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1. Review Articles

Ref. 346  A review on the broad applicability of Pycnogenol® for personalized health care, for prevention as well as treatment.
Strong J
French maritime pine bark extract (Pycnogenol®) and the use of health supplements in the age of personalized medicine.

Ref. 326  A comprehensive review of the composition and pharmacology of Pycnogenol® as well as the published medical research.
Maimoona A, Naeem I, Saddiqe Z, Jameel K
A review on biological, nutraceutical and clinical aspects of French maritime pine bark extract.
J Ethnopharmacol 133: 261-277, 2011

Ref. 269  A clinical overview based on the full monograph covering published scientific and clinical research on Pycnogenol®.
Oliff H
Scientific and clinical monograph on Pycnogenol®.
The American Botanical Council 2009

Ref. 266  A comprehensive review of research on Pycnogenol® in the field of venous insufficiency.
Gulati OP
Pycnogenol®: a nutraceutical for venous health.
Biomedical Reviews 19: 33-43, 2008

Ref. 261  This review article covers the wide range of contributions of Pycnogenol® for diabetic people, such as lowering of blood glucose and helping with a majority of diabetic complications.
Rohdewald P
Regulation of diabetes by Pycnogenol®.

Ref. 259  A comprehensive review of Pycnogenol®'s anti-inflammatory activity and its role for controlling diverse inflammatory disorders.
Farid R
Pycnogenol® in the treatment of inflammatory diseases: osteoarthritis, asthma and heart disease.
<p>| Ref. 228 | Introduction to the pathology of myocarditis and a discussion on mechanisms by which Pycnogenol® may help the heart to recover. Matsumori A Treatment Options in Myocarditis. Herz 32: 452-456, 2007 |</p>
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Review Articles

**Ref. 038**

This article reviews the antioxidant activity of Pycnogenol® and its effects on the immune system and modulation of inducible nitric oxide synthase.

Virgili F, Kobuchi H, Noda Y, Cossins E, Packer L

Procyanidins from Pinus maritima bark: Antioxidant activity, effects on the immune system and Modulation of Nitrogen Monoxide Metabolism.


**Ref. 034**

An introduction to the chemistry, antioxidant activity and biologic properties of Pycnogenol®.

Packer L, Rimbach G, Virgili F

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


**Ref. 031**

The history of ancient pine bark uses to the present day development of Pycnogenol®.

Drehsen G

From ancient pine bark uses to Pycnogenol®

2. Cardiovascular System


Ref. 295  CLINICAL STUDY: Pycnogenol® reduces the disturbing “ringing” or “hissing” noise sensation in tinnitus patients which is suggested to result from an improved blood flow to the cochlea of the ears. Grossi MG, Belcaro G, Cesarone MR, Duggall M, Hosoi M, Cacchio M, Ippolito E, Bavera P Improvement in cochlear flow with Pycnogenol® in patients with tinnitus: a pilot evaluation. Panminerva Med 52 (suppl. 1 to No. 2): 63-67, 2010


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Ref. 283
CLINICAL STUDY: Pycnogenol® taken as an adjunct to hypertensive medication improves kidney flow and function and further improves blood pressure.
Kidney Flow and Function in Hypertension: Protective Effects of Pycnogenol® in Hypertensive Participants-A Controlled Study.

Ref. 281
Pycnogenol® protects the kidneys from damage caused by oxidative stress and ischemia in an animal model.
Ozer Sehirli A, Sener G, Ercan F
Protective effects of Pycnogenol® against ischemia reperfusion-induced oxidative renal injury in rats.
Ren Fail 31: 690-697, 2009

Ref. 274
Pycnogenol® improves heart function in experimentally induced heart damage in diabetic rats.
Pycnogenol® improves left ventricular function in streptozotocin-induced diabetic cardiomyopathy in rats.
Phyother Res 24: 969-974, 2010

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Watson RR, Argüelles MC
Pycnogenol® and cardiovascular health.

