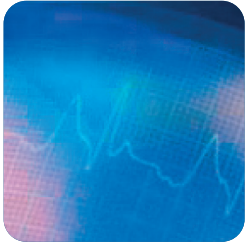




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1. Review Articles

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4. Diabetic Syndrome

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Steigerwalt R, Belcaro G, Cesarone MR, Di Renzo A, Grossi MG, Ricci A, Dugall M, Cacchio M, Schönlau F
Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.
J Ocul Pharmacol Ther 25: 537-540, 2009
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- 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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- Ref. 195** **CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers.**
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 Clin Appl Thromb Hemost 12: 318-323, 2006
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 Kamuren ZT, McPeck CG, Sanders RA, Watkins JB
 Effects of low-carbohydrate diet and Pycnogenol® treatment on retinal antioxidant enzymes in normal and diabetic rats.
 J Ocul Pharmacol Ther 22: 10-18, 2006
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 Effects of Antioxidant Treatment on Normal and Diabetic rat retinal enzyme activities.
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 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: 345-352, 2004
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 Liu X, Wei J, Tan F, Zhou S, Würthwein G, Rohdewald P
 Antidiabetic effect of Pycnogenol® French maritime pine bark extract in patients with diabetes type II.
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 French maritime pine bark extract Pycnogenol® dose-dependently lowers glucose in type II diabetic patients.
 Diabetes Care 27: 839, 2004
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Zhang TM, Han CH, Han YW, Gong H, Zhang EY, Zhang Y
Inhibitory effect of Pycnogenol® on generation of advanced glycation end products *in vitro*.
Chin Pharmacol Bull 19: 437-440, 2003
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Maritim A, Dene BA, Sanders RA, Watkins JB
Effect of Pycnogenol® treatment on oxidative stress in streptozotocin-induced diabetic rats.
J Biochem Mol Toxicol 17: 193-199, 2003
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- Ref. 092** **CLINICAL STUDY:** The review presents results of five clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® for patients with diabetic retinopathy.
Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.
Int Ophthalmol 24: 161-171, 2002
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Devaraj S, Vega-López S, Kaul N, Schönlau F, Rohdewald P, Jialal, I
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile.
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5. Eye Health

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- Ref. 271** **CLINICAL STUDY: Pycnogenol® taken at early stages of diabetic retinopathy may partially restore vision further to strengthening retinal capillaries.**
Steigerwalt R, Belcaro G, Cesarone MR, Di Renzo A, Grossi MG, Ricci A, Dugall M, Cacchio M, Schönlau F
Pycnogenol® improves microcirculation, retinal edema, and visual acuity in early diabetic retinopathy.
J Ocul Pharmacol Ther 25: 537-540, 2009
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Nakanishi-Ueda T, Kamegawa M, Ishigaki S, Tsukahara M, Yano S, Wada K, Yasuhara H
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.
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Effects of low-carbohydrate diet and Pycnogenol® treatment on retinal antioxidant enzymes in normal and diabetic rats.
J Ocul Pharmacol Ther 22: 10-18, 2006
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- 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.
J Ocul Pharmacol Ther 21: 28-35, 2005
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- Ref. 092** **CLINICAL STUDY: The review contains results of 5 clinical studies with Pycnogenol® showing the efficacy of Pycnogenol® supplementation for patients with diabetic retinopathy.**
Schönlau F, Rohdewald P
Pycnogenol® for diabetic retinopathy: A review.
Int Ophthalmol 24: 161-171, 2002
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- Ref. 075** **CLINICAL STUDY: Pycnogenol® shows beneficial effects in retinopathy.**
Spadea L, Balestrazzi E
Treatment of vascular retinopathies with Pycnogenol®.
Phytother Res 15: 219-223, 2001
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Ref. 051 Pycnogenol® protects the retina against oxidative damage more effectively than any other antioxidant tested. Pycnogenol® shows synergistic antioxidant effectiveness when combined with other antioxidants such as Coenzyme Q₁₀.
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In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.
Ophthalmic Res 31: 407-415, 1999.

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Ueda T, Ueda T, Armstrong D
Preventive effect of natural and synthetic antioxidants on lipid peroxidation in the mammalian eye.
Ophthalmic Res 28: 184-192, 1996.

6. Inflammation

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 Cesarone MR, Belcaro G, Stuard S, Schönlau F, Di Renzo A, Grossi MG, Dugall M, Cornelli U, Cacchio M, Gizzi G, Pellegrini L.
 Kidney Flow and Function in Hypertension: Protective Effects of Pycnogenol® in Hypertensive Participants--A Controlled Study.
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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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- Ref. 250** **CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.**
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 Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.
 Redox Rep 13: 271-276, 2008
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- Ref. 208** **Pycnogenol® *in vitro* study provides evidence of chemoprevention.**
 Buz'Zard AR, Lau BHS
 Pycnogenol® reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures.
 Phytother Res 21: 579-586, 2007
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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.**
 Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
 Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
 J Inflamm 3: 1-6, 2006
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Ref. 183 Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: histomorphological evidence in rats.
 Ramos FM, Schönlau 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.
 Phytother Res 20: 676-679, 2006

Ref. 176 Pycnogenol® non-selectively inhibits the activity of enzymes involved in pain sensation during inflammation.
 Schäfer A, Chovanová Z, Muchová J, Sumegová K, Liptáková A, Duracková Z, Högger P
 Inhibition of COX-1 and COX-2 activity by plasma of human volunteers after ingestion of French maritime pine bark extract (Pycnogenol®).
 Biomed Pharmacother 60: 5-9, 2005

Ref. 154 Pycnogenol® significantly counteracts inflammatory damage of the colon in an experimental animal model.
 Mochizuki M, Hasegawa N
 Therapeutic efficacy of Pycnogenol® in experimental inflammatory bowel diseases.
 Phytother Res 18: 1027-1028, 2004

Ref. 107 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
 Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
 J Free Radic Biol Med 36: 811-822, 2004

Ref. 074 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
 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.
 J Free Radic Biol Med 30: 154-160, 2001

Ref. 019 Pycnogenol® produces anti-inflammatory and anti-oedema effects in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
 Blazso G, Gabor M, Rohdewald P
 Antiinflammatory activities of procyanidin containing extracts from *Pinus pinaster* Ait. after oral and cutaneous application.
 Pharmazie 52: 380-382, 1997



Ref. 010

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

Blazso G, Gabor M, Sibbel R, Rohdewald P

Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. and its fractions.

