Ulcers of the lower legs heal faster after oral plus topical application of Pycnogenol®
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®. *Angiology* 56(6): 699-705

**Ref. 195** Pycnogenol® accelerates healing of diabetic ulcers.

**Ref. 134** Pycnogenol® prevents thrombosis and thrombophlebitis in long-haul flights.

**Ref. 116** Pycnogenol® in combination with nattokinase prevents deep vein thrombosis in long-haul flights.

www.pycnogenol.com
Pycnogenol® is effective against swelling of ankles during long flights based on the subjective and objective data in a double-blind, placebo-controlled study.


Review article: describes efficacy and safety profile of Pycnogenol® in treating venous disorders in humans. Mechanisms of reducing oedema are also discussed.


Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.


The efficacy of Pycnogenol® has been confirmed on the basis of objective and subjective signs and symptoms of static oedema in a double blind study in 40 patients suffering from chronic venous insufficiency. Pycnogenol® is a safe veno- protector.


Pycnogenol® produces a vaso-protective effect at the level of capillaries as shown in clinical studies. Pycnogenol® decreases oedema and haemorrhagic tendencies in conditions characterised by increased capillary permeability.

Ref. 067  Pycnogenol® tested in a placebo-controlled, double-blind phase as well as in open phase clinical trial, has been shown to produce significant relief and disappearance of symptoms of chronic venous insufficiency. Safety is confirmed by lack of side effects, changes in blood biochemistry and haematological parameters.
Pycnogenol® in chronic venous insufficiency.
*Phytomedicine, 7(5):* 383-388

Ref. 066  Pycnogenol® tested in a placebo-controlled, double-blind clinical trial, has been shown to produce significant relief and disappearance of symptoms of chronic venous insufficiency.
Pycnogenol® in chronic venous insufficiency.
*Fitoterapia, 71:* 236-244

Ref. 079  Pycnogenol® demonstrated higher efficacy in a lower dosage compared to horse chestnut seed extract in a clinical trial.
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
*Phytotherapy Research, 16:* 1-5.

Ref. 112  Addition of Pycnogenol® to troxerutin enhances significantly efficacy of treatment and prolongs symptom relief.

Efficacia della troxerutina assoziata al Picnogenol nel trattamento farmacologico dell’insufficienza venosa.

Efficacy of Troxerutine in association with Pycnogenol® in the treatment of venous insufficiency
*European Bulletin of Drug Research, 12 (1):* 7-12
4. Economy class syndrome

**Ref. 151** Pycnogenol® is effective against swelling of ankles during long flights based on the subjective and objective data in a double-blind, placebo-controlled study.
Prevention of edema in long flights with Pycnogenol®.  

**Ref. 134** Pycnogenol® prevents thrombosis and thrombophlebitis in long-haul flights.
Prevention of Venous Thrombosis and Thrombophlebitis in Long-Haul Flights with Pycnogenol®.  

**Ref. 135** Zinopin® - Rationale of its use as Food Supplement in Traveller's thrombosis and motion sickness.
Review article: Zinopin® - the Rationale for its use as Food Supplement in Traveller's thrombosis and motion sickness.  
*Phytotherapy Research,* 18: 687 – 695

**Ref. 036** Pycnogenol® inhibits platelet aggregation in dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce increase in bleeding time.
Inhibition of smoking-induced platelet aggregation by Aspirin and Pycnogenol.  
*Thrombosis Research,* 95: 155-161.

**Ref. 027** Pycnogenol® counteracts the constriction of blood vessels due to stress. The vaso-relaxant activity of Pycnogenol® is mediated through nitric oxide.
Endothelium-dependent vascular effects of Pycnogenol.  
*Journal of Cardiovascular Pharmacology,* 32: 509-515.