Ref. 237
CLINICAL STUDY: 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.
Zibadi S, Rohdewald P, Park D, Watson RR
Reduction of cardiovascular risk factors in subjects with Type 2 Diabetes by Pycnogenol® supplementation.
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| 233  | Pycnogenol® lowers platelet hyperactivity more effectively than aspirin in a type I diabetes pharmacologic model suggesting a protective effect from thrombosis in diabetes.  
Nocun M, Ulicna O, Muchova J, Durackova Z, Watala C  
French maritime pine bark extract (Pycnogenol®) reduces thromboxane generation in blood from diabetic male rats.  
| 230  | CLINICAL STUDY: Pycnogenol® increases endothelium-dependent vasodilation by 42%, by enhancing the synthesis of nitric oxide in young healthy men.  
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.  
Hypertens Res 30: 775-780, 2007 |
| 229  | Pycnogenol® counteracts viral infection and prevents development of virus-induced heart muscle inflammation.  
Matsumori A, Higuchi H, Shimada M  
French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.  
| 216  | Pycnogenol® prevents heart failure damage in mice.  
Zibadi S, Yu Q, Rohdewald PJ, Larson DF, Watson RR  
Impact of Pycnogenol® on cardiac extracellular matrix remodeling induced by L-NAME administration to old mice.  
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| 207  | Pycnogenol® shows strengthening of heart muscle cells in vitro.  
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A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.  
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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.
Watson RR
Nutraceutical Synergism: Pycnogenol® and Coenzyme Q10 Enhance Cardiovascular Health.
Evid Based Integrative Med 2: 67-70, 2005

Ref. 168  Pycnogenol® as a nutraceutical in cardiovascular health and diabetes (Review).
Gulati OP
The Nutraceutical Pycnogenol®: its role in cardiovascular health and blood glucose control.
Biomed Rev 16: 49-57, 2005

Ref. 140  Pycnogenol® increases red blood cell membrane fluidity and protects erythrocytes against oxidative stress.
Sivonova M, Waczulikova I, Klanczyk E, Hrnciarova M, Bryszewska M, Klapnert B, Durackova Z
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Gen Physiol Biophys 23: 39-51, 2004

Ref. 117  CLINICAL STUDY: Pycnogenol® as an adjunct to hypotensive medication with Nifedipine improves endothelial function and allows for lowering the drug dosage.
Pycnogenol® French maritime pine bark extract, improves endothelial function of hypertensive patients.
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Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
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Koch R
Comparative study of Venostasin® and Pycnogenol® in chronic venous insufficiency.
Phytother Res 16: 1-5, 2002

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Hosseini S, Lee J, Sepulveda RT, Rohdewald P, Watson RR
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.

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Pine bark extract reduces platelet aggregation.
Int Med 2: 73-77, 1999

Ref. 043  CLINICAL STUDY: Pycnogenol® inhibits platelet aggregation and adhesion and improves blood micro-circulation in heart disease patients.
The effect of Pycnogenol® on the microcirculation, platelet function and ischemic myocardium in patients with coronary artery diseases.
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Control of Edema in Hypertensive Subjects Treated With Calcium Antagonist (Nifedipine) or Angiotensin-Converting Enzyme Inhibitors with Pycnogenol®.

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

CLINICAL STUDY: 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.

CLINICAL STUDY: 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®.
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CLINICAL STUDY: Pycnogenol® effectively counteracts ankle swellings occurring during long-haul travelling in a double-blind, placebo-controlled study.
Prevention of edema in long flights with Pycnogenol®.
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CLINICAL STUDY: Addition of Pycnogenol® to troxerutin significantly enhances the efficacy of chronic venous insufficiency treatment and prolongs symptom relief.  
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Koch R  
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**Ref. 067**  
CLINICAL STUDY: Pycnogenol® provides significant symptoms relief from chronic venous insufficiency symptoms.  
Petrassi C, Mastromarino A, Spartera C  
Pycnogenol® in chronic venous insufficiency.  
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CLINICAL STUDY: Pycnogenol® significantly improves chronic venous insufficiency and relieves disappearance of symptoms of chronic venous insufficiency.  
Arcangeli P  
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In pharmacological experiments Pycnogenol® is demonstrated to protect renal cells from glucose damage in a diabetic nephropathy model.  
Kim YJ, Kim YA, Yokozawa T  
Pycnogenol® modulates apoptosis by suppressing oxidative stress and inflammation in high glucose-treated renal tubular cells.  

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Pycnogenol® provides antioxidant protective effects to the liver in an animal diabetes model.  
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Protective effects of Pycnogenol® on hyperglycemia-induced oxidative damage in the liver of type 2 diabetic rats.  