Pharm Parmacol Lett 3: 217-220, 1994

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- Ref. 272** **CLINICAL STUDY: Pycnogenol® inhibits the generation of COX-2 and 5-LOX enzymes in pharmacological investigations of inflammatory processes in humans.**
Canali R, Comitato R, Schonlau F, Virgili F
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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- Ref. 250** **CLINICAL STUDY: Pycnogenol® significantly lowers the inflammatory marker CRP in patients with osteoarthritis, thus demonstrating its anti-inflammatory potency.**
Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M, Rohdewald P
Variations in C-reactive protein, plasma free radicals and fibrinogen values in patients with osteoarthritis treated with Pycnogenol®.
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- Ref. 249** **CLINICAL STUDY: Pycnogenol® improves flexibility of osteoarthritic joints, lowers pain and allows patients to decrease their pain medication.**
Cisar P, Jany R, Waczulikova I, Sumegova K, Muchova J, Vojtassak J, Durackova Z, Lisy M, Rohdewald P
Effect of pine bark extract (Pycnogenol®) on symptoms of knee osteoarthritis.
Phytother Res 22: 1087-1092, 2008
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- Ref. 223** **CLINICAL STUDY: Pycnogenol® improves pain and mobility in osteoarthritis in 156 patients.**
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Treatment of osteoarthritis with Pycnogenol®. The SVOS (San Valentino Osteo-Arthrosis Study). Evaluation of Signs, Symptoms, Physical Performance and Vascular Aspects.
Phytother Res 22: 518-523, 2008
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- Ref. 188** **CLINICAL STUDY: In osteoarthritis Pycnogenol® reduces pain and joint stiffness and decreases the required NSAID medication.**
Farid R, Mirfeizi Z, Mirheidari M, Rezaieyazdi Z, Mansouri H, Esmaili H, Zibadi S, Rohdewald P, Watson RR
Pycnogenol® supplementation reduces pain and stiffness and improves physical function in adults with knee osteoarthritis.
Nutr Res 27: 692-697, 2007
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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.**
Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
J Inflamm 3: 1-6, 2006
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- Ref. 176** **Pycnogenol® non-selectively inhibits the activity of enzymes involved in pain sensation during inflammation in humans.**
Schäfer A, Chovanová Z, Muchová J, Sumegová K, Liptáková A, Duracková Z, Högger P
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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- Ref. 107** **Pycnogenol® as well as its metabolites found in blood of humans potently inhibit matrix metalloproteinases, enzymes involved in cartilage destruction.**
Grimm T, Schäfer A, Högger P
Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
J Free Radic Biol Med 36: 811-822, 2004
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8. Allergy & Asthma

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- Ref. 270** In animal experiments Pycnogenol® suppressed an immediate immunoglobulin type E mediated allergic response. This suggests that Pycnogenol® would have general anti-allergic effectiveness.
Choi YH, Yan GH
Pycnogenol® inhibits immunoglobulin E-mediated allergic response in mast cells.
Phytother Res 23: 1691-1695, 2009
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- Ref. 149** **CLINICAL STUDY: Pycnogenol® improves pulmonary functions and reduces symptoms of asthma in children.**
Lau BHS, Riesen SK, Truong KP, Lau EW, Rohdewald P, Barreta RA
Pycnogenol® as an adjunct in the management of childhood Asthma.
J Asthma 41: 825-832, 2004
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- Ref. 089** Pycnogenol® blocks release of histamine from mast cells *in vitro* to the same extent as the antiasthmatic drug DNCG.
Sharma SC, Sharma S, Gulati OP
Pycnogenol® inhibits the release of histamine from mast cells.
Phytother Res, 17: 66-69, 2003
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- Ref. 077** **CLINICAL STUDY: Pycnogenol® reduces asthma symptoms and improves lung function of asthmatic patients in a placebo-controlled, cross-over study.**
Hosseini S, Pishnamazi S, Sadrzadeh MH, Farid F, Farid R, Watson RR
Pycnogenol® in the management of asthma.
J Med Food 4: 201-209, 2001
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9. Fertility & the Reproductive System