**Ref. 041** Review article: describes efficacy and safety profile of Pycnogenol® in treating venous disorders in humans. Mechanisms of reducing oedema are also discussed.
Pycnogenol® in venous disorders: A review.  
Ref. 067  Pycnogenol® tested in a placebo-controlled, double-blind phase as well as in open phase clinical trial, has been shown to produce significant relief and disappearance of symptoms of chronic venous insufficiency. Safety is confirmed by lack of side effects, changes in blood biochemistry and haematological parameters.

5. Cholesterol Lowering

Ref. 090  **Pycnogenol® supplementation reduced blood levels of the "bad" cholesterol LDL in human volunteers.**
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
*Lipids* **37 (10)**: 931-934.

Ref. 079  **Pycnogenol® lowered LDL significantly in patients with chronic venous insufficiency while horse chestnut seed extract had no effect.**
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
*Phytotherapy Research* **16**: 1-5.

Ref. 093  **Pycnogenol® supplementation lowered total cholesterol and LDL and increased HDL, resulting in a better atherosclerotic index.**
Lipid metabolism and erectile function improvement by Pycnogenol®, extract from the bark of *Pinus pinaster* in patients suffering from erectile Dysfunction - a pilot study.
6. Eye Health

Ref. 092 The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.

Ref. 075 Pycnogenol® shows beneficial effects in retinopathy

Ref. 051 Pycnogenol® protects retina of the eye against damage caused by oxidative stress. The effect is more pronounced when compared to other antioxidant bioflavonoids. Pycnogenol® enhances the effects of other antioxidants like Coenzyme Q10 when combined together.

Ref. 018 Pycnogenol® protects the retina of the eye against free radicals damage.

Ref. 184 Pycnogenol increases anti-oxidative enzyme concentrations in the retina of rats, suggesting a lower risk for retinopathy and cataract formation.

Ref. 156 Pycnogenol® either alone or in combination with other antioxidants stimulates antioxidant enzyme activities in the retina of diabetic rats.
7. Diabetic Syndrome

**Ref. 092** The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.

Pycnogenol® for diabetic retinopathy: A review.

**Ref. 109** In a dose-finding study Pycnogenol® lowers glucose levels of type II diabetic patients and improves endothelial function.

French maritime pine bark extract Pycnogenol dose-dependently lowers glucose in type II diabetic patients.
*Diabetes Care*, 27(3): 839.

**Ref. 195** Pycnogenol® accelerates healing of diabetic ulcers.

Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®

**Ref. 142** Pynogenol® supplementation to diabetic patients lowers glucose levels.

Antidiabetic effect of Pycnogenol® French maritime pine bark extract in patients with diabetes type II.

**Ref. 105** Pycnogenol® lowers blood glucose and increases intracellular antioxidant defense mechanism in diabetic rats.

Effect of Pycnogenol treatment on oxidative stress in streptozotocin-induced diabetic rats.

**Ref. 153** Pycnogenol® either alone or in combination with other antioxidants reduces parameters of oxidative stress in diabetic rats.

Influence of treatment of Diabetic rats with combinations of Pycnogenol, beta-carotene, and alpha-lipoic acid on parameters of oxidative stress.
*J Biochem Mol Toxicol*, 18(6): 345-52

**Ref. 156** Pycnogenol® either alone or in combination with other antioxidants stimulates antioxidant enzyme activities in the retina of diabetic rats.

Effects of Antioxidant Treatment on Normal and Diabetic rat retinal enzyme activities.

www.pycnogenol.com
Pycnogenol increases anti-oxidative enzyme concentrations in the retina of rats, suggesting a lower risk for retinopathy and cataract formation.
Effects of Low-Carbohydrate Diet and Pycnogenol® Treatment on Retinal Antioxidant Enzymes in Normal and Diabetic Rats.

Pycnogenol® inhibits in vitro the undesirable modification of proteins in presence of glucose, which occurs in proteins of diabetic patients.
Inhibitory effect of Pycnogenol on generation of advanced glycation end products in vitro.