**Ref. 300**  
Pycnogenol® is shown in an in vitro model to facilitate better glucose uptake by fat cells which suggests anti-diabetic benefits.  
Lee HH, Kim K-J, Lee OH, KJ, Lee BY  
Effect of Pycnogenol® on glucose transport in mature 3T3-L1 adipocytes.  
Phytother Res 24: 1242-1249, 2010

**Ref. 293**  
CLINICAL STUDY: Pycnogenol® improves kidney function of metabolic syndrome patients as judged by lowered urinary albumins and improved kidney perfusion.  
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Effects of melatonin and Pycnogenol® on small artery structure and function in spontaneously hypertensive rats.  
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Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.

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

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.
Nocun M, Ulicna O, Muchova J, Durackova Z, Watala C
French maritime pine bark extract (Pycnogenol®) reduces thromboxane generation in blood from diabetic male rats.

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Schäfer A, Högger P
Oligomeric procyanidins of French maritime pine bark extract (Pycnogenol®) effectively inhibit alpha-glucosidase.
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Ref. 199

**CLINICAL STUDY: Pycnogenol® reduces diabetic microangiopathy.**


Ref. 195

**CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers.**


Ref. 184

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

Kamuren ZT, McPeek CG, Sanders RA, Watkins JB


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


Ref. 153

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**CLINICAL STUDY: Pycnogenol® supplementation to diabetic patients lowers glucose levels.**


Antidiabetic effect of Pycnogenol® French maritime pine bark extract in patients with diabetes type II. Life Sci, 75: 2505-2513, 2004
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Inhibitory effect of Pycnogenol® on generation of advanced glycation end products in vitro.

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

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Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.

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Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
Lipids 37: 931-934, 2002

Ref. 080  CLINICAL STUDY: 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.
Hosseini S, Lee J, Sepulveda RT, Rohdewald P, Watson RR
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.
5. Eye Health

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

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.  

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**CLINICAL STUDY:** Pycnogenol® significantly lowers the inflammatory marker CRP in hypertensive patients with chronic kidney disease.  
Kidney Flow and Function in Hypertension: Protective Effects of Pycnogenol® in Hypertensive Participants--A Controlled Study.  

**Ref. 272**  
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The anti-inflammatory pharmacology of Pycnogenol® in humans involves COX-2 and 5-LOX mRNA expression in leukocytes.  
Int Immunopharmacol 9: 1145-1149, 2009

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**CLINICAL STUDY:** Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.  
Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.  

**Ref. 208**  
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**Ref. 185**  
**CLINICAL STUDY:** Pycnogenol® inhibits key triggers involved in the initiation of an inflammation in a pharmacological investigation in humans.  
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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<td>183</td>
<td>Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histomorphological evidence in rats. Ramos FM, Schönlaub F, Novaes PD, Manzi FR, Bóscolo FN, Almeida SM</td>
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<td>154</td>
<td>Pycnogenol® significantly counteracts inflammatory damage of the colon in an experimental animal model. Mochizuki M, Hasegawa N</td>
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<td>Matrix metalloproteinases, enzymes involved in connective tissue destruction, are potently inhibited by Pycnogenol® as well as its metabolites found in blood of humans. Grimm T, Schäfer A, Högger P</td>
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<td>CLINICAL STUDY: Pycnogenol® dose-dependently inhibits UV-induced erythema in humans. This effect was found to be associated to the anti-inflammatory potency of Pycnogenol®. Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, Watson RR, Packer L</td>
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<td>Pycnogenol® inhibits several mechanisms related to recruitment of leukocytes to tissue which results in anti-inflammatory activity. Peng Q, Wei Z, Lau BHS</td>
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**Ref. 183**
Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histomorphological evidence in rats.
Ramos FM, Schönlaub F, Novaes PD, Manzi FR, Bóscolo FN, Almeida SM
Pycnogenol® protects against ionizing radiation as shown in the intestinal mucosa of rats exposed to X-rays.

**Ref. 176**
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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

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Therapeutic efficacy of Pycnogenol® in experimental inflammatory bowel diseases.
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Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).

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Takano T, Kozai Y, Kawamata R, Wakao H, Sakurai T, Kashima I  
Inhibitory effect of maritime pine bark extract (Pycnogenol®) on deterioration of bone structure in the distal femoral epiphysis of ovariectomized mice.  
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The anti-inflammatory pharmacology of Pycnogenol® in humans involves COX-2 and 5-LOX mRNA expression in leukocytes.  
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Ref. 250  CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.  
Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.  

Ref. 249  CLINICAL STUDY: Pycnogenol® improves flexibility of osteoarthritic joints, lowers pain and allows patients to decrease their pain medication.  
Effect of pine bark extract (Pycnogenol®) on symptoms of knee osteoarthritis.  

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