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- Ref. 220** **CLINICAL STUDY: Pycnogenol® significantly lowers menstrual pain and the quantity of required analgesic medication in a multi-center study with four hospitals in Japan.**
Suzuki N, Uebaba K, Kohama T, Moniwa N, Kanayama N, Koike K
French Maritime Pine Bark Extract Significantly Lowers the Requirement for Analgesic Medication in Dysmenorrhea. A multicenter, randomized, double-blind, placebo-controlled study.
J Reprod Med 53: 338-346, 2008
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- Ref. 219** **CLINICAL STUDY: Pycnogenol® reduces pain from endometriosis, shows less side effects than hormonal treatment and enabled some women to conceive.**
Kohama T, Herai K, Inoue M
Effect of French Maritime Pine Bark Extract on endometriosis as compared with Leuporelin acetate.
J Reprod Med 52: 703-708, 2007
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- Ref. 187** **CLINICAL STUDY: Pycnogenol® improves a broad range of climacteric symptoms in a study with 200 menopausal women.**
Yang H-M, Liao M-F, Zhu SY, Liao M-N, Rohdewald P
A randomized, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
Acta Obstet Gynecol Scand 86: 978-985, 2007
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- Ref. 174** **CLINICAL STUDY: Pycnogenol® reduces low-back pain in late period of pregnancy.**
Kohama T, Inoue M
Pycnogenol® Alleviates Pain Associated with Pregnancy.
Phytother Res 20: 232-234, 2006
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- Ref. 145** **CLINICAL STUDY: Pycnogenol® produces analgesic effect in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.**
Kohama T, Suzuki N, Ohno S, Inoue M
Analgesic efficacy of French maritime pine bark extract in dysmenorrhea. An open clinical trial.
J Reprod Med 49: 828-832, 2004
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- Ref. 091** **CLINICAL STUDY: After treatment with Pycnogenol® increase in functionally normal sperm may allow infertile couples to forgo *in vitro* fertilization.**
Roseff SJ
Improvement in sperm quality and function with French maritime pine tree bark extract.
J Reprod Med 47: 821-824, 2002
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Ref. 046 CLINICAL STUDY: Pycnogenol® improves the morphology of spermatozoa. The percentage of non-deformed sperms in sub-fertile men was increased by 99% after supplementation with Pycnogenol®.
Roseff S, Gulati R
Improvement of sperm quality by Pycnogenol®.
Eur Bull Drug Res 7: 33-36, 1999

Ref. 045 CLINICAL STUDY: Pycnogenol® helps in gynaecological disorders such as endometriosis and dysmenorrhea. It reduces menstrual cramps, abdominal pain and tenderness.
Kohama T, Suzuki N
The treatment of gynaecological disorders with Pycnogenol®.
Eur Bull Drug Res 7: 30-32, 1999

10. Sport & Endurance

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- Ref. 230** **CLINICAL STUDY: Pycnogenol® consumption increases vasodilatation by 42% in young healthy men, which warrants sufficient blood and oxygen supply to performing muscle.**
Nishioka K, Hidaka T, Nakamura S, Umemura T, Jitsuiki D, Soga J, Goto C, Chayama K, Yoshizumi M, Higashi Y
Pycnogenol®, French Maritime Pine Bark Extract, augments endothelium-dependent vasodilation in humans.
Hypertens Res 30: 775-780, 2007
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- Ref. 189** **CLINICAL STUDY: Pycnogenol® reduces muscular pain and cramps in athletes and in patients with vascular problems or poor blood circulation of the legs.**
Vinciguerra G, Belcaro G, Cesarone MR, Rohdewald P, Stuard S, Ricci A, Di Renzo A, Hosoi M, Dugall M, Ledda A, Cacchio M, Acerbi G, Fano F
Cramps and muscular pain: prevention with Pycnogenol® in normal subjects, venous patients, athletes, claudicants and in diabetic microangiopathy.
Angiology 57: 331-339, 2006
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- Ref. 044** **CLINICAL STUDY: Pycnogenol® increases exercise endurance in recreational athletes by 21% on a treadmill.**
Pavlovic P
Improved endurance by use of antioxidants.
Eur Bull Drug Res 7: 26-29, 1999
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11. Cognitive Function

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- Ref. 241** **CLINICAL STUDY: Pycnogenol® significantly improves memory in 101 senior citizens with memory deficits and saves their poly-unsaturated fatty acids, such as from neuronal membranes, from oxidative destruction.**
 Ryan J, Croft K, Wesnes K, Stough C
 An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.
 J Psychopharmacol 22: 553-562, 2008
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- Ref. 231** **CLINICAL STUDY: Pycnogenol® lowers stress-hormones in children with ADHD.**
 Dvorakova M, Jezova D, Blazicek P, Trebaticka J, Skodacek I, Suba J, Waczulikova I, Rohdewald P, Durackova Z
 Urinary catecholamines in children with attention deficit hyperactivity disorder (ADHD): modulation by a polyphenolic extract from pine bark (Pycnogenol®).
 Nutr Neurosci 10: 151-157, 2007
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- Ref. 205** **CLINICAL STUDY: Pycnogenol® improves antioxidant status in children with Attention Deficit Hyperactivity Disorder (ADHD).**
 Dvorakova M, Sivonova M, Trebaticka J, Skodacek I, Waczulikova I, Muchova J, Durackova Z
 Research Article: The effect of polyphenolic extract from pine bark, Pycnogenol®, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).
 Redox Rep 11: 163-172, 2006
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- Ref. 204** **CLINICAL STUDY: Pycnogenol® protects DNA against oxidation in children with Attention Deficit Hyperactivity Disorder (ADHD).**
 Chovanova Z, Muchova J, Sivonova M, Dvorakova M, Zitnanova I, Waczulikova I, Trebaticka J, Skodacek I, Durackova Z
 Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/hyperactivity disorder.
 Free Radic Res 40: 1003-1010, 2006
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- Ref. 190** **CLINICAL STUDY: Pycnogenol® relieves hyperactivity and improves attention in children with ADHD in a double-blind placebo controlled study.**
 Trebaticka J, Kopasova S, Hradecna Z, Cinovsky K, Skodacek I, Suba J, Muchova J, Zitnanova I, Waczulikova I, Rohdewald P, Durackova Z
 Treatment of ADHD with French maritime pine bark extract, Pycnogenol®.
 Eur Child Adolesc Psychiatry 15: 329-335, 2006
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- 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®.
Peng QL, Buz'Zard AR, Lau BHS
Pycnogenol® protects neurones from amyloid β peptide-induced apoptosis.
Brain Res Mol Brain Res 104: 55-65, 2002
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- 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.
Liu F, Lau BHS, Peng Q, Shah V
Pycnogenol® protects vascular endothelial cells from β -amyloid-induced injury.
Biol Pharm Bull 23: 735-737, 2000
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- Ref. 052** Pycnogenol® improves learning impairment and loss of memory, common symptoms of the ageing process.
Liu F, Zhang Y, Lau BHS
Pycnogenol® improves learning impairment and memory deficit in senescence-accelerated mice.
J Anti Aging Med 2: 349-355, 1999
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- Ref. 048** **CLINICAL STUDY:** Pycnogenol® is recommended for treatment of Attention Deficit Disorder.
Hanley JL
Attention Deficit Disorder.
Impact Communications Inc., Green Bay, WI, USA, 17-19, 1999
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- Ref. 047** **CLINICAL STUDY:** Positive experience with Pycnogenol® in treating ADHD is mentioned in this letter to the Editor.
Heimann SW
Pycnogenol® for ADHD?
J Am Acad Child Adolesc Psychiatry 38: 357-358, 1999
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12. 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.
Kim YJ, Kang KS, Yokozawa T
The anti-melanogenic effect of Pycnogenol® by its anti-oxidative actions.
Food and Chemical Toxicol 46: 2466-2471, 2008