Pycnogenol® reduces blood pressure, as shown in a randomized, double-blind, placebo-controlled study performed in mildly hypertensive patients. Furthermore, Pycnogenol® significantly decreases the level of the vasoconstrictor factor (thromboxane) in blood of these patients.
A randomized, double-blind, placebo-controlled, prospective, 16 week crossover study to determine the role of Pycnogenol® in modifying blood pressure in mildly hypertensive patients.

Pycnogenol® supplementation reduced blood levels of the "bad" cholesterol LDL in human volunteers.
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
Lipids 37 (10): 931-934.

Pycnogenol® helps fighting against heart disease by inhibiting adhesion and aggregation of platelets and improving microcirculatory blood flow in humans.
The effect of Pycnogenol® on the microcirculation, platelet function and ischemic myocardium in patients with coronary artery diseases.

Review of the positive effects of Pycnogenol® for cardiovascular health, based on the published clinical studies in the cardiovascular area.
Pycnogenol® and cardiovascular health.
Evidence Based Integrative Medicine, 1(1): 27-32.
Ref. 042  Pycnogenol® helps to maintain a healthy circulation through vasodilatation, anti-platelet-aggregation, free radical scavenging and capillary sealing effects. The role of endothelial nitric oxide (NO) is also discussed.
Rohdewald, P. (1999)
Reducing the risk for stroke and heart infarction with Pycnogenol®.
8. Anti-Aging

**Ref. 098** Pycnogenol® delays the aging process as shown by an increased life-span of fruit flies.

**Ref. 099** Pycnogenol® in combination with other antioxidants administered as a dietary supplement increases life-span of mice. The findings support its beneficial effects against neurogenerative diseases.

**Ref. 052** Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.

**Ref. 029** Pycnogenol® slows down the aging related process of decline in activities of immune- and blood cells generating systems and restores their functions to normal.

**Ref. 069** Pycnogenol® produces significant reduction in vascular damage caused by β-amyloid protein. β-amyloidosis is one of the neuropathological hallmarks of Alzheimer’s disease(AD). This explains the role of Pycnogenol® in reducing the risk of AD.

**Ref. 083** Neuronal apoptosis (early cell death) is induced by the amyloid-β-peptide in the brain of Alzheimer patients. In vitro experiments demonstrated an inhibition of cell death of neurons by Pycnogenol®.
9. Inflammation

**Ref. 185** Pycnogenol® inhibits key triggers of inflammation.
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol).
*Journal of Inflammation, 3: 1*, 1-6

**Ref. 176** Pycnogenol® inhibits the most important pro-inflammatory enzymes, signaling Pycnogenol’s bioavailability.
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol).
*Biomedicine & Pharmacotherapy* 60:5-9.

**Ref. 107** The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited in vitro. Release of these enzymes from inflammatory cells is also inhibited by Pycnogenol® and its metabolites.
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol).
*Free Radicals Biology and Medicine, 36(6):* 811-822.

**Ref. 180** Pycnogenol’s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc.
Nutritional supplements in clinical practice.
*Progressive Medicine 24:* 1503-1510.

**Ref. 010** Pycnogenol® scavenges superoxide radicals in vitro and inhibits oedema in vivo. The anti-inflammatory and free radical scavenging activities are closely correlated.
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. and its fractions.

**Ref. 183** Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histo-morphological evidence in rats.
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.
*(Submitted in PTR)*
**Ref. 111**  
Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.  
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.  

**Ref. 013**  
Applied topically, Pycnogenol® significantly reduces UVB radiation induced-erythema, the procyanidins are the protecting factors.  
Anti-inflammatory activities of procyanidin-containing extracts from *Pinus pinaster sol.*  

**Ref. 019**  
Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.  
Antiinflammatory activities of procyanidin containing extracts from *Pinus pinaster Ait.* after oral and cutaneous application.  
*Pharmazie, 52 (5):* 380-382.

**Ref. 193**  
Oral administration of Pycnogenol® is able to delay and to reduce skin cancer following UV radiation.  
Cancer chemopreventive effects of *Pinus maritima* bark extract on ultraviolet radiation and ultraviolet radiation -7,12 dimethylbenz(a) anthracene induced skin carcinogenesis of hairless mice.  

