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Ref. 180  Pycnogenol®‘s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc, pregnancy associated pain.
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Gulati, O.P. (2005)  
The Nutraceutical Pycnogenol®: Its role in cardiovascular health and blood glucose control.  

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**Ref. 114**  
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Ref. 039  Review article: Describes the cardiovascular pharmacologic profile of Pycnogenol®, mainly highlighting its inhibitory effects on the smoking-induced platelet aggregation in humans.
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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®.
Procyanidins from Pinus maritima bark: Antioxidant activity, effects on the immune system and Modulation of Nitrogen Monoxide Metabolism.

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®.
Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (Pinus maritima) bark, Pycnogenol®.

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Reduction of cardiovascular risk factors in subjects with Type 2 Diabetes by Pycnogenol® supplementation.

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Ref. 230  Pycnogenol® increases endothelium-dependent vasodilation by 42%, by enhancing synthesis of nitric oxide in young healthy men.
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Impact of Pycnogenol® on cardiac extracellular matrix remodeling induced by L-NAME administration to old mice.
Cardiovascular System

Ref. 207 Pycnogenol® in vitro study provides evidence of strengthening heart muscle.
Pycnogenol® Increases the Probability of the Contraction State in Chick Embryonic Cardiomyocytes, indicating Inotropic Effects.

Ref. 200 Pycnogenol® reduces oedema side effects in hypertensive subjects taking anti-hypertensive therapy.
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Control of Edema in Hypertensive Subjects Treated With Calcium Antagonist (Nifedipine) or Angiotensin-Converting Enzyme Inhibitors With Pycnogenol®.

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

Ref. 176 Pycnogenol® inhibits the most important pro-inflammatory enzymes, showing a strikingly rapid bioavailability.
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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®).

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The effect of Pycnogenol® on the erythrocyte membrane fluidity.
Ref. 117  
**Pycnogenol® improves endothelial function of hypertensive patients and helps to lower the dose of the antihypertensive drug (Nifedipine) when administered simultaneously.**

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

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

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.**

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.**
Cardiovascular System

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. 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.

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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.

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Endothelium-dependent vascular effects of Pycnogenol®.

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Ref. 200  Pycnogenol® reduces oedema side effects in hypertensive subjects taking anti-hypertensive therapy.
Control of Edema in Hypertensive Subjects Treated With Calcium Antagonist (Nifedipine) or Angiotensin-Converting Enzyme Inhibitors With Pycnogenol®.

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

Ref. 182  Pycnogenol® demonstrates superior activity versus Daflon® in treatment of chronic venous insufficiency in a comparative clinical study.
Comparison of Pycnogenol® and Daflon® in Treating Chronic Venous Insufficiency: A Prospective, Controlled Study.
Venous Disorders

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®.

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. 116  Pycnogenol® in combination with nattokinase prevents deep vein thrombosis in long-haul flights.
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### Venous Disorders

| 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 or changes in blood biochemistry and haematological parameters. Petrassi, C., Mastromarino, A. and Spartera, C. (2000) 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. Arcangeli, P. (2000) Pycnogenol® in chronic venous insufficiency. *Fitoterapia, 71*: 236-244. |
Venous Disorders

Ref. 012  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.
Le pycnogérol: une substance douée de propriétés angioprotectrices dans le traitement de l’insuffisance veineuse chronique.

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Le pycnogérol: Thérapeutique médicamenteuse de l’œdème statique.

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Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertonischen Ratten.
4. Cholesterol Lowering

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A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.  

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.  

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.  
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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.  
*Phytother Res*, 16: 1-5.
5. Diabetic Syndrome

Ref. 237  Pycnogenol® given in addition to diabetic and hypertensive medication significantly further improves blood sugar and cardio-vascular risk factors and allows a majority of patients to lower anti-hypertensive medication.

Ref. 233  Pycnogenol® lowers platelet hyperactivity more effectively than aspirin in a type I diabetes pharmacologic model suggesting a protective effect from thrombosis in diabetes.

Ref. 209  Pycnogenol® inhibits dietary carbohydrate absorption by inhibition of alpha-glucosidase.

Ref. 199  Pycnogenol® reduces diabetic microangiopathy.

Ref. 195  Pycnogenol® accelerates healing of diabetic ulcers.
Diabetic Syndrome

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**Diabetic Syndrome**

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| 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.  
| 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.  
| 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.  
| 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.  
| 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.  
| 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.  
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®.
6. Eye Health

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.  