Ref. 195 **CLINICAL STUDY: Pycnogenol® accelerates healing of diabetic ulcers in humans.**
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Gizzi G, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Cipollone G, Ruffini I, Fano F, Hosoi M
Diabetic Ulcers: Microcirculatory Improvement and Faster Healing with Pycnogenol®.
Clin Appl Thromb Hemost 12: 318-323, 2006

Ref. 193 **Oral administration of Pycnogenol® is able to delay and to reduce skin cancer following UV radiation.**
Kyriazi M, Yova D, Rallis M, Lima A
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.
Cancer Lett 237: 234-241, 2006

Ref. 185 **CLINICAL STUDY: Pycnogenol® inhibits release of enzymes involved in breaking-down collagen and elastin in inflamed skin in humans.**
Grimm T, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Inhibition of NF-kappaB activation and MMP-9 secretion by plasma of human volunteers after ingestion of maritime pine bark extract (Pycnogenol®).
J Inflamm 3: 1-6, 2006

Ref. 172 **CLINICAL STUDY: Ulcers of the lower legs heal faster with orally and topically applied Pycnogenol®.**
Belcaro G, Cesarone MR, Errichi BM, Ledda A, Di Renzo A, Stuard S, Dugall M, Pellegrini L, Rohdewald P, Ippolito E, Ricci A, Cacchio M, Ruffini I, Fano F, Hosoi M
Venous Ulcers: Microcirculatory Improvement and Faster Healing with Local Use of Pycnogenol®.
Angiology 56: 699-705, 2005

Ref. 150 **Pycnogenol® shows antimicrobial activity at very low concentration.**
Torras MAC, Faura CA, Schönlaui F, Rohdewald P
Anti-microbial activity of Pycnogenol®.
Phytother Res 19: 647-648, 2005

Ref. 211 **Beneficial effects of Pycnogenol® in wrinkles - A review article.**
 Rona C, Vailati F, Berardesca E
 The cosmetic treatment of wrinkles.
 J Cosmet Dermatol 3: 26-34, 2004

Ref. 137 **Evidence of percutaneous absorption of Pycnogenol® in human skin.**
 Sarikaki V, Rallis M, Tanojo H, Panteri I, Dotsikas Y, Loukas YL, Papaioannou G, Demetzos C, Weber S, Moini H, Maibach HI, Packer L
In vitro percutaneous absorption of pine bark extract (Pycnogenol®) in human skin.
 J Toxicol Cutaneous Ocul Toxicol 23: 149-158, 2004

Ref. 133 **Topically applied Pycnogenol® dose-dependently speeds-up the wound healing process and reduces scar formation.**
 Blazso G, Gabor M, Schönlau F, Rohdewald P
 Pycnogenol® accelerates wound healing and reduces scar formation.
 Phytother Res 18: 579-581, 2004

Ref. 132 **CLINICAL STUDY: Supplementation with Pycnogenol® in combination with vitamins, minerals improves skin smoothness and elasticity in women.**
 Segger D, Schönlau F
 Supplementation with Evelle® improves smoothness and elasticity in a double blind, placebo-controlled study with 62 women.
 J Dermatolog Treat 15: 222-226, 2004

Ref. 111 **Pycnogenol® applied topically after sunburn inhibits photocarcinogenesis.**
 Sime S, Reeve VE
 Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.
 Photochem Photobiol 79: 193-198, 2004

Ref. 107 **CLINICAL STUDY: The collagen and elastin destroying enzymes are potently inhibited by Pycnogenol® as well as its metabolites prevailing in humans after oral consumption.**
 Grimm T, Schäfer A, Högger P
 Antioxidant activity and inhibition of matrix metalloproteinases by metabolites of maritime pine bark extract (Pycnogenol®).
 J Free Radic Biol Med 36: 811-822, 2004

Ref. 094 **Review summarizing the beneficial effects of Pycnogenol® for skin care.**
 Schönlau F
 The cosmeceutical Pycnogenol®.
 J Appl Cosmetol 20: 241-246, 2002