**Ref. 074**  
Pycnogenol® inhibits UV-induced erythema in humans. This effect was concentration dependent indicating the beneficial effects of Pycnogenol® in skin disorders induced by UV radiation.  
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.  
*Free Radical Biol. & Med., 30 (2):* 154-160
10. Skin Care

Ref. 172 Ulcers of the lower legs heal faster after oral plus topical application of Pycnogenol®
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®
*Angiology* **56**(6): 699-705

Ref. 195 Pycnogenol® accelerates healing of diabetic ulcers.
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®

Ref. 133 Pycnogenol dose-dependently speeds-up the wound healing process and reduces scar formation.
*Short communication*: Pycnogenol® accelerates wound healing and reduces scar formation
*Phytotherapy Research*, **18**: 579-581.

Ref. 081 Pycnogenol® shows beneficial effects in melasma.
Treatment of melasma with Pycnogenol®
*Phytotherapy Research*, **16**: 567-571

Ref. 094 Review summarizing the positive effects for skin care
Schönlau, F. (2002)
The cosmeceutical Pycnogenol®
*Journal Applied Cosmetology*, **20**: 241-246

Ref. 132 Supplementation with Evelle® improves skin smoothness and elasticity.
Supplementation with Evelle® improves smoothness and elasticity in a double blind, placebo- controlled study with 62 women.
Ref. 074  Pycnogenol® inhibits UV-induced erythema in humans. This effect was concentration dependent indicating the beneficial effects of Pycnogenol® in skin disorders induced by UV radiation.
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.
*Free Radical Biol. & Med.*, **30 (2)**: 154-160

Ref. 111  Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.

Ref. 193  Oral administration of Pycnogenol® is able to delay and to reduce skin cancer following UV radiation.
Cancer chemopreventive effects of Pinus maritima bark extract on ultraviolet radiation and ultraviolet radiation -7,12 dimethylbenz(a) anthracene induced skin carcinogenesis of hairless mice.

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

Ref. 013  Applied topically, Pycnogenol® significantly reduces UVB radiation induced-erythema, the procyanidins are the protecting factors.
Anti-inflammatory activities of procyanidin-containing extracts from Pinus pinaster sol.

Ref. 008  Pycnogenol® protects the skin from ultraviolet-radiation-induced oxidative stress injury (lipid peroxidation and cytotoxicity). The protective effects were related to dose, with the highest concentration providing the greatest benefits.
Ultraviolet radiation-induced oxidative stress in cultured human skin fibroblasts and antioxidant protection.

www.pycnogenol.com
Pycnogenol® affects favourably the gene expression profile in human keratinocytes in vitro, thus having a great potential in treatment of psoriasis and dermatoses.
From ancient remedies to modern therapeutics: Pine bark uses in skin disorders revisited.
Phytotherapy Research, 15: 76-78.

Evidence of percutaneous absorption of Pycnogenol® in human skin.
In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol) in Human Skin.
Journal of Toxicology: Cutaneous and Ocular Toxicology, 23 (3): 149-158

The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited in vitro. Release of these enzymes from inflammatory cells is also inhibited by Pycnogenol® and its metabolites.
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol).
Free Radicals Biology and Medicine, 36(6): 811-822.

Pycnogenol® inhibits key triggers of inflammation.
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol).
Journal of Inflammation, 3: 1, 1-6

Pycnogenol® inhibits Interferon -γ (IFN-γ)-induced ICAM-1 expression in human skin cells (keratinocytes). This effect is dose and time dependent indicating the therapeutic potential of Pycnogenol® in inflammatory skin disorders.
Pine bark extract Pycnogenol down regulates IFN-γ - induced adhesion of T cells to human keratinocytes by inhibiting inducible ICAM-1 expression.
Free Radical Biology Medicine, 28 (2): 219-227.