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.  
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# 7. Inflammation

| Ref. 249 | Pycnogenol® lowers pain and improves flexibility of osteoarthritic joints.  
Effect of pine bark extract (Pycnogenol®) on symptoms of knee osteoarthritis.  
| Ref. 223 | Pycnogenol® improves pain and mobility and lowers required pain medication in osteoarthritis.  
| Ref. 208 | Pycnogenol® *in vitro* study provides evidence of chemoprevention.  
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.  
| Ref. 202 | Pycnogenol® reduces symptoms of knee osteoarthritis.  
Effect of Pine Bark Extract (Pycnogenol®) On Symptoms Of Knee Osteoarthritis.  
| 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. 188**  
Pycnogenol® reduces pain and stiffness of knee osteoarthritis.  
Pycnogenol® supplementation reduces pain and stiffness and improves physical function in adults with knee osteoarthritis.  

**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®).  

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

**Ref. 180**  
Pycnogenol®s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc and pregnancy associated pain.  
Nutritional supplements in clinical practice.  
*Progr Med*, **24**: 1503-1510.

**Ref. 176**  
Pycnogenol® inhibits the most important pro-inflammatory enzymes, showing a strikingly rapid bioavailability.  
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.

**Ref. 111**  
Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.  
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.  
The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited \textit{in vitro}. Release of these enzymes from inflammatory cells is also inhibited by Pycnogenol® and its metabolites.


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.


Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.


Applied topically, Pycnogenol® significantly reduces UVB radiation induced-erythema, the procyanidins are the protecting factors.


Pycnogenol® scavenges superoxide radicals \textit{in vitro} and inhibits oedema \textit{in vivo}. The anti-inflammatory and free radical scavenging activities are closely correlated.


8. Joint Health

Ref. 249  Pycnogenol® lowers pain and improves flexibility of osteoarthritic joints.
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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®).

Ref. 176  Pycnogenol® consumption non-selectively, inhibits cox enzyme, which are involved in pain sensation during inflammation.
Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).
The tissue destroying enzymes (matrix metalloproteinases) collagenase, elastase and gelatinase are inhibited \textit{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®).

9. Allergies and Asthma

Ref. 149  Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children.
Pycnogenol® as an adjunct in the management of childhood Asthma.
J Asthma, 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.

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.
10. Menstrual Disorders, Pregnancy Associated Pain and Endometriosis

Ref. 220 Pycnogenol® significantly lowers menstrual pain and the quantity of required analgesic medication in a multi-center study with four hospitals in Japan. 

Ref. 219 Pycnogenol® reduces pain from endometriosis and shows less side effects compared to hormonal treatment.  

Ref. 187 Pycnogenol® improves a broad range of climacteric symptoms in menopausal women.  

Ref. 180 Pycnogenol®’s beneficial effects in a series of painful conditions as stiff shoulder, endometriosis, herniated disc and pregnancy associated pain.  
*Progr Med, 24*: 1503-1510.

Ref. 174 Pycnogenol® reduces low-back pain in late period of pregnancy.  
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.

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.

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®.
## 11. Sport & Endurance

### Ref. 230

Pycnogenol® increases vasodilation by 42% in young healthy men to warrant, 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.

### 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.


### 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.


### Ref. 044

Pycnogenol® increases human endurance during exercise by 21% providing antioxidant reserves.


Improved endurance by use of antioxidants.

# 12. Attention Deficit Hyperactivity Disorder (ADHD)

**Ref. 231**  
Pycnogenol® lowers stress-hormones in children with ADHD.  
Urinary catecholamines in children with attention deficit hyperactivity disorder (ADHD): modulation by a polyphenolic extract from pine bark (Pycnogenol®).  

**Ref. 205**  
Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).  
The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).  

**Ref. 204**  
Pycnogenol® protects DNA against oxidation in children with Attention Deficit Hyperactivity Disorder (ADHD).  
Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/hyperactivity disorder.  

**Ref. 190**  
Pycnogenol® provides relief of hyperactivity and improves attention in children with ADHD in a double-blind placebo controlled study.  
Treatment of ADHD with French maritime pine bark extract, Pycnogenol®.  

**Ref. 048**  
Pycnogenol® is recommended for treatment of Attention Deficit Disorder.  
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Attention Deficit Disorder.  
*Impact Communications Inc., Green Bay, WI, USA*, 17-19.
Ref. 047  Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor.

Pycnogenol® for ADHD?
13. Skin Care

Ref. 243  Pycnogenol® inhibits pigment formation in skin cells four times more potently than kojic acid, a compound commonly used in skin-whitening products.
The anti-melanogenic effect of Pycnogenol® by its anti-oxidative actions.

Ref. 211  Beneficial effects of Pycnogenol® in wrinkles - A review article.
The cosmetic treatment of wrinkles.