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- Ref. 081** **CLINICAL STUDY: Pycnogenol® counteracts skin hyper-pigmentation in women.**
 Ni Z, Mu Y, Gulati O
 Treatment of melasma with Pycnogenol®.
 Phytother Res 16: 567-571, 2002
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- Ref. 074** **CLINICAL STUDY: Pycnogenol® dose-dependently inhibits UV-induced erythema in humans, demonstrating a potent anti-photoageing effect.**
 Saliou C, Rimbach G, Moini H, McLaughlin L, Hosseini S, Lee J, Watson RR, Packer L
 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.
 J Free Radic Biol Med 30: 154-160, 2001
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- Ref. 073** **Pycnogenol® favourably affects the gene expression profile in human keratinocytes, indicating a promising potential for improving inflammatory skin disorders such as psoriasis and dermatoses.**
 Rihn B, Saliou C, Bottin MC, Keith G, Packer L
 From ancient remedies to modern therapeutics: Pine bark uses in skin disorders revisited.
 Phytother Res 15: 76-78, 2001
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- Ref. 057** **Pycnogenol® inhibits the production of adhesion molecules in human skin cells during inflammation which would contribute to relieving inflammatory skin disorders.**
 Bito T, Roy S, Sen CK, Packer L
 Pine bark extract Pycnogenol® down regulates IFN- γ - induced adhesion of T cells to human keratinocytes by inhibiting inducible ICAM-1 expression.
 J Free Radic Biol Med 28: 219-227, 2000
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- Ref. 030** **Pycnogenol® prolongs the lifetime of vitamin C which will contribute to higher vitamin C presence in the skin.**
 Cossins E, Lee R, Packer L
 ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
 Biochem Mol Biol Int 45: 583-597, 1998
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- Ref. 026** **Pycnogenol® protects α -tocopherol from oxidation and extends its life-time in endothelial cells.**
 Virgili F, Kim D, Packer L
 Procyanidins extracted from pine bark protect α -tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide peroxynitrite.
 FEBS Lett 431: 315-318, 1998
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Ref. 019 Pycnogenol® produces an anti-oedema effect in two different models. Topical application of Pycnogenol® gel protects the skin against UV radiation.
Blazso G, Gabor M, Rohdewald P
Anti-inflammatory activities of procyanidin containing extracts from *Pinus pinaster* Ait. after oral and cutaneous application.
Pharmazie 52: 380-382, 1997

Ref. 009 Pycnogenol® increases 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.
Gabor M, Engi E, Sonkodi S
Die Kapillarwandresistenz und ihre Beeinflussung durch wasserlösliche Flavonderivate bei spontan hypertensischen Ratten.
Phlebologie 22: 178-182, 1993

Ref. 008 Pycnogenol® dose-dependently protects the skin from ultraviolet-radiation-induced oxidative stress injury (lipid peroxidation and cytotoxicity).
Guochang Z
Ultraviolet radiation-induced oxidative stress in cultured human skin fibroblasts and antioxidant protection.
Bio Res Rep Univ Jyväskylä 33: 1-86, 1993

13. Oral Health Care

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- Ref. 150** Pycnogenol® inhibits growth of gram-positive and negative bacteria and *candida albicans* at concentrations of 0.025%.
Torras MAC, Faura CA, Schönlau F, Rohdewald P
Short Communication: Antimicrobial activity of Pycnogenol®.
Phytother Res 19: 647-648, 2005
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- Ref. 133** Local application of Pycnogenol® dose-dependently speeds-up the wound healing process and reduces scar formation.
Blazso G, Gabor M, Schönlau F, Rohdewald P
Pycnogenol® accelerates wound healing and reduces scar formation.
Phytother Res 18: 579-581, 2004
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- Ref. 084** **CLINICAL STUDY:** Pycnogenol® administered in chewing gum reduced bleeding of the gum and reduced plaque formation on the teeth in a controlled clinical trial.
Kimbrough C, Chun M, de la Roca G, Lau BHS
Pycnogenol® chewing gum minimizes gingival bleeding and plaque formation.
Phytomed 9: 410-413, 2002
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- Ref. 030** Pycnogenol® prolongs the lifetime of vitamin C more than other flavonoids.
Cossins E, Lee R, Packer L
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
Biochem Mol Biol Int 45: 583-597, 1998
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14. Benefits for Travelers

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- Ref. 244** **CLINICAL STUDY: Pycnogenol® significantly lowers the severity of a wide range of typical jet-lag symptoms of flight passengers travelling intercontinental routes.**
Belcaro G, Cesarone MR, Steigerwalt RJ, Di Renzo A, Grossi MG, Ricci A, Stuard S, Ledda A, Dugall M, Cornelli U, Cacchio M
Jet-lag: Prevention with Pycnogenol®. Preliminary report: evaluation in healthy individuals and in hypertensive patients.
Minerva Cardioangiol 56(5 Suppl): 3-9, 2008
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- Ref. 151** **CLINICAL STUDY: Pycnogenol® effectively counteracts swelling of the lower-legs and ankles of passengers during long flights in a double-blind, placebo-controlled study.**
Cesarone MR, Belcaro G, Rohdewald P, Pellegrini L, Ippolito E, Scozzianti M, Ricci A, Dugall M, Cacchio M, Ruffini I, Fano F, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Mucci F
Prevention of edema in long flights with Pycnogenol®.
Clin Appl Thromb Hemost 11: 289-294, 2004
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- 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.**
Scurr JH, Gulati OP
Review article: Zinopin®- the Rationale for its use as Food Supplement in Traveller’s thrombosis and motion sickness.
Phytother Res 18: 687-695, 2004
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- Ref. 134** **CLINICAL STUDY: Pycnogenol® prevents thrombosis in passengers on long haul flights in a double-blind, placebo-controlled trial with 200 participants.**
Belcaro G, Cesarone MR, Rohdewald P, Ricci A, Ippolito E, Dugall M, Griffin M, Ruffini I, Acerbi G, Vinciguerra MG, Bavera P, Di Renzo A, Errichi BM, Cerritelli F
Prevention of Venous Thrombosis and Thrombophlebitis in Long-Haul Flights with Pycnogenol®.
Clin Appl Thromb Hemost 10: 373-377, 2004
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- Ref. 116** **CLINICAL STUDY: Pycnogenol® in combination with nattokinase prevents deep vein thrombosis in long-haul flights.**
Cesarone MR, Belcaro G, Nicolaidis AN, Ricci A, Geroulakos G, Ippolito E, Brandolini R, Vinciguerra G, Dugall M, Griffin M, Ruffini I, Acerbi G, Corsi M, Riordan N, Stuard S, Bavera P, Di Renzo A, Kenyon J, Errichi BM
Prevention of venous thrombosis in long-haul flights with Flite Tabs: The Lonflit- Flite randomized controlled trial.
Angiology 54: 531-539, 2003
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Ref. 036

CLINICAL STUDY: 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.