Pycnogenol® shows antimicrobial activity in vitro.
Anti-microbial activity of Pycnogenol®.
Phytotherapy Research, 19, 647-648

Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
**Ref. 026**  Pycnogenol® protects α-tocopherol in endothelial cells.
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.
*FEBS letters*, **431**: 315-318.

**Ref. 009**  Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.
Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertoni schen Ratten.
*Phlebologie*, **22**: 178-182.
11. Oral Health Care

Ref. 084 A Pycnogenol® - containing chewing gum tested in a clinical trial reduced bleeding of the gum and plaque formation on the teeth.

Ref. 099 Pycnogenol® increases the pathologically low capillary wall resistance. Pycnogenol® is shown to be the most potent among other bioflavonoids tested. Pycnogenol® provides strength to capillary walls and makes them less permeable and thus contributes to anti-oedema, anti-inflammatory effects.

Ref. 133 Pycnogenol dose-dependently speeds-up the wound healing process and reduces scar formation.

Ref. 150 Pycnogenol® shows antimicrobial activity *in vitro*.

Ref. 030 Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
12. Immunology

Ref. 082  Pycnogenol® shows beneficial effects in case of lupus erythematosus
Stefanescu, M., Matache, C., Onu, A., Tanaseanu, S., Dragomir, C.,
Constantinescu, I., Schönlau, F., Rohdewald, P., Szegli G. (2001)
Pycnogenol® Efficacy in the Treatment of Systemic Lupus Erythematosus Patients
Phytotherapy Research, 15: 698-704

Ref. 029  Pycnogenol® slows down the aging related process of decline in the
activities of immune- and blood cells generating systems and restores their
functions to normal.
Pycnogenol enhances immune and haemopoietic functions in senescence-accelerated
mice.

Ref. 016  Pycnogenol® enhances the activity of the immune system in mice infected
with a leukemia-causing retrovirus. Pycnogenol® increases the natural killer
cell cytotoxicity.
Cheshier, J.E., Ardestani-Kaboudanian, S., Liang B., Araghi Niknam, M., Chung, S.,
Immunomodulation by Pycnogenol® in retro-virus infected or ethanol-fed mice.

Ref. 055  Pycnogenol® increases TNF-α secretion in the macrophage system in a
concentration and time dependent manner indicating that it acts as
modulator of the immune response in macrophages.
Activity of monomeric, dimeric, and trimeric flavonoids on NO production, TNF-alpha
secretion, and NF-kappaB-dependent gene expression in RAW 264.7 macrophages.

Ref. 095  Pycnogenol® activates in vitro macrophages to kill more effectively
invading bacteria.
Pycnogenol® augments macrophage phagocytosis and cytokine secretion

Ref. 111  Pycnogenol® applied after sunburn inhibits UV-induced suppression of
immune system.
Protection from inflammation, immunosuppression and carcinogenesis induced by UV
radiation in mice by topical Pycnogenol®.
**Ref. 173**  
**Pycnogenol® selectively kills cancerous ovarian germ cells.**  
Research article: Selective toxicity of Pycnogenol® for malignant ovarian germ cells *in vitro.*  

**Ref. 059**  
**Pycnogenol® selectively kills cancerous human mammary cells (MCF-7), without affecting the normal mammary cells (MCF-10).**  
Selective induction of apoptosis in human mammary cancer cells (MCF-7) by Pycnogenol.  
*Anticancer Research, 20:* 2417-2420.
13. Allergies and Asthma

Ref. 077  **Pycnogenol® reduces asthma symptoms and improves lung function of asthmatic patients in a placebo-controlled, cross-over study.**
Pycnogenol® in the management of asthma.  
*Journal of Medicinal Food, 4 (4):* 201-209.

Ref. 149  **Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children**
Pycnogenol® as an adjunct in the management of childhood Asthma.  
*Journal of Asthma, Vol. 41 (8):* 825-832

Ref. 089  **Pycnogenol® blocks release of histamine from mast cells in vitro to the same extent as the antiasthmatic drug DNCG.**
Pycnogenol® inhibits the release of histamine from mast cells.  
*Phytotherapy Research* **17:** 66-69
14. Sport & Endurance

**Ref. 044**  Pycnogenol® increases human endurance during exercise by 21% providing antioxidant reserves.
Improved endurance by use of antioxidants.
*European Bulletin of Drug Research, 7(2)*: 26-29.