Ref. 195  Pycnogenol® accelerates healing of diabetic ulcers.
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with 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. 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®).
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### Ref. 094
Review summarizing the positive effects for skin care.
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The cosmeceutical Pycnogenol®.

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

### 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.

### Ref. 073
Pycnogenol® affects favourably the gene expression profile in human keratinocytes \textit{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.
*Phytother Res*, 15: 76-78.

### Ref. 057
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.
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| 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.  
| 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.  
| 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 Ait. after oral and cutaneous application.  
| 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.  
| 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 hypertonischen Ratten.  
| 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.  
14. Oral Health Care

Ref. 150  Pycnogenol® shows antimicrobial activity in vitro.
Short Communication: Antimicrobial activity of 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.

Ref. 084  A Pycnogenol®-containing chewing gum tested in a clinical trial reduced bleeding of the gum and plaque formation on the teeth.
Pycnogenol® chewing gum minimizes gingival bleeding and plaque formation.
*Phytomedicine*, 9: 410-413.

Ref. 030  Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
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Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertonischen Ratten.
15. 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. 135 Zinopin® (a combination of Pycnogenol® and Standardized Ginger Root Extract) – 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.

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

Ref. 116 Pycnogenol® in combination with nattokinase prevents deep vein thrombosis in long-haul flights.
Prevention of venous thrombosis in long-haul flights with Flite Tabs: The Lonflit- Flite randomized controlled trial.
Angiology, 54(5): 531-539.
### Ref. 067
Pycnogenol® tested in a placebo-controlled, double-blind as well as in open 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 or changes in blood biochemistry and haematological parameters.

Pycnogenol® in chronic venous insufficiency.

### 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. 036
Pycnogenol® inhibits platelet aggregation in a dose-dependent manner in humans. The effect lasts for more than 6 days and unlike aspirin, it does not produce an increase in bleeding time.

Inhibition of smoking-induced platelet aggregation by Aspirin and Pycnogenol®.

### 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®.
## 16. Anti-Aging

**Ref. 241** 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.  
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.  

**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.  
Reduction of inclusion body pathology in ApoE-deficient mice fed a combination of antioxidants.  

**Ref. 098** Pycnogenol® delays the aging process as shown by an increased life-span of fruit flies.  
Role of Pycnogenol® in aging by increasing the Drosophila’s life-span.  

**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®.  
Pycnogenol® protects neurons from amyloid β peptide-induced apoptosis.  

**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.  
Pycnogenol® protects vascular endothelial cells from β-amyloid-induced injury.  
### Ref. 052
Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.
Pycnogenol® improves learning impairment and memory deficit in senescence-accelerated mice.

### 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.
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.
17. Fertility

Ref. 143  Pycnogenol® and Ginkgo biloba supplementation showed beneficial effects in erectile dysfunction.
The effect of natural polyphenols (Extract from Pinus pinaster (Pycnogenol®) and Ginkgo biloba (EGB 761) on the oxidative stress and erectile function in patients suffering from erectile dysfunction.
Proceedings. (Abstract No L 61)

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. 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®.
18. Anti-microbial and anti-viral activity

Ref. 247 Pycnogenol® decreases HIV viral replication and T-cell interaction in cell culture experiments.
Pycnogenol®, a procyanidin-rich extract from French maritime pine, inhibits intracellular replication of HIV-1 as well as its binding to host cells.

Ref. 229 Pycnogenol® inhibits viral replication in the heart muscle of mice.
French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.
*J Card Fail*, 13 (9), 785-791.

Ref. 225 Pycnogenol® inhibits growth of *Helicobacter pylori* and their adherence to mucosal cells of the stomach.
*In vitro* inhibition of *Helicobacter pylori* growth and adherence to gastric mucosal cells by Pycnogenol®.

Ref. 150 Pycnogenol® shows antimicrobial activity *in vitro*.
Short Communication: Anti-microbial activity of Pycnogenol®.
19. Immunology

Ref. 236  Pycnogenol® increases phagocytosis of macrophages suggesting better defence against pathogenic infections.
Proteomic analysis of Pycnogenol effects in RAW 264.7 macrophage reveals induction of cathepsin D expression and enhancement of phagocytosis.

Ref. 228  Pycnogenol® inhibits viral replication in myocarditis.
Matsumori, A. (2007)
Treatment Options in Myocarditis.

Ref. 221  Pycnogenol® inhibits the harmful effects of two mutagenic chemicals.
Antimutagenic *In Vitro* Activity of Plant Polyphenols: Pycnogenol® and *Ginkgo biloba* Extract (EGb 761).
*Phytother Res*, **22**: 384-388.