Pütter M, Grotemeyer KHM, Würthwein G, Araghi-Niknam M, Watson RR, Hosseini S, Rohdewald P

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

Thromb Res 95: 155-161, 1999

15. Immunology, Anti-Microbial & Anti-Viral Activity

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- Ref. 247** Pycnogenol® decreases HIV viral replication and T-cell interaction in cell culture experiments.
Feng WY, Tanaka R, Inagaki Y, Saitoh Y, Chang MO, Amet T, Yamamoto N, Yamaoka S, Yoshinaka Y
Pycnogenol®, a procyanidin-rich extract from French maritime pine, inhibits intracellular replication of HIV-1 as well as its binding to host cells.
Jpn J Infect Dis 61: 279-285, 2008
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- Ref. 245** **CLINICAL STUDY: Pycnogenol® helps to lower a wide range of typical side-effects patients suffer from during cancer chemo- and radiotherapy.**
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Pycnogenol® may alleviate adverse effects in oncologic treatment.
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Wu TF, Hsu CY, Huang HS, Chou SP, Wu H
Proteomic analysis of Pycnogenol® effects in RAW 264.7 macrophage reveals induction of cathepsin D expression and enhancement of phagocytosis.
J Agric Food Chem 55: 9784-9791, 2007
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French maritime pine bark extract inhibits viral replication and prevents development of viral myocarditis.
J Card Fail 13: 785-791, 2007
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- Ref. 228** Pycnogenol® inhibits viral replication in myocarditis.
Matsumori A
Treatment Options in Myocarditis.
Herz 32: 452-456, 2007
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- Ref. 225** Pycnogenol® inhibits growth of *Helicobacter pylori* and their adherence to mucosal cells of the stomach.
Rohdewald P, Beil W
In vitro inhibition of *Helicobacter pylori* growth and adherence to gastric mucosal cells by Pycnogenol®.
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Antimutagenic *in vitro* Activity of Plant Polyphenols: Pycnogenol® and Ginkgo biloba Extract (EGb 761).
Phytother Res 22: 384-388, 2007
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- Ref. 150** Pycnogenol® shows broad anti-microbial activity *in vitro*.
Torras MAC, Faura CA, Schönlau F, Rohdewald P
Antimicrobial activity of Pycnogenol®.
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Int J Cancer Prev 1: 207-212, 2004
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Sime S, Reeve VE
Protection from inflammation, immunosuppression and carcinogenesis induced by UV radiation in mice by topical Pycnogenol®.
Photochem Photobiol 79: 193-198, 2004
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Shah V, Bayeta E, Lau BHS
Pycnogenol® augments macrophage phagocytosis and cytokine secretion.
Pak J Nutr 1: 196-201, 2002
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Stefanescu M, Matache C, Onu A, Tanaseanu S, Dragomir C, Constantinescu I, Schönlau F, Rohdewald P, Szegli G
Pycnogenol® Efficacy in the Treatment of Systemic Lupus Erythematosus Patients.
Phytother Res 15: 698-704, 2001
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Huynh HT, Teel RW
Selective induction of apoptosis in human mammary cancer cells (MCF-7) by Pycnogenol®.
Anticancer Res 20: 2417-2420, 2000
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- 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.
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Activity of monomeric, dimeric, and trimeric flavonoids on NO production, TNF-alpha secretion, and NF-kappaB-dependent gene expression in RAW 264.7 macrophages.
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- 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.
Liu FJ, Zhang YX, Lau BHS
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.
Cell Mol Life Sci 54: 1168-1172, 1998
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Cheshier JE, Ardestani-Kaboudanian S, Liang B, Araghi Niknam M, Chung S, Lane L, Castro A, Watson RR
Immunomodulation by Pycnogenol® in retro-virus infected or ethanol-fed mice.
Life Sci 58: 87-96, 1996
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16. Antioxidant-& Anti-Ageing Activity