**Ref. 189**  Pycnogenol® reduces muscular pain and cramps in athletes and in patients with chronic venous insufficiency, diabetes or poor circulation in the legs.
Cramps and Muscular Pain: Prevention with Pycnogenol® in Normal Subjects, Venous Patients, Athletes, Claudicants and in Diabetic Microangiopathy.
*Angiology 57(3)*: 331-339.

**Ref. 096**  Pycnogenol® stimulates Human Growth Hormone (HGH) secretion in vitro thousand times more effectively than other natural compounds. Treatment with HGH increases muscle mass and decreases fat mass.
Kyolic and Pycnogenol® increase human growth hormone secretion in genetically-engineered keratinocytes.
*Growth hormone & IGF Research, 12*: 34-40
15. Menstrual Disorders, Pregnancy Associated Pain and Endometriosis

**Ref. 174** Pycnogenol® reduces low-back pain in late period of pregnancy.
Pycnogenol® Alleviates Pain Associated with Pregnancy.
*Phytotherapy Research* **20**: 232-234

**Ref. 145** Pycnogenol® produces analgesic effect in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
Analgesic efficacy of French maritime pine bark extract in dysmenorrhea. - An open clinical trial

**Ref. 045** Pycnogenol® helps in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
The treatment of gynaecological disorders with Pycnogenol®.

**Ref. 180** Pycnogenol’s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc.
Nutritional supplements in clinical practice.
*Progressive Medicine* **24**: 1503-1510.

**Ref. 118** Caffeic and protocatechic acids (components of Pycnogenol®) produce anti-spasmodic activity contributing to beneficial effects of Pycnogenol® in Premenstrual syndrome (PMS)
Antispasmodic activity on rat smooth muscle of polyphenol compounds caffeic and protocatechic acids.
16. Fertility

Ref. 046 Pycnogenol® improves the morphology of spermatozoa. The percentage of non-deformed sperms in sub-fertile men was increased by 99% after supplementation with Pycnogenol® for three months.
Improvement of sperm quality by Pycnogenol®.

Ref. 091 After treatment with Pycnogenol® increase in functionally normal sperm may allow infertile couples to forgo in vitro fertilization.
Improvement in sperm quality and function with French maritime pine tree bark extract.

Ref. 143 Pycnogenol® and Ginkgo biloba supplementation showed beneficial effects in erectile dysfunction
The effect of natural phyphenols (Extract from Pinus pinaster (Pycnogenol®) and Ginkgobiloba (EGB 761) on the oxidative stress and erectile function in patients suffering from erectile dysfunction.
17. Attention Deficit Hyperactivity Disorder (ADHD)

Ref. 190  **Pycnogenol®** provides relief of hyperactivity and improves attention in children with ADHD in a double-blind placebo controlled study.

Ref. 047  **Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor**

Ref. 048  **Pycnogenol® is recommended for treatment of Attention Deficit Disorder.**
18. Antioxidant and Free Radical Scavenger

Ref. 090  Pycnogenol® increases antioxidant capacity and lowers cholesterol in obese volunteers in a double-blind, placebo-controlled study.
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
*Lipids 37 (10):* 931-934.

Ref. 183  Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histo-morphological evidence in rats.
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.
*(Submitted in PTR)*

Ref. 021  Pycnogenol® is shown to be the strongest hydroxyl and superoxide radical scavenger among other extracts tested. In addition, Pycnogenol® is resistant to heat and ascorbate oxidase.
Hydroxyl and superoxide anion radical scavenging activities of natural source antioxidants using the computerized JES-FR30 ESR spectrometer system.
*Biochem. & Mol. Biol. Int., 42 (1):* 35-44.

Ref. 030  Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.