Ref. 208  Pycnogenol® reduces cancerogenesis in human ovarian cells.
Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.

Ref. 173  Pycnogenol® selectively kills cancerous ovarian germ cells.
Research article: Selective toxicity of Pycnogenol® for malignant ovarian germ cells *in vitro*.

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®.
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20. Antioxidant and Free Radical Scavenger

Ref. 241  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.
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.

Ref. 239  Pycnogenol® antagonises the neurotoxicity of alcohol, suggesting mitigation of hangover symptoms.
Protective mechanisms of Pycnogenol® in ethanol-insulted cerebellar granule cells.

Ref. 227  Pycnogenol® and Lutein display synergistic antioxidant effects for prevention of lipid peroxidation.
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.

Ref. 218  Pycnogenol® lowers oxidative stress in the liver of rats challenged with a chemical toxin.
Ameliorative Effects of Pycnogenol® on Carbon Tetrachloride-Induced Hepatic Oxidative Damage in Rats.

Ref. 215  Pycnogenol® protects liposomes from lipid peroxidation and shows synergistic protective effects with vitamin C and vitamin E.
The Combined Effect of Pycnogenol® with Ascorbic Acid and Trolox on the Oxidation of Lipids and Proteins.
Ref. 205  Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).
The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).

Ref. 204  Pycnogenol® protects DNA against oxidation in children with Attention Deficit Hyperactivity Disorder (ADHD).
Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/hyperactivity disorder.

Ref. 203  Pycnogenol® prevents accumulation of oxidative damaged proteins and may reduce the risk of Alzheimer’s, Parkinson’s and Huntington’s diseases.
Ferritin oxidation and proteasomal degradation: Protection by antioxidants.

Ref. 183  Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histomorphological evidence in rats.
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.

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. 090  Pycnogenol® increases antioxidant capacity and lowers cholesterol in obese 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. 086

**Pycnogenol® in combination with whey increases antioxidative capacity of plasma.**


Determination of the antioxidative potential of human plasma after supplementation with Pycnogenol® and whey.

*Food Res Intern, 35*: 257-266.

### Ref. 072

**Pycnogenol® selectively enhances activity of intracellular antioxidative enzymes.**


Pycnogenol® inhibits generation of inflammatory mediators in macrophages.


### 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.

*Arch Biochem Biophys, 374(2)*: 347-355.

### Ref. 063

**Pycnogenol® shows free radical scavenging activity against reactive oxygen species.**

It inhibits the generation of pro-inflammatory mediators confirming the anti-inflammatory and immuno-modulatory profile of Pycnogenol®.


Effect of bioflavonoids extracted from the bark of Pinus maritime on proinflammatory cytokine interleukin-1 production in lipopolysaccharide-stimulated raw 264.7.


### Ref. 062

**Pycnogenol® blocks oxidative modification of cellular proteins more effectively than other antioxidants.**


Effect of select antioxidants on malondialdehyde modification of proteins.

*Nutrition, 16*: 1079-1081.

### 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. 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®.

### 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 and peroxynitrite.

### 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 Dev Ind Pharm, 24*(2): 139-144.

### Ref. 022
Pycnogenol® in addition to its free radical scavenging property, modulates the production of nitric oxide radicals in activated inflammatory cells.
Procyanidins extracted from Pinus maritima (Pycnogenol®): scavengers of free radical species and modulators of nitrogen monoxide metabolism in activated murine raw 264.7 macrophages.

### 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.
Pycnogenol® stimulates synthesis of antioxidative enzymes inside cells of the arteries thereby doubling the amount of antioxidative enzymes.

Pycnogenol® enhances endothelial cell antioxidant defenses.

Pycnogenol® protects the endothelial cells which line the blood vessels from free radicals damage. Damage to endothelial cells is considered a prime cause for atherosclerosis.

Pycnogenol® protects vascular endothelial cells from t-butyl hydroperoxide induced oxidant injury.

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.

Pycnogenol® is proven an excellent radical scavenger of enzymatically produced hydroxyl and singlet oxygen free radicals, two of the most dangerous free radicals.

Radical scavenger properties of leucocyanidine.
21. Bio-Availability and Metabolism

Ref. 197  Pycnogenol® is bioavailable after oral administration.
Single and multiple dose pharmacokinetics of maritime pine bark extract (Pycnogenol®) after oral administration to healthy volunteers.

Ref. 137  Evidence of percutaneous absorption of Pycnogenol® in human skin.
*In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol®) in Human Skin.

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.

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. 040  Pycnogenol® is shown to be bioavailable based on its therapeutic effects in vivo: 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®.
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