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- Ref. 241** **CLINICAL STUDY:** Pycnogenol® significantly decreases F2-isoprostane plasma levels in 101 senior citizens indicating that poly-unsaturated fatty acids, such as those from neuronal membranes, are saved from oxidative destruction.
Ryan J, Croft K, Wesnes K, Stough C
An examination of the effects of the antioxidant Pycnogenol® on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population.
J Psychopharmacol 22: 553-562, 2008
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- Ref. 218** Pycnogenol® lowers oxidative stress in the liver of rats challenged with a chemical toxin.
Ahn T-H, Yang Y-S, Lee J-C, Moon C-J, Kim S-H, Jun W, Park S-C, Kim J-C
Ameliorative Effects of Pycnogenol® on Carbon Tetrachloride-Induced Hepatic Oxidative Damage in Rats.
Phytother Res 21: 1015-1019, 2007
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- Ref. 187** **CLINICAL STUDY:** Pycnogenol® significantly increases total antioxidant status (TAS) in a double-blind, placebo-controlled study with 155 menopausal women.
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A randomised, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women.
Acta Obstet Gynecol Scand 86: 978-985, 2007
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Nakanishi-Ueda T, Kamegawa M, Ishigaki S, Tsukahara M, Yano S, Wada K, Yasuhara H
Inhibitory Effect of Lutein and Pycnogenol® on Lipid Peroxidation in Porcine Retinal Homogenate.
J Clin Biochem Nutr 38: 204-210, 2006
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The Combined Effect of Pycnogenol® with Ascorbic Acid and Trolox on the Oxidation of Lipids and Proteins.
Gen Physiol Biophys 25: 379-396, 2006
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 Dvorakova M, Sivonova M, Trebaticka J, Skodacek I, Waczulikova I, Muchova J, Durackova Z
 The effect of polyphenolic extract from pine bark, Pycnogenol® on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD).
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 Chovanova Z, Muchova J, Sivonova M, Dvorakova M, Zitnanova I, Waczulikova I, Trebaticka J, Skodacek I, Durackova Z
 Effect of polyphenolic extract, Pycnogenol®, on the level of 8-oxoguanine in children suffering from attention deficit/hyperactivity disorder.
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 Voss P, Horakova L, Jakstadt M, Kiekebusch D, Grune T
 Ferritin oxidation and proteasomal degradation: Protection by antioxidants.
 Free Radic Res 40: 673-683, 2006
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- Ref. 183** **Pycnogenol® protects intestinal mucosa against radiotherapy induced damage: Histomorphological evidence in rats.**
 Ramos FM, Schönlau F, Novaes PD, Manzi FR, Bóscolo FN, Almeida SM
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 Sivonová M, Waczulíková I, Kilanczyk E, Hrnčiarová M, Bryszewska M, Klajnert B, Duracková Z
 The effect of Pycnogenol® on the erythrocyte membrane fluidity.
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 Maritim A, Dene BA, Sanders RA, Watkins JB
 Effect of Pycnogenol® treatment on oxidative stress in streptozotocin-induced diabetic rats.
 J Biochem Mol Toxicol 17: 193-199, 2003
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Reduction of inclusion body pathology in ApoE-deficient mice fed a combination of antioxidants. J Free Radic Biol Med 34: 1070-1077, 2003
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Shuguang L, Xinwen Z, Sihong X, Gulati OP
Role of Pycnogenol® in aging by increasing the Drosophila's life-span. Eur Bull Drug Res 11: 39-45, 2003
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Durackova Z, Trebaticky B, Novotny V, Zitnanova I, Breza J
Lipid metabolism and erectile function improvement by Pycnogenol®, extract from the bark of *Pinus pinaster* in patients suffering from erectile dysfunction-a pilot study. Nutr Res 23: 1189-1198, 2003
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Devaraj S, Vega-López S, Kaul N, Schönlaue F, Rohdewald P, Jialal I
Supplementation with a pine bark extract rich in polyphenols increases plasma antioxidant capacity and alters plasma lipoprotein profile. Lipids 37: 931-934, 2002
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- Ref. 086** Pycnogenol® in combination with whey increases antioxidative capacity of plasma.
Janisch K, Hippeli S, Dornisch K, Kern S, Elstner EF
Determination of the antioxidative potential of human plasma after supplementation with Pycnogenol® and whey. Food Res Intern 35: 257-266, 2002
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- Ref. 072** Pycnogenol® selectively enhances activity of intracellular antioxidative enzymes.
Bayeta E, Lau BHS
Pycnogenol® inhibits generation of inflammatory mediators in macrophages. Nutr Res 20: 249-259, 2000
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Bors W, Michel C, Stettmaier K
Electron paramagnetic resonance studies of radical species of proanthocyanidins and gallate esters.
Arch Biochem Biophys 374: 347-355, 2000
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- 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®.
Cho K-J, Yun C-H, Yoon D-Y, Cho Y-S, Rimbach G, Packer L, Chung A-S
Effect of bioflavonoids extracted from the bark of Pinus maritime on proinflammatory cytokine interleukin-1 production in lipopolysaccharide-stimulated raw 264.7.
Toxicol Appl Pharmacol 168: 64-71, 2000
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- Ref. 062** Pycnogenol® blocks oxidative modification of cellular proteins more effectively than other antioxidants.
Kim J, Chehade J, Pinnas JL, Mooradian AD
Effect of select antioxidants on malondialdehyde modification of proteins.
Nutrition 16: 1079-1081, 2000
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- Ref. 051** In a comparative study Pycnogenol® shows more potent antioxidant activity than vitamin C and E, α -lipoic acid, Co-Q₁₀ and grape seed. In combination Pycnogenol® enhances the effects of other antioxidants like Coenzyme Q₁₀.
Chida M, Suzuki K, Nakanishi-Ueda T, Ueda T, Yasuhara H, Koide R, Armstrong D
In vitro testing of antioxidants and biochemical end-points in bovine retinal tissue.
Ophthalmic Res 31: 407-415, 1999
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- 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.
Guo Q, Zhao B, Packer L
Electron spin resonance study of free radicals formed from a procyanidin-rich pine (Pinus maritime) bark extract, Pycnogenol®.
J Free Radic Biol Med 27: 1308-1312, 1999
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- Ref. 030** Pycnogenol® protects vitamin C from oxidation and recycles oxidized vitamin C more effectively than other flavonoids.
Cossins E, Lee R, Packer L
ESR studies of vitamin C regeneration, order of reactivity of natural source phytochemical preparations.
Biochem Mol Biol Int 45: 583-597, 1998
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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.
Liu FJ, Zhang YX, Lau BHS
Pycnogenol® enhances immune and haemopoietic functions in senescence-accelerated mice.
Cell Mol Life Sci 54: 1168-1172, 1998