Ref. 026  Pycnogenol® protects α-tocopherol in endothelial cells.
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.
*FEBS letters,* 431:315-318.

Ref. 033  Pycnogenol® is an efficient antioxidant due to the relative stability of its corresponding radical and its regeneration by vitamin C and vitamin E homologue Trolox.
Electron spin resonance study of free radicals formed from a procyanidin-rich pine (Pinus maritime) bark extract, Pycnogenol.
*Free Radical Biology Medicine,* 27 (11-12): 1308-1312

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Ref. 025 Pycnogenol® inhibits the effect of oxidative stress and minimises hydroxyl radical-induced DNA damage in vitro.
Pycnogenol inhibits macrophage oxidative burst, lipoprotein oxidation and hydroxyl radical-induced DNA damage.
*Drug Development and Industrial Pharmacy, 24 (2):* 139-144.

Ref. 020 Pycnogenol® stimulates synthesis of antioxidative enzymes inside cells of the arteries thereby doubling the amount of antioxidative enzymes.
Pycnogenol enhances endothelial cell antioxidant defenses.
*Redox Report, 3(4):* 219-224.

Ref. 072 Pycnogenol® selectively enhances activity of intracellular antioxidative enzymes.
Pycnogenol® inhibits generation of inflammatory mediators in macrophages.

Ref. 105 Pycnogenol® lowers blood glucose and increases intracellular antioxidant defense mechanism in diabetic rats.
Effect of Pycnogenol treatment on oxidative stress in streptozotocin-induced diabetic rats.

Ref. 051 Pycnogenol® protects retina of the eye against damage caused by oxidative stress. The effect is more pronounced when compared to other antioxidant bioflavonoids. Pycnogenol® enhances the effects of other antioxidants like Coenzyme Q10 when combined together.
In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.

Ref. 010 Pycnogenol® scavenges superoxide radicals in vitro and inhibits oedema in vivo. The anti-inflammatory and free radical scavenging activities are closely correlated.
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. And its fractions.

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Ref. 070  Pycnogenol® by virtue of its high content of procyanidins is more potent antioxidant than other herbal-sourced antioxidants containing relatively higher content of regular flavon(ol)s. This fact is explained on structural and functional basis. Bors, W., Michel C and Stettmaier, K (2000) Electron paramagnetic resonance studies of radical species of proanthocyanidins and gallate esters. *Archives of Biochemistry and Biophysics, 374 (2): 347-355.*


Ref. 086  Pycnogenol® in combination with whey increases antioxidative capacity of plasma.
*Food Research International*, **35**: 257-266.
19. Bio-Availability and Metabolism

Ref. 040  Pycnogenol® is shown to be bioavailable based on its therapeutic effects in viva: the prevention of platelet aggregation and the capillary sealing effect. Valerolactones as sulphates or glucuronides appear in the urine and they represent the active metabolites of Pycnogenol®.
Rohdewald, P. (1999)
Bioavailability and metabolism of Pycnogenol®.

Ref. 058  Pycnogenol®, its components and metabolites are bio-available in human for more than 24 hours to produce their beneficial effects.
Urinary metabolites of French maritime pine bark extract in humans.

Ref. 060  Bio-kinetics (absorption, metabolism and excretion) of Pycnogenol® in healthy human subjects has been demonstrated by studying the excretion pattern of ferulic acid (one of the components of Pycnogenol®).
Ferulic acid excretion as a marker of consumption of a French maritime pine (Pinus maritima) bark extract.
Free Radical Biology & Medicine, 28 (8): 1249-1256.

Ref. 137  Evidence of percutaneous absorption of Pycnogenol® in human skin.
In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol) in Human Skin.
Journal of Toxicology: Cutaneous and Ocular Toxicology. 23 (3): 149-158
20. Anti-microbial and anti-viral activity

Ref. 150  **Pycnogenol® shows antimicrobial activity in vitro.**
Short Communication: Antimicrobial activity of Pycnogenol®.
*Phytotherapy research, 19:* 647-648.