Ref. 026 Pycnogenol® protects α -tocopherol in endothelial cells.
Virgili F, Kim D, Packer L
Procyanidins extracted from pine bark protect α -tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide and peroxynitrite.
FEBS Lett 431: 315-318, 1998

Ref. 025 Pycnogenol® inhibits the effect of oxidative stress and minimises hydroxyl radical-induced DNA damage *in vitro*.
Nelson AB, Lau BHS, Ide N, Rong Y
Pycnogenol® inhibits macrophage oxidative burst, lipoprotein oxidation and hydroxyl radical-induced DNA damage.
Drug Dev Ind Pharm 24: 139-144, 1998

Ref. 022 Pycnogenol® in addition to its free radical scavenging property, modulates the production of nitric oxide radicals in activated inflammatory cells.
Virgili F, Kobuchi H, Packer L
Procyanidins extracted from *Pinus maritima* (Pycnogenol®): scavengers of free radical species and modulators of nitrogen monoxide metabolism in activated murine raw 264.7 macrophages.
J Free Radic Biol Med 24: 1120-1129, 1998

Ref. 021 Pycnogenol® is shown to be the strongest hydroxyl- and superoxide radical scavenger among other extracts tested. In addition, Pycnogenol® is shown to be resistant to heat.
Noda Y, Anzai K, Mori A, Kohno M, Shinmei M, Packer L
Hydroxyl and superoxide anion radical scavenging activities of natural source antioxidants using the computerized JES-FR30 ESR spectrometer system.
Biochem Mol Biol Int 42: 35-44, 1997

Ref. 020 Pycnogenol® stimulates synthesis of antioxidative enzymes in cell lining arteries thereby doubling their amount.
Wei ZH, Peng QL, Lau BHS
Pycnogenol® enhances endothelial cell antioxidant defenses.
Redox Rep 3: 219-224, 1997



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- Ref. 014** Pycnogenol® protects endothelial cells lining from free radical damage. Damage to endothelial cells is considered a primary cause for atherosclerosis.
Rong Y, Li L, Shah V, Lau BHS
Pycnogenol® protects vascular endothelial cells from t-butyl hydroperoxide induced oxidant injury.
Biotechnol Ther 5: 117-126, 1995
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- Ref. 010** Pycnogenol® scavenges superoxide radicals *in vitro* and inhibits oedema *in vivo*. The anti-inflammatory and free radical scavenging activities are closely correlated.
Blazso G, Gabor M, Sibbel R, Rohdewald P
Anti-inflammatory and superoxide radical scavenging activities of a procyanidins containing extract from the bark of *Pinus pinaster* sol. and its fractions.
Pharm Parmacol Lett 3: 217-220, 1994
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- Ref. 007** Pycnogenol® is proven an excellent radical scavenger of enzymatically produced hydroxyl and singlet oxygen free radicals, two of the most dangerous free radical species.
Elstner EF, Kleber E
Radical scavenger properties of leucocyanidine.
In: Das NP, ed. Flavonoids in Biology & Medicine III: Current issues in Flavonoid Research:
National University of Singapore Press: 227-235, 1990
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17. Analytics, Bio-Availability & Metabolism

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- Ref. 197** **CLINICAL STUDY: This study presents the appearance of Pycnogenol® constituents and metabolites in blood after oral administration in humans.**
Grimm T, Skrabala R, Chovanova Z, Muchova J, Sumegova K, Liptakova A, Durackova Z, Högger P
Single and multiple dose pharmacokinetics of maritime pine bark extract (Pycnogenol®) after oral administration to healthy volunteers.
BMC Clin Pharmacol 6: 1472-6904, 2006
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- Ref. 239** **Pycnogenol® antagonises the neurotoxicity of alcohol, suggesting mitigation of hang-over symptoms.**
Siler-Marsiglio KI, Paiva M, Madorsky I, Serrano Y, Neeley A, Heaton MB
Protective mechanisms of Pycnogenol® in ethanol-insulted cerebellar granule cells.
J Neurobiol 61: 267-276, 2004
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- Ref. 171** **USP Monograph.**
Maritime Pine Bark Extract – USP 30.965-966
The United States Pharmacopeia, United States Pharmacopeial Convention, Inc. official from May 1, 2007
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- Ref. 170** **USP Monograph.**
Maritime Pine – USP-30.964-965
The United States Pharmacopeia, United States Pharmacopeial Convention, Inc. official from May 1, 2007
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- Ref. 137** **Evidence of percutaneous absorption of Pycnogenol® in human skin.**
Sarikaki V, Rallis M, Tanojo H, Panteri I, Dotsikas Y, Loukas YL, Papaioannou G, Demetzos C, Weber S, Moini H, Maibach HI, Packer L
In vitro Percutaneous Absorption of Pine Bark Extract (Pycnogenol®) in Human Skin.
J Toxicol Cutaneous Ocul Toxicol 23: 149-158, 2004
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- Ref. 060** **CLINICAL STUDY: 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®).**
Virgili F, Pagana G, Bourne L, Rimbach G, Natella F, Rice-Evance C, Packer L
Ferulic acid excretion as a marker of consumption of a French maritime pine (*Pinus maritima*) bark extract.
J Free Radic Biol Med 28: 1249-1256, 2000
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- Ref. 058** CLINICAL STUDY: Pycnogenol®, its components and metabolites are bio-available in humans for more than 24 hours to exert their beneficial effects.
Grosse-Düweler K, Rohdewald P
Urinary metabolites of French maritime pine bark extract in humans.
Pharmazie 55: 364-368, 2000
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- 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
Bioavailabilty and metabolism of Pycnogenol®.
Eur Bull Drug Res 7: 5-7, 1999
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